



Residency In-service
Training Examination

**2025 DISCUSSION &
REFERENCE MANUAL**

The American Academy of Neurology Institute owns all copyright rights in the RITE® examination materials, including the examination questions, images, and discussions. If you are interested in receiving a license from the AANI to create study materials based on these materials, please contact Academy staff at therite@aan.com.

Question #

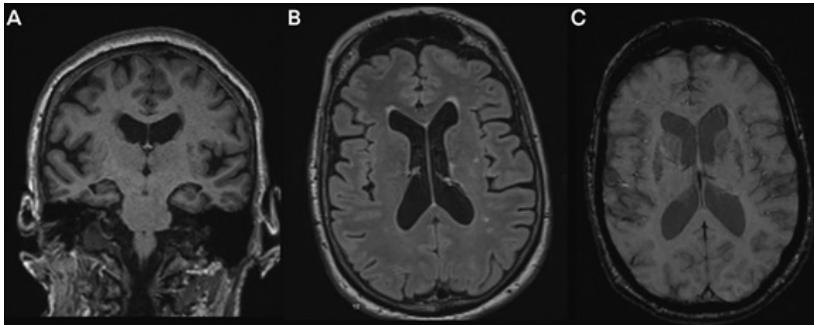
4 ADULT NEUROLOGY**Clinical Aspects of Disease**

This patient has limbic-predominant, age-related TDP-43 encephalopathy (LATE), a disease believed to be the second most common cause of neurodegeneration after Alzheimer disease. Characteristic features include prominent unilateral or bilateral hippocampal atrophy on imaging studies and normal measures of amyloid and phosphorylated tau on CSF analysis. Cognitive testing shows relatively isolated impairment on tests of episodic and working memory. The most common pathology associated with this condition is accumulation of phosphorylated TDP-43 in the limbic system.

MAPT is a tau gene linked to FTD-tau pathology; alternative splicing of this gene results in different tau isoforms associated with progressive supranuclear palsy, corticobasal degeneration, global glial tauopathy, and argyrophilic grain disease.

Alpha-synuclein protein is associated with Parkinson disease. Progranulin is generally present with behavioral variant (bvFTD) or nonfluent variant (nfvFTD) frontotemporal dementia or corticobasal syndrome. 14-3-3 protein is associated with prion diseases.

Butler Pagnotti RM, Pudumjee SB, Cross CL et al. Cognitive and clinical characteristics of patients with limbic-predominant age-related TDP-43 encephalopathy. Neurology. 2023 Mar 20;100(19):e2027–e2035.



Question #

8 ADULT NEUROLOGY**Neuroanatomy**

This patient has simultanagnosia, which is one component of Balint syndrome. Simultanagnosia refers to a severe difficulty shifting visuospatial attention. On a Navon figure, patients will see a small letter but not the large letter; rather, they see the local form but not the global form.

Other components of Balint syndrome are optic ataxia (poor reaching under visual guidance) and ocular apraxia (abnormal eye movements to visual targets).

Simultanagnosia most commonly occurs with lesions of the bilateral parietal lobe, not with lesion of the optic nerves, occipital lobes, temporal lobes, or frontal lobes.

Prasad S, Dinkin M. Higher cortical visual disorders. *Continuum Lifelong Learning Neurol*. 2019 Oct;25(5):1329–1361.

18 ADULT NEUROLOGY**CORE KNOWLEDGE****Clinical Aspects of Disease**

Apraxia is the inability to perform a skilled motor movement in the absence of weakness or other physical impairment. Ideomotor apraxia refers to the inability to use an object (or pantomime use of an object) properly (transient ideomotor apraxia).

Visual agnosia is the inability to understand what is seen. Alien hand may be seen in some patients with corticobasal degeneration and may manifest as an "interfering" limb. Abulia is seen in frontal lesions and is a lack of interest in the environment; semantic dementia refers to loss of word meaning, seen in patients with primary progressive aphasia.

Coslett HB. Apraxia, neglect, and agnosia. *Continuum Lifelong Learning Neurol*. 2018 Jun;24(3):768–782.

Question #

41 ADULT NEUROLOGY**CORE KNOWLEDGE****Clinical Aspects of Disease**

The memory disorder of early Alzheimer disease affects impairment in word recall (recent memory) with normal digit span (immediate memory), and relatively spared remote memory. Memory for concepts (semantic memory) is generally spared, as is most procedural memory in the early stages of Alzheimer disease.

Ropper AH, Samuels MA, Klein JP, et al (eds). Adams and Victor's Principles of Neurology. 11th ed. New York: McGraw-Hill Education; 2019, p 421.

Ghoshal N, Garcia-Sierra F, Wu J, et al. Tau conformational changes correspond to impairments of episodic memory in mild cognitive impairment and Alzheimer's disease. *Exp Neurol.* 2002 Oct;177(2):475-493.

49 ADULT NEUROLOGY**Treatment/Management**

Dopaminergic agonists and inhibitors of dopamine reuptake have been used to treat the behavioral traits associated with medial frontal syndrome. Methylphenidate blocks dopamine transporters in the synapse, increasing dopamine availability. This syndrome may be seen after ischemia in the distribution of the anterior cerebral artery. The mechanism of action of the other agents listed do not work through the dopamine pathway.

Mintzer J, Lanctôt KL, Scherer RW, et al. Effect of methylphenidate on apathy in patients with Alzheimer disease: the ADMET 2 Randomized Clinical Trial. *JAMA Neurol.* 2021 Nov 1;78(11):1324-1332.

Question

60 ADULT NEUROLOGY**CORE KNOWLEDGE****Clinical Aspects of Disease**

Anosognosia (unawareness of deficit or illness) is usually associated with nondominant parietal lobe lesions. Achromatopsia is found with lesions of the inferior lip of the occipital lobe. Right-left confusion is most often seen as part of Gerstmann syndrome and localizes to the dominant (left) parietal lobe (angular gyrus). Ideomotor apraxia is the inability to carry out, on command, learned motor acts and localizes to left parietal and premotor areas. Semantic aphasia is seen with dominant hemisphere lesions (left anterior temporal).

Acharya AB, Sánchez-Manso JC. Anosognosia. [Updated 2023 Apr 24]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024, Jan-.

Uysal S. The parietal lobes and associated disorders. In: Functional Neuroanatomy and Clinical Neuroscience: Foundations for Understanding Disorders of Cognition and Behavior. Online edition. New York: Oxford Academic; 2023.

Bartolomeo P, Bachoud-Levi A-C, de Schotten MT. The anatomy of cerebral achromatopsia: a reappraisal and comparison of two case reports. *Cortex*. 2014 Jul;56:138-144.

Gorno-Tempini MF, Hillis AE, Weintraub S, et al. Classification of primary progressive aphasia and its variants. *Neurology*. 2011 Feb 16;76(11):1006-1014.

74 ADULT NEUROLOGY**CORE KNOWLEDGE****Neuroimaging**

Bilateral diffuse and asymmetric corticospinal tract findings on examination are most compatible with ischemic cerebrovascular disease and vascular dementia. The three main neuroimaging patterns in vascular dementia are large vessel stroke, small vessel disease, and microhemorrhages.

Small vessel disease usually appears as either multiple bilateral lacunae or as extensive leukoaraiosis with confluent periventricular white matter hyperintensities. Cortical microbleeds are associated with amyloid angiopathy, whereas subcortical and periventricular microbleeds are associated with arteriolosclerosis, subcortical ischemia, and vascular dementia.

Graff-Radford J. Vascular cognitive impairment. *Continuum Lifelong Learning Neurol*. 2019 Feb;25(1):147-164.

Question #

81 PEDIATRIC NEUROLOGY**Diagnostic Procedures**

This patient's history is consistent with epileptic-aphasia syndrome, previously known as Landau-Kleffner syndrome and now defined under the umbrella of DEE-SWAS (development/epileptic encephalopathy – spike wave activation in sleep), an epileptic encephalopathy that often presents with seizures and language regression. Classically, patients can have electrographic status epilepticus in sleep (ESES)/spike wave activation in sleep (SWAS). An awake EEG that does not capture sleep may miss this diagnosis.

Polysomnography typically has a single EEG lead and thus may not adequately capture abnormalities. Certain genetic abnormalities, such as *GRIN2A* mutations, place patients at higher risk for epileptic aphasia; however, a diagnosis should be made before pursuing genetic testing.

Deonna T, Roulet-Perez E. Early-onset acquired epileptic aphasia (Landau-Kleffner syndrome, LKS) and regressive autistic disorders with epileptic EEG abnormalities: the continuing debate. *Brain Dev.* 2010 Oct;32(9):746-752.

Lesca G, Møller RS, Rudolf G, et al. Update on the genetics of the epilepsy-aphasia spectrum and role of *GRIN2A* mutations. *Epileptic Disord.* 2019 Jun 1;21(S1):41-47.

83 ADULT NEUROLOGY**Clinical Aspects of Disease**

This patient presents with parkinsonism associated with brief, intermittent periods of disorientation, as well as REM behavior sleep disorder. Along with hallucinations, this would suggest dementia with Lewy bodies.

Gomperts SN. Lewy body dementia: dementia with Lewy bodies and Parkinson disease dementia. *Continuum Lifelong Learning Neurol.* 2016 Apr;22(2):435-463.

Armstrong M. Lewy body dementias. *Continuum Lifelong Learning Neurol.* 2019 Feb;25(1):128-146.

Question #

94 ADULT NEUROLOGY**CORE KNOWLEDGE****Treatment/Management**

Use of anticholinergic medications, including first-generation antihistamines such as diphenhydramine, tricyclic antidepressants, and bladder antimuscarinics, has been associated with an increased risk for dementia and can worsen confusion or other dementia symptoms.

Selective serotonin reuptake inhibitors (SSRIs) such as sertraline have been associated with an increased risk for sleep disturbance, weight gain, and sexual dysfunction, but not dementia. Similarly, medications to lower cholesterol have not been associated with an increased risk of dementia.

Lecanemab is FDA approved for mild cognitive impairment due to Alzheimer disease and mild Alzheimer disease, whereas memantine is FDA approved for moderate to severe Alzheimer disease. Because this patient has not completed an evaluation to establish a diagnosis of Alzheimer disease, these medications should not be considered at this time.

Gray SL, Anderson ML, Dublin S, et al. Cumulative use of strong anticholinergics and incident dementia: a prospective cohort study. *JAMA Intern Med.* 2015 March;175(3):401–407.

Zhang X, Wen J, Zhang Z. Statins use and risk of dementia: A dose-response meta analysis. *Medicine (Baltimore).* 2018 Jul;97(30):e11304.

Dmochowski RR, Thai S, Iglay K, et al. Increased risk of incident dementia following use of anticholinergic agents: A systematic literature review and meta-analysis. *Neurourol Urodyn.* 2021 Jan;40(1):28–37.

108 ADULT NEUROLOGY**Neuroscience and Mechanism of Disease**

Although all the genes listed, except *MAPT*, have been associated with Alzheimer disease, the presenilin 1 (*PSEN1*) mutations are the most common cause of familial Alzheimer disease and early-onset Alzheimer disease. The *PSEN1* gene encodes presenilin 1, which is the catalytic subunit of γ -secretase that generates β -amyloid (A β) peptides of varying lengths. *MAPT* mutations result in frontotemporal dementia, progressive supranuclear palsy, and corticobasal syndrome, but not Alzheimer disease.

Ringman J, Coppola G. New genes and new insights from old genes: update on Alzheimer disease. *Continuum Lifelong Learning Neurol.* 2013 Apr;19(2):358–371.

Question #

123 ADULT NEUROLOGY**CORE KNOWLEDGE****Clinical Aspects of Disease**

Progressive supranuclear palsy is a neurodegenerative disorder that begins with falls and then characterized by vertical gaze palsy, rigidity, dysarthria, cognitive decline, and parkinsonian features. Pathologic features include tau-positive inclusions that are most commonly found in the basal ganglia.

Idiopathic Parkinson disease typically presents with bradykinesia, asymmetric appendicular rigidity, and resting tremors. Dementia with Lewy bodies has parkinsonian features but also has prominent fluctuations in cognition and well-formed visual hallucinations.

Corticobasal degeneration is a progressive asymmetric movement disorder that presents with abnormalities in one limb or on one side of the body. Multiple-system atrophy has parkinsonian features as well but also has dysautonomia, pyramidal signs, or cerebellar symptoms

Greene P. Progressive supranuclear palsy, corticobasal degeneration, and multiple system atrophy. *Continuum Lifelong Learning Neurol*. 2019 Aug;25(4):919–935.

Jankovic JJ, Tolosa E (eds). *Parkinson's Disease and Movement Disorders*. 6th ed. Philadelphia: Wolters Kluwer; 2015.

Williams D, Litvan I. Parkinsonian syndromes. *Continuum Lifelong Learning Neurol*. 2013 Oct;19(5):1189–1212.

Question #

137 ADULT NEUROLOGY**CORE KNOWLEDGE****Diagnostic Procedures**

Semantic memory refers to the acquisition of factual information about the world and is the most common aspect of memory tested during standard clinical assessments of memory.

Episodic memory refers to the recording and conscious recollection of personal experiences, together with their context in terms of time, place, and associated emotions. Remote memory refers to distant past memory on the order of years and decades; it is a type of episodic memory in which learning occurs outside the lab or clinic setting. Both semantic and episodic memory are considered aspects of declarative memory and are anatomically dependent on the integrity of the hippocampus and its related structures.

Nondeclarative memory involves memory tasks that can be performed successfully by patients who have sustained damage to the hippocampus and associated structures. Procedural memory, which is a form of nondeclarative memory, is applied to tasks that assess the acquisition of motor or cognitive skills, such as riding a bike.

Priming, another form of nondeclarative memory, refers to identification of perceptual objects from reduced cues as a consequence of previous exposure to those objects. Standard clinical assessments of memory do not actively test these forms of memory.

Weiss L, Roberts MD (eds). The American Psychiatric Association Publishing Textbook of Psychiatry. 7th ed. Washington DC: American Psychiatric Publishing; 2019.

Rich JB. Remote memory. In: Encyclopedia of Clinical Neuropsychology. 2nd ed. New York: Springer; 2018.

145 ADULT NEUROLOGY**Clinical Aspects of Disease**

Simultanagnosia is a deficit in which an individual cannot simultaneously perceive more than one stimulus item or more than one part of a complex pattern. This syndrome is occasionally seen in Alzheimer disease.

Hemispatial neglect is defined as failure to respond to or notice one half of space (usually the left). In this case, the patient could not perceive an object that initially was on one side of space and then on the opposite side. Anosognosia refers to the denial of deficit.

Haque S, Vaphiades MD, Lueck CJ. The visual agnosias and related disorders. J Neuroophthalmol. 2018 Sep;38(3):379-392.

Question #

160 ADULT NEUROLOGY**Treatment/Management**

A black box warning has been issued by the FDA concerning increased mortality and risk of neuroleptic malignant syndrome associated with atypical antipsychotic drugs such as risperidone. These agents should be used with extreme caution in patients with dementia and only when other treatment options have failed.

Stroup TS, McEvoy JP, Swartz MS, et al. The National Institute of Mental Health Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) Project: schizophrenia trial design and protocol development. *Schizophr Bull*. 2003;29(1):15–31.

Lieberman JA, Stroup TS, McEvoy JP, et al. Effectiveness of antipsychotic drugs in patients with chronic schizophrenia. *New Engl J Med*. 2005 Sep; 353(12):1209–1223.

Zheng L, Mack WJ, Dagerman KS, et al. Metabolic changes associated with second-generation antipsychotic use in Alzheimer's disease patients: the CATIE-AD study. *Am J Psychiatry*. 2009 May;166(5):583–590.

Yunusa I, Alsumali A, Garba AE, et al. Assessment of reported comparative effectiveness and safety of atypical antipsychotics in the treatment of behavioral and psychological symptoms of dementia: a network meta-analysis. *JAMA Netw Open*. 2019;2(3):e190828.

Rubino A, Sanon M, Ganz ML, et al. Association of the US Food and Drug Administration antipsychotic drug boxed warning with medication use and health outcomes in elderly patients with dementia. *JAMA Netw Open*. 2020;3(4):e203630.

170 ADULT NEUROLOGY**Clinical Aspects of Disease**

The video shows a patient with a faciobrachial dystonic seizure (FBDS), a disorder classically associated with LGI1 encephalitis. The other antibodies listed (GFAP, Ma2, GAD, Ri) can be associated with movement disorders.

Ri and Ma2 are associated with opsoclonus-myoclonus syndrome and parkinsonism. Ri and GAD are associated with stiff person syndrome. GFAP is associated with ataxia and tremor.

Hsieh PC, Wu Yr. Diagnosis and clinical features in autoimmune-mediated movement disorders. *J Mov Disord*. 2022 May;15(2):95–105.

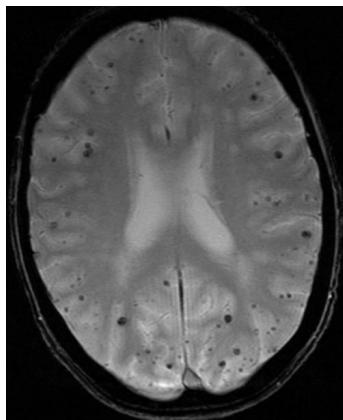
Video credit: Schmerler DA, Roller S, Espay AJ. Teaching Video NeurolImages: Faciobrachial dystonic seizures. Pathognomonic phenomenology. *Neurology*. 2016 Feb 9;86(6):e600–e61

Question #

181 ADULT NEUROLOGY**CORE KNOWLEDGE****Neuroimaging**

This patient's presentation is consistent with cerebral amyloid angiopathy, most commonly seen in Alzheimer disease. The other genetic defects listed (factor V Leiden, homocysteine methyltransferase, methylene tetrahydrofolate reductase, *NOTCH3*) have no correlation with intraparenchymal microhemorrhages.

Ropper AH, Samuels MA, Klein JP, et al (eds). Adams and Victor's Principles of Neurology. 11th ed. New York: McGraw-Hill Education; 2019.

**196 ADULT NEUROLOGY****Neuroanatomy**

Dominant angular gyrus lesions may cause Gerstmann syndrome (acalculia, agraphia, right-left disorientation, and finger agnosia). Impaired writing skills (agraphia) are often present.

Abulia is a frontal lobe sign. Simultanagnosia is often a feature of Balint syndrome, which is caused by bilateral parietal-occipital lesions. Acquired prosopagnosia is usually associated with bilateral or right-sided lesions of the occipital or temporal lobes. Anosognosia typically occurs from nondominant lesions or bilateral lesions affecting the cortical and subcortical regions.

Silbersweig DA, Safar LT, Daffner KR. Neuropsychiatry and Behavioral Neuroscience: Principles and Practice. New York: McGraw-Hill; 2021.

Pia L, Neppi-Modona M, Ricci R, Berti A. The anatomy of anosognosia for hemiplegia: a meta-analysis. Cortex 2004;40:367-377.

Question

208 NO SPECIFIED PATIENT AGE**SUBSPECIALTY KNOWLEDGE****Neuroanatomy**

The cingulate gyrus projects fibers to the ventral striatum (limbic striatum), which includes the ventral caudate, nucleus accumbens, and olfactory tubercle. Fibers from these regions then project, via direct and indirect loops, to the dorsomedial nucleus of the thalamus, which then relay fibers back to the cortex. This circuit subserves motivation.

Mavridis IN. How deep brain stimulation of the nucleus accumbens affects the cingulate gyrus and vice versa. *Brain Sci.* 2019 Jan;9(1):5.

220 PEDIATRIC NEUROLOGY**CORE KNOWLEDGE****Diagnostic Procedures**

This patient presents with global developmental delay without features suggestive of a specific syndrome, along with a negative family history and reassuring perinatal course. Guidance from the American College of Medical Genetics suggests clinical exome or genome testing as first- or second-tier evaluation for pediatric congenital anomalies or intellectual disability/global developmental delay.

MRI/MR spectroscopy can be considered in patients with features suggestive of perinatal injury or an abnormal neurologic exam, including macro- or microcephaly. Targeted testing for Rett syndrome (*MECP2*) and fragile X syndrome should be pursued in situations of high clinical concern; otherwise, exome/genome should be considered first.

Manickam K, McClain MR, Demmer LA, et al; ACMG Board of Directors. Exome and genome sequencing for pediatric patients with congenital anomalies or intellectual disability: an evidence-based clinical guideline of the American College of Medical Genetics and Genomics (ACMG). *Genet Med.* 2021 Nov;23(11):2029–2037.

231 NO SPECIFIED PATIENT AGE**Clinical Aspects of Disease**

The amnesia of transient global amnesia (TGA) affects recall of recent events and impairs new learning (anterograde memory). There is often some retrograde memory loss but generally involving only recent events. Patients are usually disoriented as to date and location, most likely due to their inability to build upon new memory. TGA spares immediate recall, remote memory, language and procedural memory (playing a musical instrument). Details of identity are also spared.

Romero-Fernandez R. Memory dysfunction. *Continuum Lifelong Learning Neurol.* 2021 Dec;27(6):1562–1585.

Question #

245 ADULT NEUROLOGY**CORE KNOWLEDGE****Treatment/Management**

Choice of an antidepressant for an individual is based on the side effect profile of the medication and how it fits with the patient's needs. Mirtazapine is an antidepressant that promotes weight gain and helps with sleep. Both are important for this elderly patient, who has lost 15 lb and has disrupted sleep.

Paroxetine often results in weight gain, but it can also cause insomnia. It is also the most anticholinergic of the SSRIs and therefore not preferred in dementia. The most commonly observed adverse events consistently associated with the use of bupropion are dry mouth and insomnia; however, weight is not usually affected.

Sertraline typically does not cause weight gain, and insomnia occurs with about the same frequency as somnolence. Insomnia and anorexia are more typical adverse events with imipramine than weight gain or sleepiness.

Schulz PE, Arora G. Depression. Continuum Lifelong Learning Neurol. 2015 Jun;21(3): 756-771.

260 ADULT NEUROLOGY**Diagnostic Procedures**

The Trail Making Test measures perseveration, set-shifting, and response inhibition, abilities that are altered in patients with a frontal lobe dementia as in this patient. The Wechsler Memory Scale assesses memory. The Boston Naming Test evaluates language, and the WAIS-III Arithmetic Subtest evaluates calculation abilities. The Rey Complex Figure Test and Recognition Trial measures visuospatial abilities.

Llinàs-Reglà J, Vilalta-Franch J, Lopez-Pousa S, et al. The Trail-Making Test. Assessment. 2017 Mar;24(2):183-196.

Gonzalez Kelso I, Tadi P. Cognitive assessment. [Updated 2020 Nov 20]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021.

Question #

279 ADULT NEUROLOGY**Clinical Aspects of Disease**

Several key risk factors are associated with amyloid-related imaging abnormalities (ARIA). Carriers of the apolipoprotein E-ε4 (APOE-ε4), especially homozygotes, face a heightened risk of both ARIA-E (effusion) and ARIA-H (hemorrhage). In this scenario, the oldest patient who has more than one copy of the APOE-ε4 allele is at greatest risk.

Cerebral microhemorrhages seen on baseline MRI scans also significantly increase the likelihood of ARIA-H. Factors such as older age and a history of cerebrovascular disease also correlate with a higher incidence of ARIA-H.

Use of antithrombotic agents can also lead to an increased risk of ARIA-H. Higher doses of anti-amyloid antibodies are associated with a greater incidence of ARIA, suggesting a dose-dependent relationship in the manifestation of these imaging abnormalities.

Doran SJ, Russell PS. Risk factors in developing amyloid related imaging abnormalities (ARIA) and clinical implications. *Front Neurosci.* 2024 Jan 19;18:1326784.

292 ADULT NEUROLOGY**Neuroanatomy**

This patient appears to have problems with working memory, as evidenced by his trouble immediately remembering numbers, tasks, and information after he hears them. The prefrontal cortex and parietal association cortex are important to working memory. The medial temporal lobes, mammillary bodies, and anterior thalamus are important for episodic memory – memory of personal events. The supplemental motor cortex is important for procedural memory – memory of learned movements.

Matthews BR. Memory dysfunction. *Continuum Lifelong Learning Neurol.* 2015 Jun;21(3):613–626.

Gliebus GP. Memory dysfunction. *Continuum Lifelong Learning Neurol.* 2018 Jun;24(3):727–744.

Question #

305 ADULT NEUROLOGY**CORE KNOWLEDGE****Clinical Aspects of Disease**

Loss of all remote memory (including autobiographical memory) with spared new learning ability suggests psychogenic amnesia. Memory loss in early Alzheimer disease most prominently affects more recent memory and somewhat spares remote memory. Korsakoff amnestic syndrome affects remote memory, but autobiographical details generally are not affected. Limbic encephalitis and Pick disease would likewise not be expected to impair such basic facets of remote memory as hometown and family names while sparing 5-minute object recall.

Harrison NA, Johnston K, Corno F, et al. Psychogenic amnesia: syndromes, outcome, and patterns of retrograde amnesia. *Brain*. 2017 Sep;140(9):2498–2510.

Serraa L, Faddaa L, Buccionea I, et al. Psychogenic and organic amnesia: a multidimensional assessment of clinical, neuroradiological, neuropsychological and psychopathological features. *Behav Neurol*. 2007;18(1):53–64.

321 PEDIATRIC NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Treatment/Management**

Atomoxetine, which is a second-line agent for attention-deficit/hyperactivity disorder selectively blocks the uptake of norepinephrine.

Khoodoruth MAS, Ouanes S, Khan YS, A systematic review of the use of atomoxetine for management of comorbid anxiety disorders in children and adolescents with attention-deficit hyperactivity disorder. *Res Dev Disabil*. 2022 Sep;128:104275.

Daughton JM, Kratochvil CJ. Review of ADHD pharmacotherapies: advantages, disadvantages, and clinical pearls. *J Am Acad Child Adolesc Psychiatry*. 2009 Mar;48(3):240–248.

Question #

323 ADULT NEUROLOGY**Clinical Aspects of Disease**

This patient is unable to read simple words (alexia) but has preserved ability to write (without agraphia). This disorder is typically caused by a left occipital lobe lesion with involvement of the splenium of the corpus callosum.

A left occipital lobe lesion causes a right homonymous hemianopia. The lesion of the left splenium of the corpus callosum prevents preserved vision from the right occipital lobe to be transmitted to Wernicke's area in the left temporal lobe for the reading of written words.

Amusia is typically caused by temporal lobe lesions, particularly in the nondominant hemisphere. Astereognosis is caused by contralateral parietal lobe lesions.

Jauregui R, Greenberg J, Kuball P, et al. Alexia without agraphia: from infarctions to malignancies. Pract Neurol. 2024 Sept 23;pn-2024-004235. Online ahead of print.

335 ADULT NEUROLOGY**CORE KNOWLEDGE****Neuroimaging**

A patient with a 4- to 5-day history of headache, malaise, behavioral disturbances, anterograde memory deficit, and fever should be presumed to have herpes simplex virus type 1 encephalitis until proven otherwise. The most commonly affected areas of the brain are the medial temporal and orbitofrontal lobes; the cingulate gyrus is less commonly affected. The treatment of choice is IV acyclovir 10 mg/kg every 8 hours for 2 weeks.

Boland R, Verduin M, Ruiz P (eds). Kaplan and Sadock's Synopsis of Psychiatry: Behavioral Sciences/Clinical Psychiatry. 12th ed. Philadelphia: Wolters Kluwer; 2021.

Question #

347 ADULT NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Clinical Aspects of Disease**

Capgras syndrome is a delusional misidentification disorder that can be seen in schizophrenia, traumatic brain injury, Alzheimer dementia, parietal lobe stroke, and Lewy body dementia.

Phantom boarder syndrome is a delusional belief that an uninvited guest is living in one's home, characterized by visual and auditory hallucinations.

In Fregoli syndrome, a person believes that a stranger or acquaintance is someone known but in disguise. This syndrome is thought to be a result of a breakdown in normal facial recognition.

The Cotard delusion is a delusional misidentification syndrome in which patients believe they are already dead or dying.

Pseudocyesis is a belief that a person is pregnant when they are not.

Barrelle A, Luauté J-P. Capgras syndrome and other delusional misidentification syndromes. *Front Neurol Neurosci*. 2018;42:35-43.

357 ADULT NEUROLOGY**CORE KNOWLEDGE****Diagnostic Procedures**

Alzheimer disease (AD) is a progressive neurodegenerative disorder affecting memory, thinking, and behavior and is the most common cause of dementia. CSF biomarkers seen in AD include low β -amyloid protein and increased total and phosphorylated tau protein levels.

The presence of CSF 14-3-3 protein is associated with Creutzfeldt-Jakob disease (CJD), a type of rapidly progressive neurodegenerative dementia caused by prion disease. High CSF neurofilament light chain is nonspecific and suggestive of inflammation. Positive real-time quaking-induced conversion (RT-QuIC) is a marker for CJD.

McDade EM. Alzheimer disease. *Continuum Lifelong Learning Neurol*. 2022 Jun;28(3):648-675.

Question #

366 ADULT NEUROLOGY**CORE KNOWLEDGE****Neuroanatomy**

Witzelsucht (inappropriate jocularity) is seen in patients with orbitofrontal cortex lesions. Lesions in this region are also characterized by disinhibited and antisocial behavior.

Amygdala impairment can lead to Kluver Bucy syndrome, a rare impairment characterized by inappropriate sexual behaviors, mouthing objects, and loss of normal fear or anger. Anterior insula impairment can lead to dysfunction in language and possible loss of addiction to substances such as nicotine. Lesions of the dorsolateral prefrontal cortex and posterior cingulate are characterized by difficulty with working memory, attention, cognitive slowing, and depression.

Moore KL, Dalley AF, Agur AMR (eds). Moore's Clinically Oriented Anatomy. 8th ed. Philadelphia: Wolters Kluwer; 2018.

Question #

378 ADULT NEUROLOGY**Diagnostic Procedures**

Amyloid-related imaging abnormalities (ARIA) are related to the increased permeability of amyloid-laden blood vessels to fluid or blood products that can occur in the setting of cerebral amyloid angiopathy and as a result of amyloid mobilization by lecanemab.

The ClarityAD phase 3 trial reported infusion-related reactions and ARIA, specifically ARIA with hemosiderin (ARIA-H) and ARIA-edema/effusion (ARIA-E). The edema seen in ARIA-E is vasogenic, not cytotoxic. The incidence of ARIA-H reactions (eg, microhemorrhages and superficial siderosis) was 17.3% in patients taking lecanemab compared with 9% in those receiving a placebo. The incidence of ARIA-E reactions was 12.6% in the treatment group compared with 1.7% in the placebo group.

MRI recommendations include the following: at baseline before initiation of treatment and then before the fifth, seventh, and fourteenth infusions to monitor for ARIA-E or ARIA-H.

Based on a patient's clinical symptoms and the severity the findings seen on imaging studies, clinical judgment is needed when considering to continue dosing or temporarily or permanently discontinue lecanemab. The appearance of new microhemorrhages would warrant a pause in treatment, assessment of the patient, and review of imaging studies.

The empty delta sign is created by a nonenhancing thrombus in the dural sinus surrounds by a triangular enhancing dura as seen on cross-section. It suggests a dural sinovenous thrombosis. The dural tail sign is a thickening and enhancement of the dura in continuity with a mass, usually highly specific for a meningioma. The hummingbird sign is significant midbrain atrophy with pons atrophy associated with progressive supranuclear palsy. The edema seen in ARIA-E is vasogenic, not cytotoxic.

van Dyck CH, Swanson CJ, Aisen P, et al. Lecanemab in early Alzheimer's disease. *N Engl J Med.* 2023 Jan 5;388(1):9–21.

Cummings J, Apostolova L, Rabinovici GD, et al. Lecanemab: appropriate use recommendations. *J Prev Alz Dis.* 2023;3(10):362–377.

Virhammar J, Blohme H, Nyholm D, et al. Midbrain area and the hummingbird sign from brain MRI in progressive supranuclear palsy and idiopathic normal pressure hydrocephalus. *J Neuroimaging.* 2022 Jan;32(1):90–96.

Chavhan GB, Shroff MM. Twenty classic signs in neuroradiology: a pictorial essay. *Indian J Radiol Imaging.* 2009 May;19(2):L135–145.

Question #

400 ADULT NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Clinical Aspects of Disease**

This patient had a stroke in his dominant (left) occipital region with expansion into the splenium. This would typically cause a syndrome of alexia without agraphia. There is a lesion in his left calcarine cortex as a result of the stroke; thus, the only visual input is coming into his right calcarine cortex.

The written words that he sees must cross through the splenium of the corpus callosum to be interpreted as words by the language centers in his dominant (left) hemisphere. Because the splenium was also involved in the stroke, words cannot cross over to the left hemisphere; therefore, he is unable to read (alexia).

Writing (graphia) is still intact because it requires more anterior regions and visual input to write letters. Left-hand agraphesthesia and astereognosis might be seen if a callosal disconnection of the parietal regions anterior to the splenium is present. Conduction aphasia typically occurs from a disconnection between the Wernicke and Broca areas on the left.

Brazis PW, Masdeu JC, Biller J. Localization in Clinical Neurology. 7th ed. Philadelphia: Lippincott Williams and Wilkins; 2017.

Blumenfeld H. Neuroanatomy Through Clinical Cases. 3rd ed. Sunderland: Sinauer Associates; 2021.

Question

7 ADULT NEUROLOGY**CORE KNOWLEDGE****Treatment/Management**

Hyponatremia can occur in various acute brain injuries, but it is commonly seen in patients with subarachnoid hemorrhage or traumatic brain injury. Syndrome of inappropriate antidiuretic hormone secretion (SIADH) and cerebral salt wasting (CSW) are frequently the causes of hyponatremia in patients with acute brain injury, but intravascular volume depletion and iatrogenic hypotonic fluid administration may also be the culprit. Therefore, serum osmolarity and urine electrolyte and osmolarity should be checked expeditiously.

Whether CSW and SIADH are two different pathologies is still debated, each exhibits distinct phenotypes. CSW is associated with hypovolemia, high urine output and high urine sodium excretion, whereas SIADH is associated with an euvolemic or hypervolemic state with normal to decreased urine output.

When selecting treatment for hyponatremia, it is important to assess how rapidly the sodium needs to be corrected. Patients with clinically significant cerebral edema or a space-occupying lesion are less likely to tolerate rapid decreases in serum osmolality; therefore, they require urgent increase of serum sodium. In contrast, patients who do not have significant cerebral edema but have chronic hyponatremia should not have such an abrupt correction, given the risk of osmotic demyelination. A bolus of hypertonic saline with a tonicity of 3% or higher is the fastest way to correct hyponatremia.

Even though the standard treatment for SIADH is free water restriction, this method will not increase serum sodium quickly enough for patients with significant space-occupying mass lesions or high intracranial pressure. Neither would oral salt tablets or oral fludrocortisone, though these may be part of maintenance strategy after the sodium is already corrected.

IV normal saline solution may paradoxically worsen hyponatremia in SIADH, particularly if the patient's urine osmolality is higher than that of normal saline (300 mmol/L). Vasopressin receptor antagonists are indicated in patients with refractory SIADH, but their clinical use is limited by their excessive cost and restricted availability.

Baba M, Alsbrook D, Williamson S, et al. Approach to the management of sodium disorders in the neuro critical care unit. *Curr Treat Opt Neurol.* 2022 Aug;24(8):327-346.

Suarez J. Diagnosis and management of subarachnoid hemorrhage. *Continuum Lifelong Learning Neurol.* 2015 Oct;21(5):1263-1287.

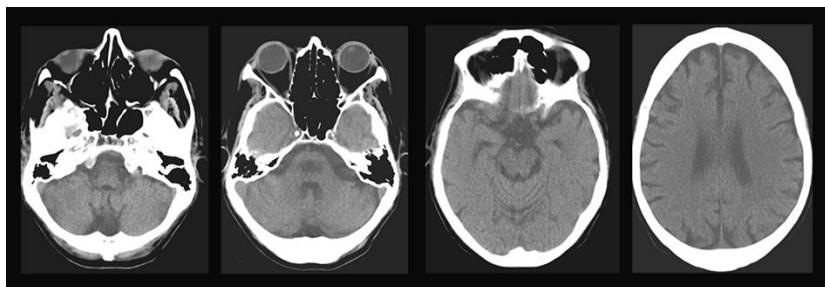
Question

55 ADULT NEUROLOGY**CORE KNOWLEDGE****Clinical Aspects of Disease**

The CT scans demonstrate an ovoid hypodensity within the central basis pontis. This lesion does not extend to the anterior or posterior margin of the pons as would be seen with a large pontine infarction. There is no vasogenic edema associated with this lesion as would be seen in an infectious process or tumor.

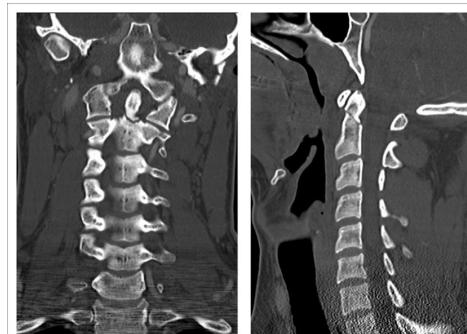
Wernicke encephalopathy can demonstrate some suggestive findings on CT scan, including hypodensities in the fornices and low-density changes along the periaqueductal region and along the margins of the third ventricle. These findings are much better demonstrated on MRI scans along with signal changes within the mammillary bodies, not seen in this case. Acute alcohol intoxication is not associated with any specific imaging findings.

Atlas S. Magnetic Resonance Imaging of the Brain and Spine. 3rd ed. Philadelphia: Williams and Wilkins; 2002.

**69 ADULT NEUROLOGY****CORE KNOWLEDGE****Neuroimaging**

The imaging studies show a C2 odontoid fracture. The clivus, C1 lateral mass, and posterior arch, and C2 spinous process appear normal.

Pryputniewicz DM, Hadley MN. Axis fractures. Neurosurgery. 2010; 66:A68–A82.



Question #

119 ADULT NEUROLOGY

Neuropathology

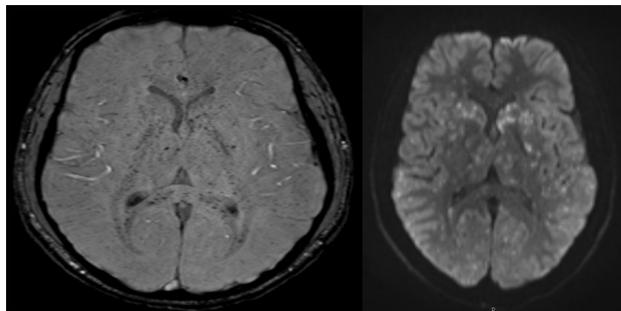
Fat embolism syndrome (FES) is caused by a shower of fatty bone marrow into the systemic circulation, most commonly associated with orthopedic surgery and long bone fractures. The risk of FES also increases with delay in surgical fixation of long bone fractures.

Fat embolization often triggers a systemic inflammatory response (SIRS) characterized by fever, acute hypoxia, and tachycardia. The pulmonary circulation is most commonly affected. Symptoms range from mild hypoxia to severe acute respiratory distress syndrome. Arterial embolization to the brain and other organ systems can also occur via cardiopulmonary shunts, causing punctate areas of restricted diffusion with small hemorrhages around small vessels.

Diffuse axonal injury can have a similar radiographic appearance, but clinically patients present with a poor level of consciousness, rather than a delayed decline.

Cerebral contusion and venous infarction tend to present with larger and more confluent hemorrhages and are not often associated with other systemic manifestations such as fever, tachycardia, and hypoxic respiratory failure. Disseminated intravascular coagulation can also present with a similar radiographic appearance, but this patient does not have coagulation abnormalities to suggest this diagnosis.

Ellison DW, Love S (eds). *Neuropathology: A Reference Text of CNS Pathology*. 3rd ed. San Francisco: Elsevier; 2013.



Question #

166 NO SPECIFIED PATIENT AGE**CORE KNOWLEDGE****Diagnostic Procedures**

This patient's clinical picture indicates acute cervical spine injury with spinal shock for which emergent imaging of the cervical spine is the highest priority.

The absence of reflexes and mute plantar responses due to spinal shock can initially be difficult to distinguish from peripheral nerve dysfunction (ie, Guillain–Barré syndrome). In this patient, however, the acuity and mechanism of injury (with resulting quadriplegia) and sensory level indicate acute spinal cord injury; therefore, evaluating the spinal cord is the most appropriate initial step.

The lesion localizes to the cervical cord based on weakness at C5/6 and caudally. A sensory level at the nipples suggests injury at T4, though the clinical sensory level can be segments below the anatomic level of injury.

Thoracic imaging may be appropriate but should not delay immediate imaging of the cervical spine. This patient's MRI scan showed cord compression at C5/6 due to a large herniated disk. The patient was taken to surgery immediately.

Several pooled analyses of randomized controlled studies looking at timing of decompressive surgery after acute spinal cord injury all indicate that early surgery (within 24 hours) is associated with better sensorimotor recovery, and that there is a steep decline in functional recovery over time within the first 24 to 36 hours. After 36 hours, motor recovery plateaus and the efficacy of early surgery is lost. These findings highlight the importance of timely diagnosis and surgical decompression following traumatic acute spinal cord injury.

Izzy S. Traumatic spinal cord injury. *Continuum Lifelong Learning Neurol*. 2024 Feb;30(1): 53–72.

Question #

195 PEDIATRIC NEUROLOGY**Contemporary Issues**

Neonatal hypoxic ischemic encephalopathy (HIE) occurs in 2 to 4 per 1,000 live births. Therapeutic hypothermia is the standard of care in neonates diagnosed with moderate or severe HIE within the first 6 hours of life. Therapeutic hypothermia to 33.5°C is continued for 72 hours, followed by slow rewarming to normothermia over the next 6 to 12 hours.

This patient's examination findings are consistent with moderate encephalopathy, characterized by her low Apgar scores, low pH (<7.0) and increased base deficit, all elements accepted in modern cooling trials.

While avoiding hyperthermia and maintaining eucarbia and normal serum glucose are neuroprotective, injection of erythropoietin does not improve outcomes in HIE. Because the family has clearly stated they want full medical management, involvement of the ethics committee is not indicated. Similarly, while early counseling regarding potential outcomes in HIE may be appropriate, the neurologic outcome shortly after resuscitation is not known. Testing for determination of death by neurologic criteria is not appropriate in this patient due to presence of pupillary reflexes and the short duration after resuscitation.

Jacobs SE, Berg M, Hunt R, et al. Cooling for newborns with hypoxic ischaemic encephalopathy. Cochrane Database Syst Rev. 2013 Jan 31;2013(1):CD003311.

215 ADULT NEUROLOGY**CORE KNOWLEDGE****Diagnostic Procedures**

The best predictor to assess the need for intubation in patients with neuromuscular respiratory failure (NMRF) is forced vital capacity (FVC). It accurately predicts diaphragmatic dysfunction and the development of mucous plugging and atelectasis due to diminished cough.

A drop in FVC is an early indicator of respiratory failure and the need for possible intubation. Drops in arterial oxygen saturation and hypercarbia occur late in the setting of NMRF. Although anti-MAG antibodies and repetitive nerve stimulation studies may assist with the diagnosis of demyelinating polyneuropathy and myasthenia gravis, neither predicts the clinical severity of disease or the need for intubation, which is the most acute concern in this patient.

Dhar R. Neuromuscular respiratory failure. Continuum Lifelong Learning Neurol. 2009 Jun;15(3):40-67.

Rabinstein A. Acute neuromuscular respiratory failure. Continuum Lifelong Learning Neurol. 2015 Oct;21(5):1324-1345.

Question #

286 NO SPECIFIED PATIENT AGE

Neuroscience and Mechanism of Disease

Hypothermia reduces the activity of the cytochrome P450 system, which can persist even after rewarming. This can prolong the effects of sedative and neuromuscular blocking agents metabolized via the liver, which can confound interpretation of neurologic and electrophysiologic exam findings and alter their accuracy for the purposes of prognostication. Fentanyl, midazolam, and vecuronium undergo extensive hepatic metabolism via the cytochrome P450 system. Continued clinical observation of these patients is strongly advised until the effects of sedation are no longer in question.

Bilateral absent corneal reflexes and absent or extensor motor responses are no longer considered reliable predictors of poor functional outcome after therapeutic hypothermia. Highly malignant EEG patterns (complete suppression, burst-suppression pattern with or without periodic discharges) are considered moderately reliable predictors for poor neurologic outcome after cardiac arrest, though care should be taken to ensure that the recordings are not obtained while patients are under the influence of sedation. Discontinuous and low-voltage backgrounds are not highly malignant features.

Two small studies demonstrated that patients experiencing out-of-hospital ventricular fibrillation who were randomized to therapeutic hypothermia had about a 50% chance for a good neurologic outcome compared with those treated with routine ICU care. These studies were criticized for lack of blinding, no protocol for withdrawal of care, and poor fever control in the routine ICU care group. Subsequent larger studies comparing therapeutic hypothermia (33 to 36°C) with normothermia failed to show similar benefit in patients treated with therapeutic hypothermia to 33°C. The optimal temperature to maintain unresponsive patients after cardiac arrest, along with duration and timing to initiate therapy, remains a topic of debate.

Initial rhythm of arrest is not predictive of neurologic outcome.

Tortorici MA, Kochanek PM, Poloyac SM. Effects of hypothermia on drug disposition, metabolism, and response: a focus of hypothermia-mediated alterations of the cytochrome P450 enzyme system. Crit Care Med 2007;35(9):2196-2204.

Westhall E, Rossetti AO, van Rootselaar AF, et al. Standardized EEG interpretation accurately predicts prognosis after cardiac arrest. Neurology. 2016 Apr 19;86(16):1482-1490.

Rajajee V, Muehlschlegel S, Wartenberg KE, et al. Guidelines for neuroprognostication in comatose adult survivors of cardiac arrest. Neurocritical Care. 2023 Jun;38(3):533-563.

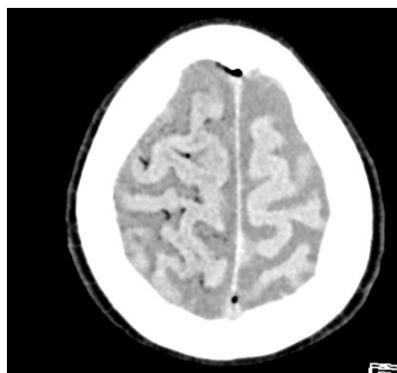
Question #

314 ADULT NEUROLOGY**CORE KNOWLEDGE****Neuroimaging**

The CT scan demonstrates air in a serpiginous pattern in the sulci consistent with venous air embolism, a complication that can occur following traumatic removal of a central line. Lumbar puncture can cause intracranial hypotension, which would not have this appearance.

Reversible cerebral vasoconstriction syndrome could cause convexal subarachnoid hemorrhage, a finding that would be hyperdense rather than hypodense. Orthopedic surgery can cause fat embolism in which infarction and/or hemorrhage would be seen. Endocarditis can cause stroke, mycotic aneurysm, and hemorrhage, none of which is seen here.

Heckmann JG, Lang CJ, Kindler K, et al. Neurologic manifestations of cerebral air embolism as a complication of central venous catheterization. Crit Care Med 2000;28:1621-1625.

**341 ADULT NEUROLOGY****CORE KNOWLEDGE****Treatment/Management**

Death by neurologic criteria (also known as brain death, which is no longer the preferred term) can be confirmed by clinical examination with apnea testing.

Ancillary testing is required only if the clinical assessment cannot be safely or fully completed. Ancillary testing demonstrating an absence of cerebral blood flow can include conventional angiogram or radionucleotide cerebral scintigraphy. In adults, transcranial Doppler ultrasound can also identify a lack of cerebral blood flow. EEGs, auditory evoked responses, or somatosensory evoked responses should not be used as ancillary tests to assist with the diagnosis of death by neurologic criteria.

Greer DM. Determination of brain death. New Engl J Med. 2021 Dec 30;385(27):2554-2561.

Greer DM, Kirschen MP, Lewis A, et al. Pediatric and Adult Brain Death/Death by Neurologic Criteria Consensus Guideline. Neurology. 2023 Dec 12;101(24):1112-1132. Erratum in: Neurology. 2024 Feb 13;102(3):e208108."

Question #

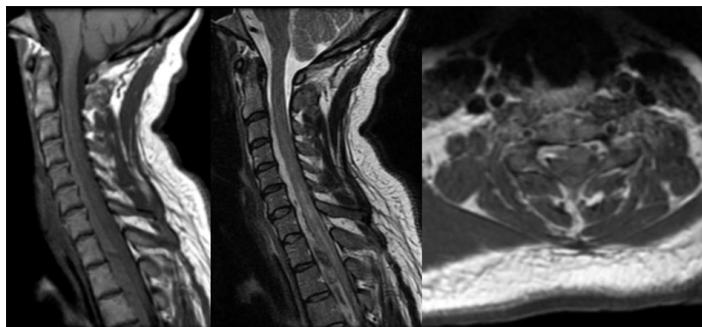
372 ADULT NEUROLOGY**Neuroimaging**

Spinal epidural hematoma is the most likely diagnosis. The MRI scans show an extradural collection that is slightly hyperintense on both T1 and T2 images with some heterogeneous hypointense signal admixed in the thoracic portion of the collection. The axial image further confirms the epidural location of the hematoma, with displacement of the dura and epidural fat by the hematoma, distinguishing the lesion from a subdural collection.

Epidural abscess is not the best response because the lesion is T1 hyperintense, suggestive of blood products. Spinal epidural lipomatosis is not the best response because the collection is not of fat signal intensity; epidural lipomatosis rarely involves the cervical spinal canal, and symptoms are typically gradual when it occurs. Spinal meningioma is typically intradural extramedullary. The lesion is extra-axial, not compatible with longitudinally extensive transverse myelitis.

Thiele RH, Hage ZA, Surdell DL, et al. Spontaneous spinal epidural hematoma of unknown etiology: case report and literature review. *Neurocrit Care*. 2008; 9:242–246.

Hussenbocus SM, Wilby MJ, Cain C, et al. Spontaneous spinal epidural hematoma: a case report and literature review. *J Emerg Med*. 2012;42(2):e31–e34.

**397 ADULT NEUROLOGY****Neuroimaging**

Hepatic encephalopathy is characterized by delirium, psychomotor slowing, asterixis, dysarthria, and nystagmus. Severe cases are associated with posturing and coma. Laboratory testing can demonstrate abnormalities in liver function, ammonia levels, and clotting. Cerebral edema is common patients with acute hepatic encephalopathy, especially in those with fulminant hepatic failure.

Wijdicks EFM. *The Practice of Emergency and Critical Care Neurology*. 2nd ed. New York: Oxford University Press; 2016.

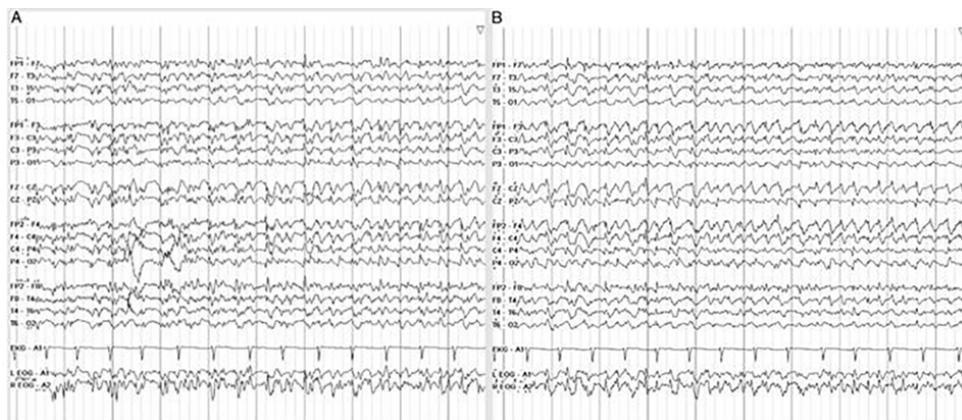
Question #

25 ADULT NEUROLOGY**Clinical Aspects of Disease**

Nonconvulsive status epilepticus can present with altered levels of consciousness or cognition. It can develop in patients with a seizure disorder, occasionally in elderly patients without a previous history of seizures or after withdrawal of an antiseizure or sedative medication.

EEG findings in Creutzfeldt-Jakob disease are characterized by repetitive, generalized 1–Hz sharp waves. Hepatic coma presents with triphasic waves on EEG. Generalized beta activity is seen with benzodiazepine toxicity. EEG findings associated with early Alzheimer disease are normal or show mild slowing of background activity.

Hocker SE. Status epilepticus. *Continuum Lifelong Learning Neurol*. 2015 Oct;21(5): 1362–1383.



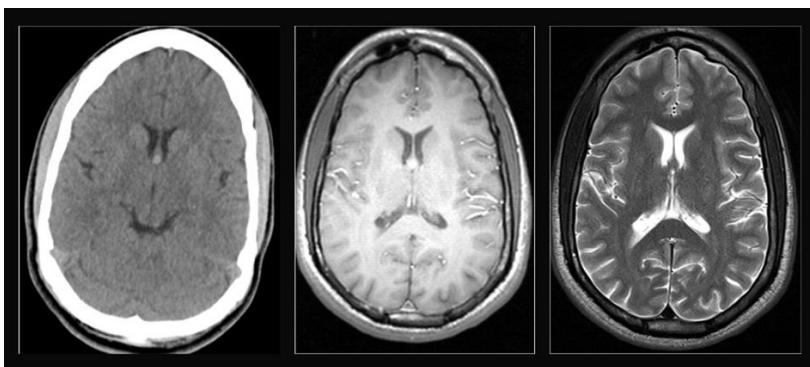
Question #

40 ADULT NEUROLOGY

Neuroimaging

The hyperdense appearance on the CT scan, the hyperintense nonenhancing appearance on the postcontrast T1-weighted MRI scan, and the isointense appearance on T2 sequence MRI scan, along with location within the third ventricle adjacent to the foramina of Monro, are typical of colloid cyst.

Jhaveri MD, Salzman KL, Osborn AG (eds). Diagnostic Imaging: Brain. 4th ed. Philadelphia: Elsevier; 2016.



Question #

46 ADULT NEUROLOGY**Treatment/Management**

This patient has tuberous sclerosis and associated remote infantile spasms for which she takes clobazam, lamotrigine, and vigabatrin. Patients taking vigabatrin require ophthalmic examination every 3 months to monitor for progressive central-sparing visual field defect. This defect pattern is secondary to preferential loss of binasal papillomacular fibers. Adults seem to be more likely to have this ophthalmic complication than children or infants.

The Tuberous Sclerosis Alliance has published guidelines outlining appropriate screening for the various multisystemic complications that can be seen in this condition. Echocardiogram is indicated in children with TSC to screen for a rhabdomyoma, though this is usually unnecessary in adult patients with TSC. Cardiac MRI is not usually required.

Genetic testing is often ordered to confirm TSC, but repeat testing would not be necessary in this patient who has already underwent genetic testing.

Brain MRI is recommended every 1 to 3 years to screen for subependymal giant cell astrocytomas (SEGAs) up to age 25. Since this patient is 40 and has no new neurologic symptoms, brain MRI is not necessary for this purpose.

Patients with TSC are at risk for fibrotic lung disease caused due to lymphangioleiomyomatosis. The prevalence of this condition is higher in women than men with TSC; thus, high-resolution lung CT is recommended in women with TSC every 5 years to screen for this disease. Lung biopsy is not needed in this asymptomatic patient.

TSC Alliance. 2021 Tuberous sclerosis complex diagnostic criteria, surveillance and management recommendations. <https://www.tscalliance.org/understanding-tsc/diagnosis-criteria/>. Reviewed November 2023. Accessed September 2024.

Northrup H, Aronow ME, Bebin EM, et al; International Tuberous Sclerosis Complex Consensus Group. Updated International Tuberous Sclerosis Complex diagnostic criteria and surveillance and management recommendations. *Pediatr Neurol*. 2021 Oct;123:50–66.

Schein Y, Miller KD, Han Y, et al. Ocular examinations, findings and toxicity in children taking vigabatrin. *JAAPOS*. 2022 Aug;26(4):187.e1–187.e6.

Oliveira C. Toxic-metabolic and hereditary optic neuropathies. *Continuum Lifelong Learning Neurol*. 2019 Oct;25(5):1265–1288.

Question #

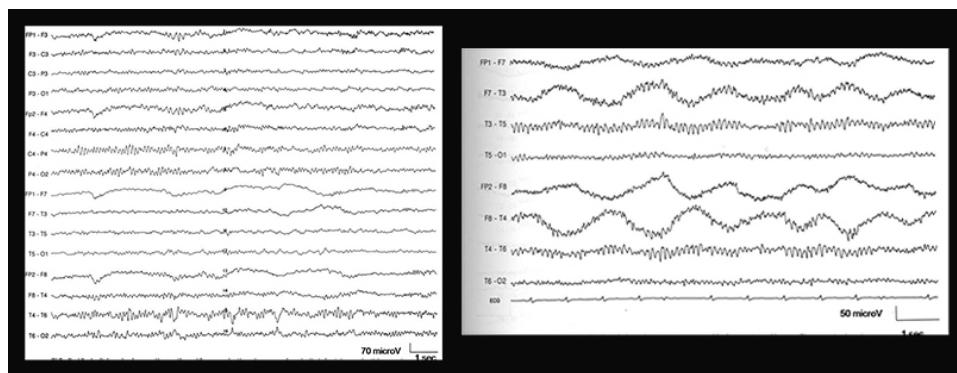
54 ADULT NEUROLOGY**CORE KNOWLEDGE****Neurophysiology**

Eye movement is a very common cause of physiologic artifact in EEG recordings. Lateral eye movements are seen on the bipolar montages; these are out-of-phase in derivations involving the F7 and F8 electrodes, as an increase in positivity at one is associated with a decrease in positivity in the other.

Muscle activity produces very brief potentials. Movement of the tongue, whose tip is electrically negative with respect to its base, may produce widely distributed, low-frequency intermittent potentials that may resemble "projected rhythms." A burst of muscle potentials may precede such low-frequency waves, serving to differentiate glossokinetic potentials from "projected" activity.

Rhythmic delta activity confined to a single electrode position likely represents pulse artifact. Sequential eye blink artifacts are identifiable by their location at Fp1, Fp2, their considerably lower amplitude at F3, F4, and their response to eye opening.

Ebersole JS, Husain AM, Nordli DR (eds). Current Practice of Clinical Electroencephalography. 4th ed. Philadelphia: Wolters Kluwer Health; 2014.

**59 ADULT NEUROLOGY****CORE KNOWLEDGE****Neuroscience and Mechanism of Disease**

HLA-B genetic testing is indicated in patients of Han-Chinese, Thai, or Malaysian ancestry prior to initiation of carbamazepine. The HLA-B 1502 allele is predictive of a severe, carbamazepine-induced rash, including Stevens-Johnson syndrome and toxic epidermal necrolysis, and therefore should be tested in patients of Asian ancestry.

Willmore L. Monitoring and antiepileptic drug safety. Continuum Lifelong Learning Neurol. 2013 Jun;19(3):801-805.

Question #

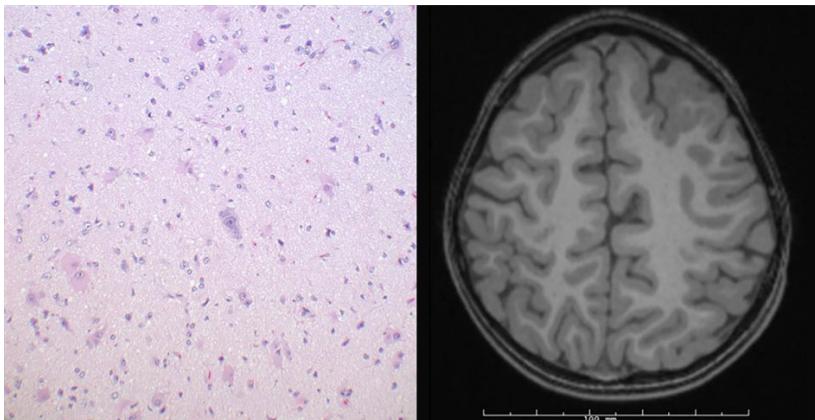
64 PEDIATRIC NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Neuropathology**

The histopathologic image shows typical dysmorphic neurons and balloon cells (with abundant pink cytoplasm) that are characteristic of focal cortical dysplasia (FCD) type IIb. Neither of these cell types is present in FCD type Ia, nor would they be present in either cavernous malformations or pleomorphic xanthoastrocytoma.

Gangliogliomas harbor dysmorphic–appearing neoplastic ganglion cells; however, balloon cells are not a feature of that tumor. Rasmussen encephalitis typically contains microglial proliferation/neuronophagia and variable chronic inflammatory infiltrates.

The T1 MPRAGE axial MRI image shows an area of focal cortical dysplasia in the left frontal lobe, characterized by thickening of the cortical ribbon in this case. A tail of tissue with gray matter intensity extending toward the ventricle would also be characteristics of FCD type IIb.

Kleinschmidt-DeMasters BK, Pekmezci M, Rodriguez F, et al (eds). Diagnostic Pathology: Neuropathology. 3rd ed. Philadelphia: Elsevier, 2021.



Question #

68 ADULT NEUROLOGY**CORE KNOWLEDGE****Clinical Aspects of Disease**

This patient has focal seizures most likely resulting from a lesion of the temporal lobe. Mesial temporal sclerosis is the most common etiology in adults with this disorder, although other structural lesions of the temporal lobe (eg, glioma, vascular malformation) are other possibilities.

The likelihood of a meningioma in a 20-year-old man is very low. Migraine usually is not associated with gustatory hallucination, and the stereotyped nature of these episodes are more consistent with epilepsy than primary psychiatric disease.

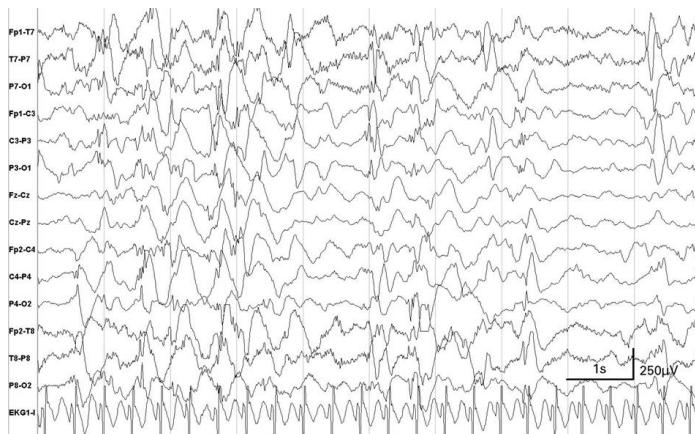
Rudzinski LA, Shih JJ. The classification of seizures and epilepsy syndromes. *Continuum Lifelong Learning Neurol*. 2010 Jun;16(3):15-35.

Sadler RM. The syndrome of mesial temporal lobe epilepsy with hippocampal sclerosis: clinical features and differential diagnosis. *Adv Neurol*. 2006;97:27-37.

76 PEDIATRIC NEUROLOGY**CORE KNOWLEDGE****Neurophysiology**

Hypsarrhythmia (interictal high-amplitude, disorganized delta activity with independent multifocal spike discharges) characterizes infantile epileptic spasm syndrome. Landau-Kleffner syndrome/DEE-SWAS occurs in children with language regression and sleep-activated spikes. Lennox-Gastaut syndrome is characterized by background activities of wakefulness that are too slow for state with interictal rhythmic 2-Hz spike-wave discharges. Childhood absence epilepsy in children occurs with generalized 3-Hz spike-wave discharges.

Arzimanoglou A, O'Hare A, Johnston M, et al (eds). *Aicardi's Diseases of the Nervous System in Childhood*. 4th ed. London: Mac Keith Press; 2018.



Question #

87 ADULT NEUROLOGY**CORE KNOWLEDGE****Clinical Aspects of Disease**

This patient's clinical presentation changes significantly after the addition of valproate to the treatment regimen. Valproate is known to interact with lamotrigine by inhibiting its metabolism in the liver, leading to an increase in lamotrigine levels in the blood. This can result in toxicity if lamotrigine dosages are not appropriately adjusted following the introduction of valproate. The symptoms of lamotrigine toxicity, as reflected in the patient's presentation, include confusion, ataxia, dizziness, and diplopia.

Abou-Khalil BW. Update on antiepileptic drugs 2019. *Continuum Lifelong Learning Neurol*. 2019 Apr;25(2):508–536.

89 NO SPECIFIED PATIENT AGE**Treatment/Management**

High-dose or prolonged administration of propofol, particularly in children, may result in potentially fatal metabolic acidosis. It is necessary to monitor acid-base balance closely when using propofol at high doses (>5 mg/kg/h) or for more than 48 hours.

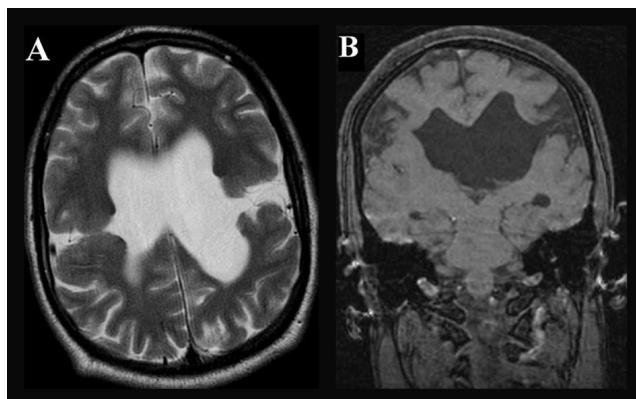
Rabinstein AA. Neurologic complications of anesthesia. *Continuum Lifelong Learning Neurol*. 2011 Feb;17(1):134–147.

Question #

98 PEDIATRIC NEUROLOGY**Neuroimaging**

This patient's MRI scans show clefts extending from the extra-axial space to the lateral ventricles bilaterally, findings characteristic of open-lip schizencephaly. In porencephaly, the cyst is not lined by cortex, as it is here. In hydranencephaly there is little brain tissue around a central cyst. The appearance of encephalomalacia due to trauma is different, with areas of mixed signal intensity in the frontal, temporal, or occipital regions.

Jhaveri MD, Salzman KL, Osborn AG (eds). Diagnostic Imaging: Brain. 4th ed. Philadelphia: Elsevier; 2016.

**104 PEDIATRIC NEUROLOGY****CORE KNOWLEDGE****Clinical Aspects of Disease**

Patients with Lennox–Gastaut syndrome have multiple types of seizures, such as tonic, atypical absence, and atonic, with age of onset 1 to 8 years. The EEG reveals slow spike-and-wave discharges of 1.5 to 2 Hz. Most children are intellectually disabled, with approximately 70% having an identifiable cause for the cognitive delay and epilepsy.

Tonic seizures are not observed in myoclonic atonic epilepsy (Doose syndrome). The syndrome described here is not absence epilepsy or juvenile myoclonic epilepsy. Landau–Kleffner syndrome (DEE–SWAS) is associated with speech regression, not intellectual disability; however, the latter may be present. Juvenile myoclonic epilepsy has later onset and is more prominent in women.

Wyllie E, Gidal BE, Goodkin HP, et al (eds). Wyllie's Treatment of Epilepsy: Principles and Practice. 7th ed. Philadelphia: Wolters Kluwer, 2021.

Question #

110 PEDIATRIC NEUROLOGY

CORE KNOWLEDGE

Treatment/Management

Phenobarbital should be the first-line antiseizure medication in neonates, regardless of etiology with one exception. Neonates who have a channelopathy involving the KCNQ2 or KCNQ3 genes should receive a sodium channel blocker such as fosphenytoin or oxcarbazepine first. If phenobarbital fails, second-line options include fosphenytoin and levetiracetam. Midazolam and lidocaine are other options.

Pressler RM, Abend NS, Auvin S, et al. Treatment of seizures in the neonate: guidelines and consensus-based recommendations – Special report from the ILAE Task Force on Neonatal Seizures. *Epilepsia*. 2023 Oct;64(10):2550–2570.

126 NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

Neurophysiology

Lateralized periodic discharges (LPDs) indicate unilateral hemispheric lesion and are the most common finding in herpes encephalitis.

A 3-Hz spike-wave discharge is a diffuse epileptic discharge composed of a spike with after-coming slow wave at 3/sec. FIRDA is a slow bifrontal discharge without a sharp component. Triphasic waves are seen in metabolic encephalopathy and are bilateral and frontally predominant. Breach rhythm is seen overlying a skull defect in which normal discharges are seen at higher than normal amplitudes.

Rubin DI, Daube JR (eds). *Clinical Neurophysiology*. 4th ed. New York: Oxford University Press; 2016.



Question #

142 PEDIATRIC NEUROLOGY**Treatment/Management**

Certain antiseizure medications (ASMs) may exacerbate myoclonic seizures. These include carbamazepine, gabapentin, lamotrigine, pregabalin, tiagabine, and vigabatrin. In addition, gabapentin, tiagabine, and vigabatrin may aggravate absence seizures.

Broad-spectrum formulations are the most appropriate ASMs for an epilepsy syndrome such as juvenile myoclonic epilepsy, which may have multiple seizure types (absence, myoclonic, generalized tonic-clonic). In addition to valproate, other broad-spectrum medications to consider include lamotrigine (may also increase myoclonus in some patients), levetiracetam, topiramate, and zonisamide.

Wirrell E. Infantile, childhood, and adolescent epilepsies. *Continuum Lifelong Learning Neurol.* 2016 Feb;22(1):60–93.

152 ADULT NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Treatment/Management**

Cenobamate is one of the latest antiseizure medications approved for focal epilepsy. The dose of clobazam should be decreased because when combined with cenobamate, the active metabolites of clobazam increase through CYP2C19 inhibition and result in significant side effects. Brivaracetam does not affect cenobamate and vice versa.

Roberti R, De Caro C, Iannone LF, et al. Pharmacology of cenobamate: mechanism of action, pharmacokinetics, drug-drug interactions and tolerability. *CNS Drugs.* 2021 Jun;35(6):609–618.

Smith MC, Klein P, Krauss GL, et al. Dose adjustment of concomitant antiseizure medications during cenobamate treatment: Expert opinion consensus recommendations. *Neurol Ther.* 2022 Dec;11(4):1705–1720.

163 PEDIATRIC NEUROLOGY**CORE KNOWLEDGE****Neurophysiology**

Absence seizures, characteristically seen in children 5 to 15 years of age, are associated with staring and may have automatisms such as repetitive chewing movements. Similar features may be seen in focal seizures, although absence seizures are shorter and may occur more frequently and typically do not have a postictal phase. A characteristic EEG obtained during an absence seizure would show 3-Hz spike-and-wave discharges.

Schomer D, Lopez de Silva F (eds). Niedermeyer's Electroencephalography: Basic Principles, Clinical Applications, and Related Fields. 7th ed. New York: Oxford University Press; 2018.

Question #

206 ADULT NEUROLOGY**CORE KNOWLEDGE****Treatment/Management**

Valproic acid is the drug of choice for patients with absence and tonic-clonic seizures, along with a 3-Hz spike-and-wave pattern on EEG, especially in male patients. In female patients, especially young women, consideration of the side effect profile, which includes teratogenicity, may lead to selection of an alternate medication. There are no other appropriate medications listed here.

Valproic acid can be used in young women, if needed, with appropriate counseling and mitigation of adverse effects. Ethosuximide, while effective for absence seizures, will not effectively treat generalized tonic-clonic seizures.

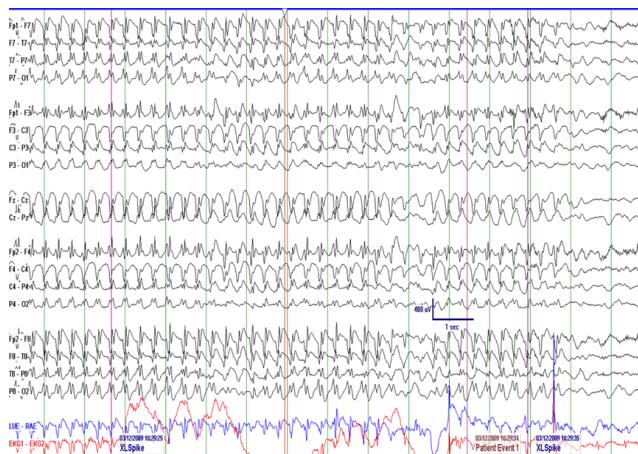
Carbamazepine and phenytoin are less effective against absence seizures. Clonazepam may be helpful for myoclonic seizures but is not first-line treatment for generalized tonic-clonic and absence seizures.

Abou-Khalil BW. Antiepileptic drugs. Continuum Lifelong Learning Neurol. 2016 Feb;22(1):132-156.

221 PEDIATRIC NEUROLOGY**CORE KNOWLEDGE****Neuroscience and Mechanism of Disease**

This patient has absence epilepsy confirmed by an EEG that demonstrates 3-Hz generalized spike-and-wave discharges. First-line treatment of childhood absence epilepsy is ethosuximide. The prevailing hypothesis for the mechanism of action of this drug is that it produces a blockade of thalamic low-threshold "transient" or "tiny" calcium (so-called T type) channels.

Patsalos PN, Bourgeois BFD. The Epilepsy Prescribers Guide to Antiepileptic Drugs. Cambridge, UK: Cambridge University Press; 2010.



Question #

233 ADULT NEUROLOGY**Treatment/Management**

This patient likely has epilepsy given the clinical history, which suggests at least two convulsive seizures, as well as confirmatory neurophysiologic findings (focal epileptiform discharges).

Sudden unexplained death in epilepsy (SUDEP) is death in a person with epilepsy that occurs separate from an identifiable cause, with no etiology revealed on postmortem examination. Among neurologic conditions, SUDEP is second only to stroke with respect to potential life lost. There is growing evidence that patients and their families prefer to be educated about SUDEP and other risks associated with epilepsy; however, neurology providers may unnecessarily avoid discussing SUDEP for fear of inciting patient anxiety. An empathetic discussion of the potential risks of epilepsy, including SUDEP, is warranted at the time of diagnosis. Neurologists should be familiar with the risk factors associated with SUDEP to provide contextualized and patient-centered counseling.

Epidemiologic data suggest that across epilepsy syndromes, tonic-clonic seizures represent the strongest risk factor for SUDEP. Additional risk factors include predominantly nocturnal seizures, and seizures that occur in patients who live or sleep alone. A variable risk of SUDEP is associated with frontal lobe seizures, and it has not been demonstrated that they confer a lower risk compared to other epilepsy syndromes. Nonadherence to antiseizure medications has been identified as one potential modifiable risk factor for SUDEP.

Mesraoua B, Tomson T, Brodie M, et al. Sudden unexpected death in epilepsy (SUDEP): definition, epidemiology, and significance of education. *Epilepsy Behav.* 2022 Jul;132:108742.

Henning O, Nakken KO, Lossius MI. People with epilepsy and their relatives want more information about risks of injuries and premature death. *Epilepsy Behav.* 2018 May;82: 6–10.

Question #

239 ADULT NEUROLOGY**Diagnostic Procedures**

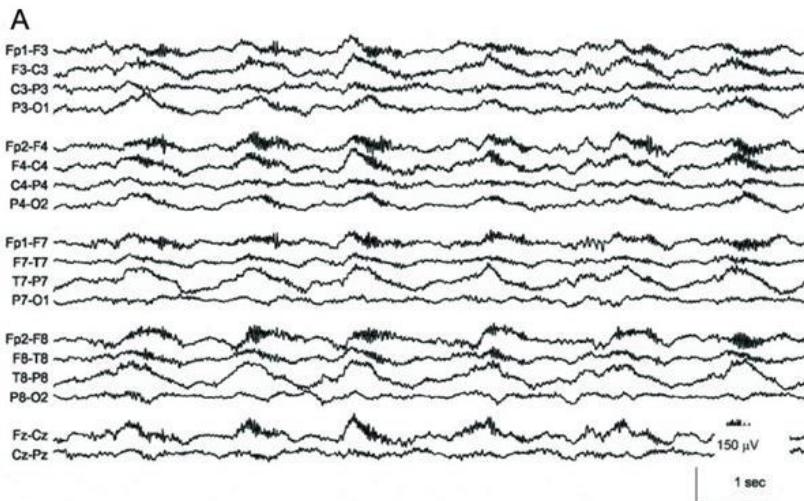
This patient's symptoms are consistent with a typical presentation of N-methyl-D-aspartate (NMDA) receptor encephalitis. The EEG reveals extreme delta brushes with rhythmic delta activity and superimposed beta, findings often seen in this syndrome. Antibodies in the CSF can confirm the diagnosis.

Though continuous EEG can aid in capturing potential seizures, it will not help confirm the diagnosis. CSF 14-3-3 protein may be helpful in the diagnosis of Creutzfeldt–Jakob disease, and the EEG may reveal periodic discharges that may be asymmetric depending on the timing of presentation.

Some chromosomal disorders, such as 16p11.2 deletion syndrome, are associated with autism and schizophrenia (and sometimes epilepsy) but typically present at a younger age and are not associated with specific EEG findings.

Gaspard N. Autoimmune epilepsy. *Continuum Lifelong Learning Neurol*. 2016 Feb; 22(1):227–245.

Schmitt SE, Pargeon K, Frechette ES, et al. Extreme delta brush: a unique EEG pattern in adults with anti-NMDA receptor encephalitis. *Neurology*. 2012 Sep 11;79(11):1094–1100.



Question #

246 ADULT NEUROLOGY**CORE KNOWLEDGE****Contemporary Issues**

In a 2008 survey of over 213 respondents with epilepsy, 19% indicated that in order to drive, they were not completely honest about their seizure frequency. Indeed, 26% reported having had a car accident because of a seizure.

It is important to recognize that the loss of a driver's license can profoundly impact an individual's life. In an effort to explore ways to encourage patient compliance, voluntarily exploring other options for driving is imperative if a physician suspects poor adherence. Neurologists, however, are not obligated to serve as policing agents if a patient is driving and is not well-controlled on medication; however, if an individual knowingly drives and injures another, that individual may be liable for both civil and even criminal damages.

Adding a second antiseizure medication will not increase adherence with the first drug. Transferring care to another neurologist is not recommended as a first step, particularly because the treating physician may have better success at least initially exploring why the patient is not adherent. Finally, although it may be germane to report a negligent parent for driving her minor children while she has inadequate seizure control because of poor adherence, it is not the ideal first step.

Elliott JO, Long L. Perceived risk, resources, and perceptions concerning driving and epilepsy: a patient perspective. *Epilepsy Behav.* 2008 Aug;13(2):381-386.

Question #

254 NO SPECIFIED PATIENT AGE**Neuroimaging**

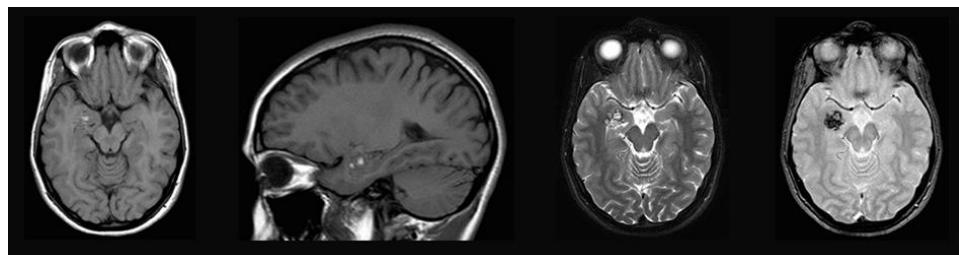
The lesion shown is a hypothalamic hamartoma. Typical presentation is gelastic seizures (defined as seizures beginning with mirthless laughter). Endocrine effects are relatively uncommon, but precocious puberty may occur. None of the other seizure types listed (focal with olfactory aura, tonic, atonic, absence) would be a consequence of a lesion in this location and with this appearance.

Wyllie E, Gidal BE, Goodkin HP, et al (eds). Wyllie's Treatment of Epilepsy: Principles and Practice. 7th edition. Philadelphia: Wolters Kluwer, 2021.

**263 ADULT NEUROLOGY****CORE KNOWLEDGE****Clinical Aspects of Disease**

The appearance of this lesion suggests a very limited differential diagnosis, mainly subtypes of cerebral cavernous malformations (also known as cavernous hemangioma, cavernoma). Features of T1 and T2 hyperintensities with T2 hypointense rings give the lesion a so-called "popcorn" appearance, which is characteristic of cavernous malformations. None of the other disorders listed (mesial temporal sclerosis, herpes encephalitis, ganglioglioma, bacterial abscess) would have this appearance.

Campbell PG, Jabbour P, Yadla S, Awad IA. Emerging clinical imaging techniques for cerebral cavernous malformations: a systematic review. Neurosurg Focus. 2010 Sep; 29(3):E6.



Question #

274 PEDIATRIC NEUROLOGY**Treatment/Management**

When multiple drugs fail, such as in this 2-year-old patient, initiation of a ketogenic diet has a higher response rate than a new antiseizure medication. Phenytoin, ethosuximide, and carbamazepine may actually worsen generalized epilepsy and are less likely to succeed in seizure control. Temporal lobectomy would not be indicated for generalized epilepsy.

Although corpus callosotomy can be used in intractable epilepsy, it is more effective for drop attacks (atonic seizures). This surgical procedure is often recommended only after other treatment options fail to improve seizure control, including vagus nerve stimulation, ketogenic diet, and other appropriate broad-spectrum antiseizure medications.

Wyllie E, Gidal BE, Goodkin HP, et al (eds). Wyllie's Treatment of Epilepsy: Principles and Practice. 7th ed. Philadelphia: Wolters Kluwer, 2021.

295 PEDIATRIC NEUROLOGY**Neuroscience and Mechanism of Disease**

Sleep-related hypermotor epilepsy (previously known as nocturnal frontal lobe epilepsy) can be an autosomal dominant disorder caused by a mutation in the gene for a nicotinic acetylcholine receptor subunit, or the result of various frontal lobe pathologies. This type of epilepsy is often mistaken for a parasomnia, panic attack, or psychogenic nonepileptic seizure. Unlike parasomnias, multiple episodes per night are characteristic.

Sleep related hypermotor epilepsy (previously known as nocturnal frontal lobe epilepsy) can be an autosomal dominant genetic disorder caused by a mutation in the gene for a nicotinic acetylcholine receptor subunit, or the result of various frontal lobe pathologies. This type of epilepsy is often mistaken for a parasomnia, panic attack, or psychogenic nonepileptic seizure. Unlike parasomnias, multiple episodes per night are characteristic.

Tinuper P, Bisulli F, Cross JH, et al. Definition and diagnostic criteria of sleep-related hypermotor epilepsy. Neurology. 2016 May 10;86(19):1834-1842.

Question #

298 ADULT NEUROLOGY**CORE KNOWLEDGE****Treatment/Management**

In this patient, treatment of status epilepticus should begin on scene with EMS administering intranasal or intramuscular midazolam. Non-IV benzodiazepines can abort status epilepticus in 80% of patients, and intranasal or intrabuccal midazolam is recommended.

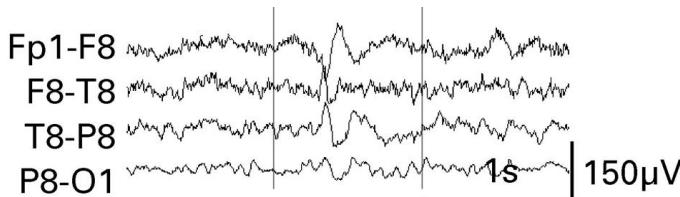
Trinka E, Leitinger M. Management of status epilepticus, refractory status epilepticus and super refractory status epilepticus. *Continuum Lifelong Learning Neurol*. 2022 Apr;28(2):559–602.

308 NO SPECIFIED PATIENT AGE**CORE KNOWLEDGE****Neurophysiology**

This EEG shows a right anterior temporal sharp wave (phase reversal at the F8 electrode with a field through right temporal chain), consistent with an epileptiform discharge and indicating a propensity for seizures arising from that region. Epileptiform discharges are sharp, stand out from the background, and have a field in surrounding electrodes and after-going slow wave. Epileptiform discharges alone do not confirm a diagnosis of epilepsy; the patient must also have seizures.

Wicket waves are a normal finding sometimes mistaken for temporal lobe epileptiform discharges. They are characterized by an arciform morphology and no after-going slow wave. Vertex waves are normal parts of sleep architecture and consist of a sharply contoured wave that phase-reverses at the central vertex with a symmetric field in both hemispheres (in an otherwise normal brain). Generalized discharges are sharp/spike and slow waves that are seen across every electrode in a full head montage (not shown here).

Schomer D, Lopez de Silva F (eds). Niedermeyer's Electroencephalography: Basic Principles, Clinical Applications, and Related Fields. 7th ed. New York: Oxford University Press; 2018.



Question #

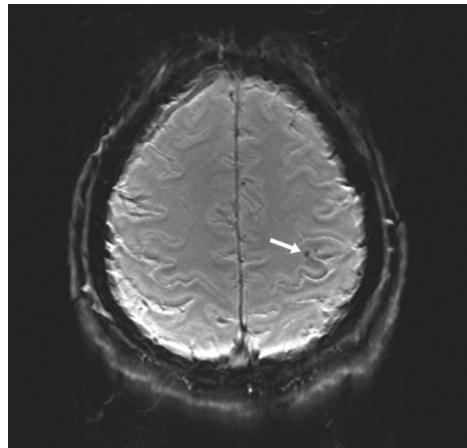
325 ADULT NEUROLOGY

Neuroanatomy

Small foci of magnetic susceptibility (arrow) is noted in the left precentral gyrus in the vicinity of the left-hand knob, most likely representing chronic hemorrhage. Chronic hemorrhage caused cortical irritability producing right finger clonic activity.

Automatisms and autonomic changes would be less likely to occur with a seizure focus involving the motor cortex, though they can be seen with seizures originating from both the temporal or insular cortices, with hand automatisms often occurring ipsilateral to the seizure focus.

Beniczky S, Tatum WO, Blumenfeld H, et al. Seizure semiology: ILAE glossary of terms and their significance. *Epileptic Disord*. 2022 Jun;24(3):447-495.



Question #

326 ADULT NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Treatment/Management**

The most recent combined estrogen and progestin contraceptive pills contain only 20 to 35 mg of ethynodiol diacetate (ED). The dose of EE in these agents is too low to ensure suppression of ovulation and serves mainly to provide proper cycle control, whereas the progestin component is responsible for the contraceptive mechanisms, which include inhibition of ovulation as well as increased viscosity of the cervical mucus and reduced endometrial suitability for ovum implantation.

Carbamazepine, phenobarbital, and phenytoin are potent enzyme inducers and can accelerate the metabolism of hormonal contraceptives, thus increasing the risk of unplanned pregnancy. Oxcarbazepine also has a lower potential to enzyme induction, but exerts a similar effect on hormonal contraceptives as carbamazepine.

Eslicarbazepine is the S-enantiomer of the active constituent of oxcarbazepine and also reduces the plasma concentrations of EE and progestins. A selective dose-dependent induction of progestin metabolism has been demonstrated for perampanel, an effect thought to be clinically significant at 12 mg.

Rufinamide is typically used in Lennox-Gastaut syndrome and would not be an optimal choice in this patient with focal epilepsy.

Available data, although sparse, suggest that neither valproate, gabapentin, levetiracetam, zonisamide, nor lacosamide affect the metabolism of combined estrogen and progestin contraceptive pills. Lamotrigine, however, may have a modest decreasing effect on the plasma level of the levonorgestrel while the EE compound is not affected.

Reimers A, Brodtkorb E, Sabers A. Interactions between hormonal contraception and antiepileptic drugs: Clinical and mechanistic considerations. *Seizure*. 2015 May;28:66-70.

Question

336 NO SPECIFIED PATIENT AGE**SUBSPECIALTY KNOWLEDGE****Treatment/Management**

In February 2016, the FDA approved brivaracetam as an add-on treatment to other medications used for partial-onset seizures in patients age 16 years and older with epilepsy. Significant reductions in partial-onset seizure frequency/week over placebo were demonstrated in the 50 mg/day group (12.8% reduction, $P = 0.025$).

Brivaracetam is a high-affinity synaptic vesicle protein 2A (SV2A) ligand; levetiracetam also binds to this same ligand. Lacosamide and eslicarbazepine are sodium channel antagonists. Perampanel is an AMPA receptor antagonist. The mechanism of action of rufinamide is unknown.

US Food and Drug Administration. FDA approves Briviant to treat partial onset seizures. <https://www.fda.gov/news-events/press-announcements/fda-approves-briviant-treat-partial-onset-seizures#:~:text=The%20U.S.%20Food%20and%20Drug,people%20to%20have%20recurring%20seizures>. Published February 2016. Accessed December 2021.

Biton V, Berkovic SF, Abou-Khalil B, et al. Brivaracetam as adjunctive treatment for uncontrolled partial epilepsy in adults: a phase III randomized, double-blind, placebo-controlled trial. *Epilepsia*. 2014 Jan;55(1):57-66.

346 BOTH/NEITHER**CORE KNOWLEDGE****Clinical Aspects of Disease**

Occasional hemiclonic seizures during sleep in a typically developing 10-year-old child with this EEG finding is consistent with self-limited epilepsy with centrotemporal spikes. Seizures in this syndrome are typically characterized by unilateral oral numbness or paresthesias, unilateral orofacial tonic or clonic contractions, speech arrest, sialorrhea, and hemiclonic activity. These seizures usually occur during sleep.

The EEG shows independent left and right centrotemporal spike and slow wave discharges that are more frequent during drowsiness. Background activity is normal with sleep augmented, biphasic, high-voltage, centrotemporal sharp and slow wave discharges, which can be bilateral.

Self-limited epilepsy with autonomic seizures (formerly known as Panayiotopoulos syndrome) occurs in typically developing children in a similar age range (although often younger), but the seizures are characterized by autonomic symptoms such as pallor, flushing, and vomiting. The interictal discharges on EEG may be, but not always, posterior when patients first present.

(continues)

Question

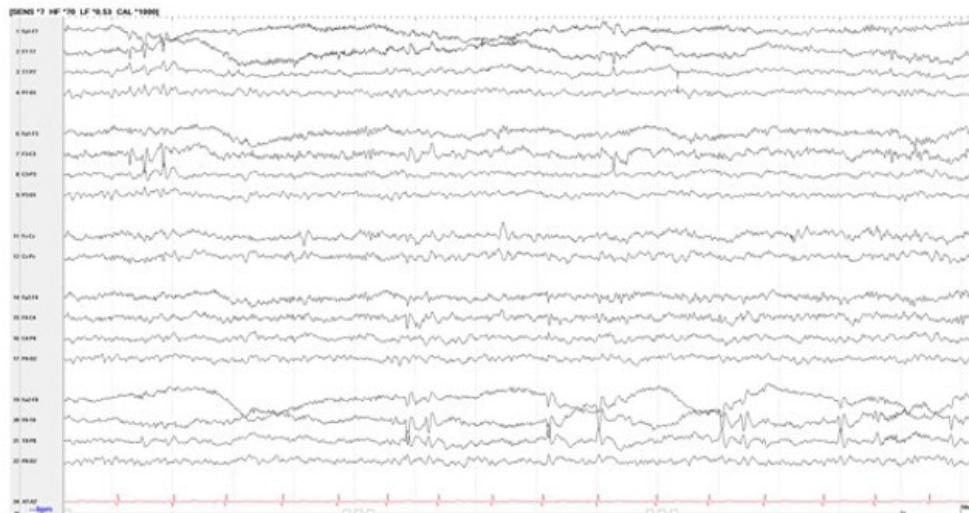
Photosensitive occipital lobe epilepsy also occurs in typically developing children in the same age range with photic-induced visual seizures. The EEG shows occipital spikes.

Sleep-related hypermotor (hyperkinetic) epilepsy occurs in typically developing children in the same age range, but the seizures are focal with hyperkinetic features. The awake EEG usually is normal.

Familial mesial temporal lobe epilepsy typically consists of focal aware seizures with *déjà vu*. The EEG is normal or shows temporal slowing or focal epileptiform discharges.

Specchio N, Wirrell EC, Scheffer IE, et al. International League Against Epilepsy classification and definition of epilepsy syndromes with onset in childhood: Position paper by the ILAE Task Force on Nosology and Definitions. *Epilepsia*. 2022 Jun;63(6):1398–1442.

Riney K, Bogacz A, Somerville E, et al. International League Against Epilepsy classification and definition of epilepsy syndromes with onset at a variable age: Position statement by the ILAE Task Force on Nosology and Definitions. *Epilepsia*. 2022 Jun;63(6):1443–1474.



Question

355 NO SPECIFIED PATIENT AGE**CORE KNOWLEDGE****Treatment/Management**

Kidney stones can be an adverse effect of either zonisamide or topiramate. Both drugs are carbonic anhydrase inhibitors, which can lead to metabolic acidosis, hypercalciuria, hypocitraturia, and elevation of urinary pH, all of which are favorable to kidney stone formation.

French JA, Gazzola DM. Antiepileptic drug treatment: new drugs and new strategies. *Continuum Lifelong Learning Neurol*. 2013 Jun;19(3):643–655.

384 PEDIATRIC NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Neuropathology**

Voltage-gated sodium channels initiate action potentials in brain neurons, and sodium channel blockers are used in therapy of epilepsy. Mutations in sodium channels are responsible for genetic epilepsy syndromes with a wide range of severity, and the NaV1.1 channel encoded by the SCN1A gene is the most frequent target of mutations. Complete loss-of-function mutations in NaV1.1 cause severe myoclonic epilepsy of infancy (Dravet syndrome), characterized by severe intractable epilepsy and comorbidities of ataxia and cognitive impairment. Antiseizure medications in which the sodium channel is the primary mechanism of action should be avoided when treating this disorder.

Catterall WA, Kalume F, Oakley JC. NaV1.1 channels and epilepsy. *J Physiol*. 2010 Jun 1;588(Pt 11):1849–1859.

394 PEDIATRIC NEUROLOGY**Treatment/Management**

This patient's presentation is consistent with infantile epileptic spasms syndrome (IESS), formerly known as West syndrome but which also includes infantile spasms without hypsarrhythmia, which is the EEG pattern described here. First-line treatment after a new diagnosis of IEES in a child without tuberous sclerosis should be with adrenocorticotrophic hormone (ACTH) or high-dose prednisone/prednisolone.

In an infant with tuberous sclerosis, first-line treatment is vigabatrin. Clonazepam, lamotrigine, and topiramate have little evidence of efficacy. Pyridoxine (vitamin B6) is effective only in the rare circumstance of pyridoxine-responsive epilepsy.

Grinspan AM, Knupp KG, Patel AD, et al. Comparative effectiveness of initial treatment for infantile spasms in a contemporary US cohort. *Neurology*. 2021 Sep 20;97(12):e1217–e1228.

Question #

6 NO SPECIFIED PATIENT AGE**CORE KNOWLEDGE****Neuroscience and Mechanism of Disease**

Corticobasal degeneration is a sporadic disorder; cases previously thought to be familial have now been reclassified as frontotemporal dementia. Dentatorubral-pallidoluysian atrophy and spinocerebellar ataxias are autosomal dominant. Friedreich ataxia is usually autosomal recessive.

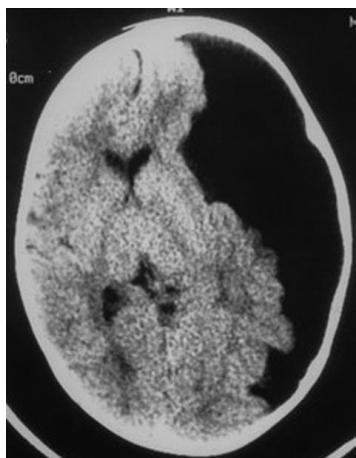
Ellison DW, Love S (eds). *Neuropathology: A Reference Text of CNS Pathology*. 3rd ed. San Francisco: Elsevier; 2013.

10 PEDIATRIC NEUROLOGY**Neuroimaging**

The large collection of CSF on the left side of the image represents an arachnoid cyst. The medial part of the Sylvian fissure is "box" shaped. The larger hemicranium proves long-standing underlying pathology.

Chronic subdural hematoma and subdural effusion would have a flattening effect on the sulci. Hemimegalencephaly is a parenchymal malformation with an abnormal enlargement of a hemisphere, not present in this study.

Jhaveri MD, Salzman KL, Osborn AG (eds). *Diagnostic Imaging: Brain*. 4th ed. Philadelphia: Elsevier; 2016.

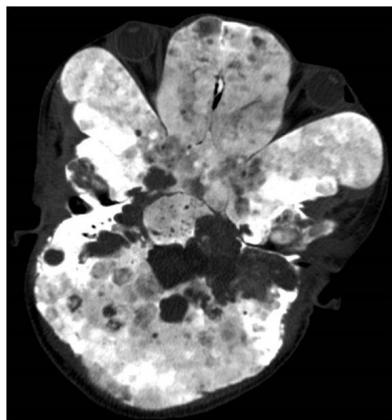


Question #

24 ADULT NEUROLOGY**Neuroimaging**

Polyostotic fibrous dysplasia can be part of McCune-Albright syndrome, with associated multiple café-au-lait spots and endocrine hyperfunction (such as precocious puberty). In neurofibromatosis type 1, bony erosions develop due to compression by adjacent neurofibromas and schwannomas, but hyperostosis is not seen. Multiple myeloma and osteosarcoma do not produce the type of lesions seen here.

Bousson V, Rey-Jouvin C, Laredo JD, et al. Fibrous dysplasia and McCune-Albright syndrome: imaging for positive and differential diagnoses, prognosis, and follow up guidelines. Eur J Radiol. 2014 Oct;83(10):1828-1842.

**30 ADULT NEUROLOGY****Neuroscience and Mechanism of Disease**

The most common cause of familial ALS is a hexanucleotide intronic repeat expansion (GGGGCC) n in the *C9orf72* gene on chromosome 9. Pertinent to this case, the mutation also causes familial frontotemporal dementia (FTD), a disorder with an autosomal dominant inheritance pattern. About 20% of people with ALS will also develop FTD.

SOD1, *FUS*, and TDP-43 mutations are associated with familial ALS but not with frontotemporal dementia. Androgen receptor repeat expansion causes bulbospinal atrophy or Kennedy disease, a form of motor neuron disease. However, Kennedy disease does not have upper motor neuron features or associated dementia.

Stavros K. Genetic myopathies. Continuum Lifelong Learning Neurol. 2024 Feb;30(1): 119-132.

Gijsselinck I, Cruts M, Van Broeckhoven C. The genetics of *C9orf72* expansions. Cold Spring Harb Perspect Med. 2018 Apr 2;8(4):a026757.

Question

45 PEDIATRIC NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Treatment/Management**

This patient's history and clinical presentation is consistent with myoclonic epilepsy of infancy (Dravet syndrome), a disorder associated with pathogenic variants in the *SCN1A* gene. The disorder is autosomal dominant, and the phenotype is caused by a haploinsufficiency of the specific sodium channel subunit encoded by *SCN1A*.

Features of Dravet syndrome include multiple seizure types, onset younger than age 1 year, prolonged febrile or afebrile generalized tonic-clonic seizures, hemiclonic seizures, and myoclonic seizures. Initial development is normal, but cognition becomes impaired over time.

Individuals with pathogenic variants in the *SCN1A* gene can present with a number of different phenotypes, ranging from febrile seizures only, to febrile seizures plus (febrile seizures persisting past age 5), to myoclonic astatic epilepsy, to Dravet syndrome. Sodium channel blocking agents (including lamotrigine) may worsen seizures in *SCN1A*-associated epilepsies, and thus are generally contraindicated.

Cross JH, Caraballo RH, Nabbout R, et al. Dravet syndrome: treatment options and management of prolonged seizures. *Epilepsia*. 2019 Dec;60 Suppl 3:S39–S48.

57 PEDIATRIC NEUROLOGY**Clinical Aspects of Disease**

Glutaric acidemias comprise different disorders resulting in an increased urinary excretion of glutaric acid. Glutaric acidemia type 1 (GA1) is an autosomal recessive disorder of lysine, hydroxylysine, and tryptophan metabolism caused by deficiency of glutaryl-CoA dehydrogenase. It results in the accumulation of 3-hydroxyglutaric and glutaric acid.

Affected patients can present with brain atrophy, macrocephaly, and with acute dystonia secondary to striatal degeneration, usually triggered by an intercurrent childhood infection with fever between 6 and 18 months of age. GA1 can be suspected based on clinical presentation or neuroimaging findings. The typical widening of Sylvian fissures with microcephalic macrocephaly is suggestive of GA1.

Hedlund GL, Longo N, Pasquali M. Glutaric acidemia type 1. *Am J Med Genet C Semin Med Genet*. 2006 May 15;142C(2):86–94.

Question #

66 NO SPECIFIED PATIENT AGE**SUBSPECIALTY KNOWLEDGE****Treatment/Management**

Tuberous sclerosis complex is caused by dysregulation of the mTOR pathway. Principal clinical features include angiofibroma, shagreen patch, ungual fibroma, cortical dysplasia, subependymal giant cell astrocytoma (SEGA), cardiac rhabdomyoma, and angiolioma.

Rapamycin and everolimus are mTOR inhibitors that can be used for SEGA, asymptomatic renal angiomyolipoma >3 cm, and moderate-to-severe or rapidly progressive lung lymphangioleiomyomatosis. However, for renal angiomyolipoma with acute hemorrhage, embolization followed by corticosteroids should be considered first-line therapy. Everolimus also has an indication for refractory focal seizures in tuberous sclerosis, but not status epilepticus.

Rosser T. Neurocutaneous disorders. *Continuum Lifelong Learning Neurol.* 2018 Feb;24(1):96–129.

77 ADULT NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Treatment/Management**

Hypokalemic periodic paralysis (HPP) usually occurs after heavy exercise or carbohydrate intake, but spontaneous weakness can occur without triggers. The genetic mutations in either *CACNA1S* or *SCN4A* are inherited in an autosomal dominant manner. Muscle strength can be restored with gentle potassium supplementation. Medications that can be used to prevent recurrent attacks include acetazolamide, a potassium-sparing diuretic (such as triamterene and spironolactone), or a potassium supplement.

Statland JM, Fontaine B, Hanna MG, et al. Review of the diagnosis and treatment of periodic paralysis. *Muscle Nerve.* 2018 Apr;57(4):522–530.

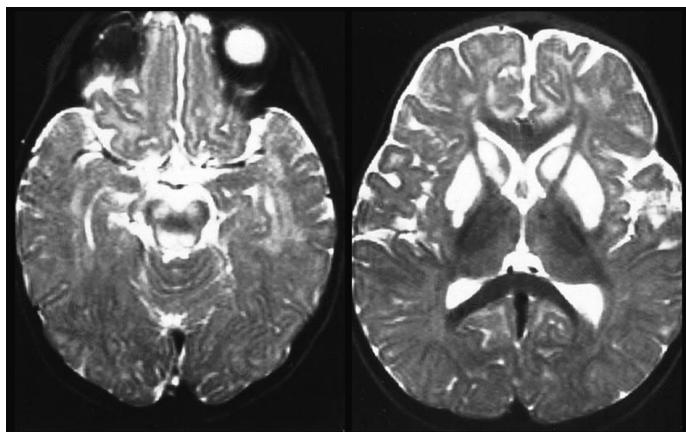
Question #

97 PEDIATRIC NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Neuroimaging**

The MRI scans are consistent with Leigh disease. The abnormal areas are seen as symmetric high signal intensity within the brainstem and basal ganglia. Such abnormalities are found in patients with metabolic acidosis and elevated serum lactate, including Leigh disease.

Herpes encephalitis usually involves the medial temporal lobe, insular cortex, and inferior frontal lobes, areas that are not involved in this case. There is also no brain swelling or mass effect, findings common in herpes. Carbon monoxide poisoning principally involves the globus pallidus but not the brainstem. Infarctions in sickle cell disease do not have such symmetry and are uncommon in the brainstem.

Arii J, Tanabe Y. Leigh syndrome: serial MR imaging and clinical follow-up. AJNR Am J Neuroradiol. 2000 Sep;21(8):1502-1509.



Question #

148 PEDIATRIC NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Treatment/Management**

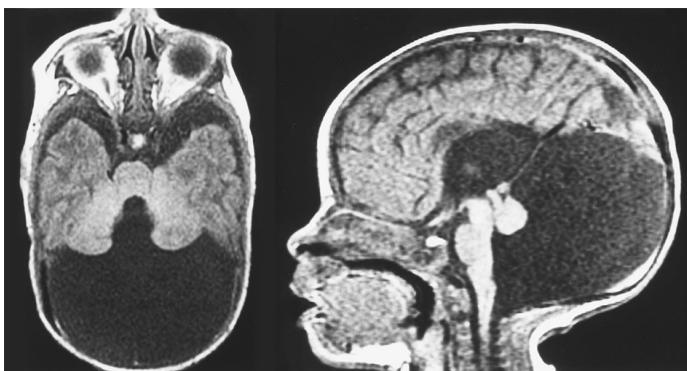
Glucose transporter type 1 deficiency syndrome (Glut1DS) is an autosomal dominant disorder characterized by deficiency of a protein required for glucose transport across the blood-brain barrier. In addition to poor growth and development, patients usually have seizures and dystonia. Low CSF glucose in the absence of hypoglycemia suggests the diagnosis and can be confirmed by genetic testing for *SLC2A1* gene pathogenic variants. Ketogenic diet is used to treat seizures in Glut1DS. The response could be prompt and dramatic.

Klepper J, Akman C, Armeno M, et al. Glut1 deficiency syndrome (Glut1DS): state of the art in 2020 and recommendations of the International Glut1DS Study Group. *Epilepsia Open*. 2020 Aug 13;53):354-365.

155 PEDIATRIC NEUROLOGY**CORE KNOWLEDGE****Neuroimaging**

Both images demonstrate the missing inferior vermis. Thus, the fourth ventricle connects with the cisterna magna, the hallmark of a Dandy-Walker malformation. The posterior fossa is enlarged.

Bvarkovich AJ, Raybaud C (eds). *Pediatric Neuroimaging*. 6th ed. Philadelphia, PA: Wolters Kluwer; 2018.



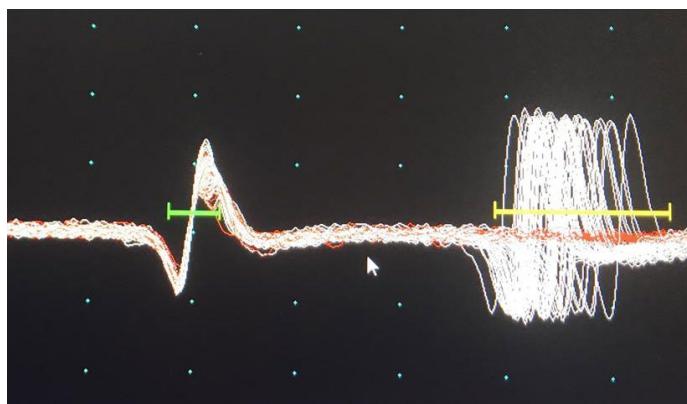
Question #

174 ADULT NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Diagnostic Procedures**

This patient's clinical picture is consistent with a neuromuscular junction disorder, with her EMG results as confirmation. Congenital or genetically determined myasthenia gravis can present during adulthood and be mistaken for "double seronegative" myasthenia gravis. Making the correct diagnosis is important as treatment differs significantly from that of autoimmune myasthenia gravis. Some forms of congenital myasthenia gravis can worsen with cholinesterase inhibitors. Immune suppression poses unnecessary risk.

Though mitochondrial disease can present with ptosis and proximal weakness, eye movements are usually affected and muscle weakness is not fatigable. In addition, mitochondrial DNA is only responsible for coding a small number of genes involved in mitochondrial function. Likewise, myotonic dystrophy causes ptosis without extraocular muscle abnormalities, but fatigable muscle weakness is not characteristic. Muscle biopsy and imaging studies are not helpful in diagnosing neuromuscular junction disorders.

Lorenzoni PJ, Ducci RD-P, Arndt RC, et al. Congenital myasthenic syndrome in a cohort of patients with 'double' seronegative myasthenia gravis. Arq Neuropsiquiatr. 2022 Jan;80(1): 69-74.



Question #

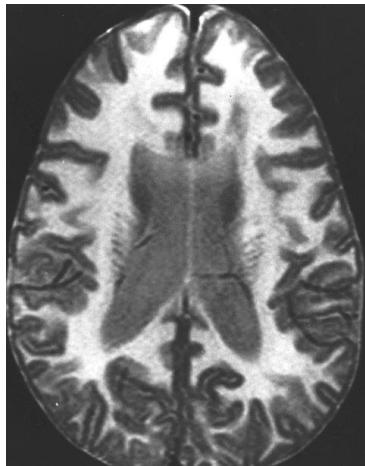
191 PEDIATRIC NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Clinical Aspects of Disease**

The MRI scan shows aspartoacylase-associated leukodystrophy (Canavan disease). The abnormality is the high signal intensity in the white matter that extends from the periventricular region to the cortex in a diffuse fashion, involving all of the white matter including the subcortical U fibers.

Periventricular leukomalacia is in the periventricular region in the frontal parietal region. Metachromatic leukodystrophy does not extend out into the subcortical U fibers, whereas adrenoleukodystrophy favors the occipital and parietal regions, sparing the frontal lobes in all but a small percentage of cases.

Adrenoleukodystrophy also tends to spare the subcortical U fibers. Krabbe disease features significant atrophy.

Barkovich AJ, Raybaud C (eds). Pediatric Neuroimaging. 6th ed. Philadelphia: Wolters Kluwer; 2019.



Question #

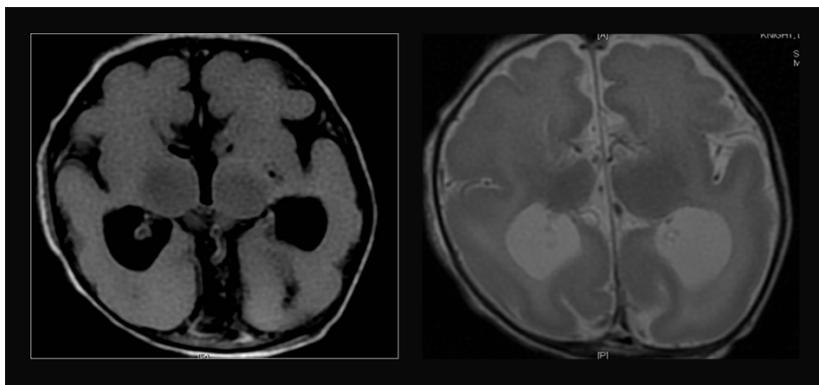
210 PEDIATRIC NEUROLOGY

CORE KNOWLEDGE

Neuroimaging

Lissencephaly is a set of neuronal migration disorders that are characterized by lack of sulcation and gyration, resulting in a "smooth" brain. Though migration abnormalities can be due to vascular compromise or in utero infections, when the abnormality is this extensive and symmetric, a genetic cause is more likely. Implicated genes include *LIS1* (also known as *PAFAH1B1*), *RELN*, *TUBA1A*, *NDE1*, *KATNB1*, *CDK5*, *ARX* and *DCX*.

Barkovich AJ, Raybaud C (eds). Pediatric Neuroimaging. 6th ed. Philadelphia, PA: Lippincott, Williams & Wilkins; 2018.



Question #

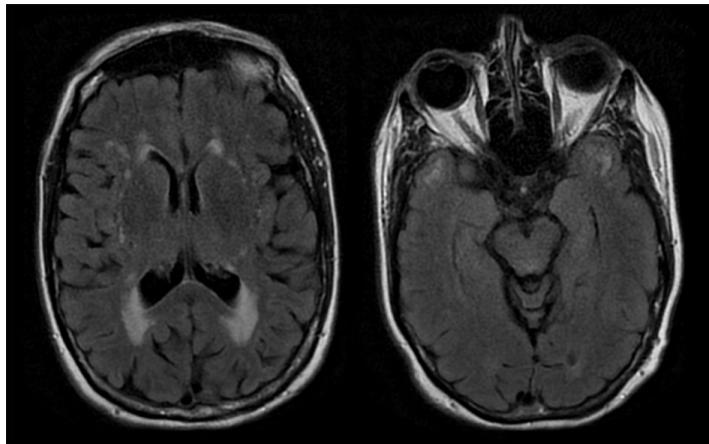
224 ADULT NEUROLOGY**Neuroscience and Mechanism of Disease**

This patient's episode of garbled speech suggests a transient ischemic event. Her history of migraines, family history of vascular dementia, and the white matter disease noted in the extreme capsule and anterior temporal poles are consistent with cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL). CADASIL is an inherited vascular disease caused by a pathogenic variant in the *NOTCH3* gene.

ABCD1 is associated with adrenoleukodystrophy, which would not feature stroke symptoms. *CSF1R* mutation is linked to adult-onset leukoencephalopathy with axonal spheroids and pigmented glia. Features include progressive cognitive/personality and movement deficits. *GFAP* mutations are associated with Alexander disease, which usually has progressive onset before age 2 years.

Mitochondrial encephalopathy, lactic acidosis, and stroke-like episodes (MELAS), a disorder that usually presents in children or young adults, is linked to *MT-TL1* pathogenic variants, though pathogenic variants in other mitochondrial genes may also cause MELAS.

Kim H, Lim Y-M, Lee E-J, et al. Clinical and imaging features of patients with cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy and cysteine-sparing NOTCH3 mutations. PLoS One. 2020 Jun 18;15(6):e0234797.



Question #

249 ADULT NEUROLOGY**Treatment/Management**

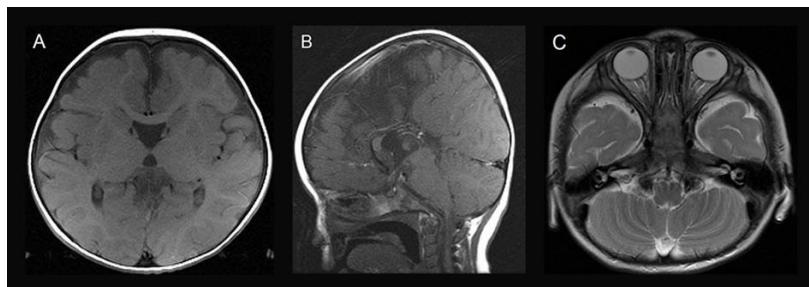
This patient has ALS. The FDA recently approved tofersen for the treatment of ALS due to *SOD1* mutations. Tofersen is an antisense oligonucleotide to *SOD1*. Other medications for additional genetic cases of ALS are in development, but no other medications are currently approved.

Izenberg A. Amyotrophic lateral sclerosis and other motor neuron diseases. *Continuum Lifelong Learning Neurol*. 2023 Oct;129(5):1538–1563.

267 PEDIATRIC NEUROLOGY**Neuroimaging**

The syndrome of septo-optic dysplasia (de Morsier syndrome) consists of hypoplasia of the optic nerves and hypoplasia or absence of the septum pellucidum. Clinical presentation may include nystagmus and diminished visual acuity. Approximately two thirds of affected patients will also have hypothalamic-pituitary dysfunction. This patient's MRI scans demonstrate absence of the septum pellucidum, hypoplasia of the corpus callosum, and hypotelorism (closely set eyes).

Barkovich AJ, Raybaud C (eds). *Pediatric Neuroimaging*. 6th ed. Philadelphia, PA: Wolters Kluwer; 2018.



Question #

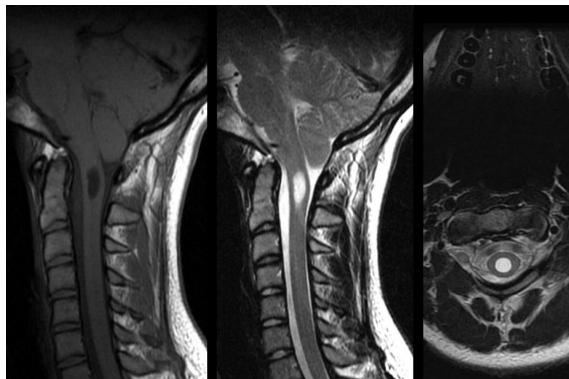
288 ADULT NEUROLOGY**CORE KNOWLEDGE****Clinical Aspects of Disease**

The images show cerebellar tonsillar ectopia (approximately 1 cm below the foramen magnum) with an associated cervical syrinx, findings consistent with Chiari type I malformation. The contents of the syrinx correspond to CSF (T1 hypointense and T2 hyperintense). The lesion has distinct margins and displaces rather than infiltrates the adjacent spinal cord.

Pilocytic astrocytomas occur in the posterior fossa and area characterized by a nodule accompanied by a large cyst. The peak age of onset is 10 to 12 years.

Basilar invagination refers to narrowing of the foramen magnum due to upward migration of the top of C2. Multiple sclerosis causes demyelinating lesions of the brain and spinal cord and is not associated with tonsillar ectopia. Chordomas are tumors of notochord remnants that most often occur in the clivus and sacrococcygeal regions.

Ropper AH, Samuels MA, Klein JP, et al (eds). Adams and Victor's Principles of Neurology. 11th ed. New York: McGraw-Hill Education; 2019.



Question

297 NO SPECIFIED PATIENT AGE**SUBSPECIALTY KNOWLEDGE****Neuroscience and Mechanism of Disease**

The histopathologic hallmark of Alexander disease is the presence of profuse numbers of Rosenthal fibers. Rosenthal fibers are composed of densely compacted glial intermediate filaments made of glial fibrillary acidic protein (GFAP). A large percentage of patients with Alexander disease have a mutation in the GFAP gene, which leads to an altered protein with toxic gain of function.

Ellison DW, Love S (eds). *Neuropathology: A Reference Text of CNS Pathology*. 3rd ed. San Francisco: Elsevier; 2013.

Messing A, Goldman JE, Johnson AB, Brenner M. Alexander disease: new insights from genetics. *J Neuropathol Exp Neurol*. 2001;60:563–573.

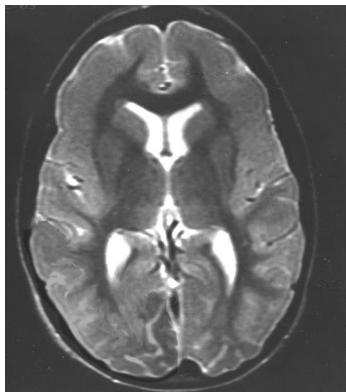
Brenner M, Johnson AB, Boespflug-Tanguy O, et al. Mutations in GFAP, encoding glial fibrillary acidic protein, are associated with Alexander disease. *Nat Genet*. 2001;27:117–120.

310 ADULT NEUROLOGY**Neuroimaging**

The axial T2-weighted image shows a symmetrical brain with normal-sized ventricles. The frontal lobe cortex is flat; the white matter, which is hypointense, does not show the normal interdigititation into the gray matter in this region. Thus, the cortex is thick. These findings are consistent with pachygryria. Such an abnormality develops during the period of neuronal radial migration, occurring during the second trimester.

Raybaud C, Widjaja E. Development and dysgenesis of the cerebral cortex: malformations of cortical development. *Neuroimag Clin N Am*. 2011; 21:483–543.

Zimmerman RA, Bilaniuk LT. Pediatric central nervous system. In: Stark DD, Bradley WG (eds). *Magnetic Resonance Imaging*. 2nd ed. St. Louis: Mosby; 1999.



Question #

319 NO SPECIFIED PATIENT AGE**CORE KNOWLEDGE****Treatment/Management**

Methylated O-6-methylguanine-DNA methyltransferase (MGMT) increases resistance to temozolomide. Patients with glioblastoma containing a methylated MGMT promotor benefit from temozolomide, but those who do not have a methylated MGMT promotor do not. The benefit is best among patients who receive temozolomide with radiation as initial treatment.

Colman H. Adult gliomas. *Continuum Lifelong Learning Neurol.* 2020 Dec;26(6):1452-1475.

Hegi ME, Diserens AC, Gorlia T, et al. MGMT gene silencing and benefit from temozolomide in glioblastoma. *N Engl J Med.* 2005 Mar 10;352(10):997-1003.

328 ADULT NEUROLOGY**Neuroscience and Mechanism of Disease**

This patient has fragile X-associated tremor/ataxia syndrome, an adult-onset progressive ataxia seen in premutation carriers for fragile X syndrome. Fragile X syndrome, described in his grandson, is caused by more than 200 CGG repeats in the *FMR1* gene.

Dentatorubral pallidoluysian atrophy (DRPLA) is caused by a CAG repeat expansion in the *ATN1* gene. SCA3 (also known as Machado-Joseph disease) is caused by CAG repeat expansion in the *ATXN2* gene. Spinocerebellar ataxia type 6 is caused by a CAG repeat in the *CACNA1A* gene.

Rosenthal LS. Neurodegenerative cerebellar ataxia. *Continuum Lifelong Learning Neurol.* 2022 Oct 1;28(5):1409-1434.

Question #

330 PEDIATRIC NEUROLOGY**Contemporary Issues**

The decision to perform genetic testing in a minor at risk for genetic disease should include several considerations. According to the AMA Code of Medical Ethics, diagnostic testing should be offered "when the child is at risk for a condition for which effective measures to prevent, treat, or ameliorate it are available," but genetic testing should not be pursued when adult onset is expected and no effective measures are available to treat or ameliorate the disorder.

Parents' need to know for psychological reasons is not the primary consideration. While a child should be included in decision making regarding genetic testing for himself, at age 10 years he does not yet have decisional capacity. He might choose differently when an adult.

Cost/insurance coverage is one, but not the primary, consideration, as many sponsored testing programs are now available. When the adult patient's (in this scenario the father) genetic diagnosis is known, targeted testing of the child is unlikely to produce false-negative results.

AMA Code of Medical Ethics. Genetic Testing of Children. <https://code-medical-ethics.ama-assn.org/ethics-opinions/genetic-testing-children>. Accessed December 2024.

342 PEDIATRIC NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Clinical Aspects of Disease**

Hyperekplexia is the result of a mutation of the glycine receptor and presents during the neonatal period with an exaggerated startle and period of generalized rigidity and apnea.

Kernicterus is caused by hyperbilirubinemia resulting in damage to the basal ganglia and is characterized by abnormalities of tone and mental status. Nonketotic hyperglycinemia is an inborn error of glycine metabolism that results in a neonatal encephalopathy with myoclonus, seizures, and hypotonia.

Infantile epileptic spasms are characterized by sudden extension or flexion of the trunk with limb contraction or extension, lasting a few seconds. Spasms tend to occur in clusters but are considered seizures and have an electrographic correlate.

Sandifer syndrome refers to gastroesophageal reflux in an infant resulting in stiffening and back arching and is often accompanied by emesis; a diagnosis of GERD, however, would not explain this infant's hypertonia.

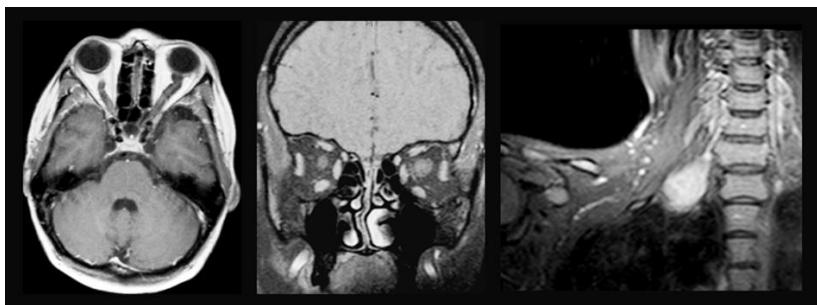
Arzimanoglou A, O'Hare A, Johnston M, et al (eds). Aicardi's Diseases of the Nervous System in Childhood. 4th ed. London: Mac Keith Press; 2018.

Question #

351 ADULT NEUROLOGY**Neuroimaging**

This patient's MRI scans demonstrate markedly enlarged optic nerves, the left greater than the right, typical of optic nerve glioma. The cervical plexus study demonstrates an ovoid homogeneous enhancing lesion typical of a nerve sheath tumor. The combination of peripheral nerve sheath tumor and optic nerve glioma is seen in conjunction with neurofibromatosis type 1 but is not a feature of the other disorders listed. Neurofibromatosis type 2 and schwannomatosis are not associated with optic nerve gliomas.

Jhaveri MD, Salzman KL, Osborn AG (eds). Diagnostic Imaging: Brain. 4th ed. Philadelphia: Elsevier; 2016.

**361 ADULT NEUROLOGY****CORE KNOWLEDGE****Neuroimaging, Treatment/Management**

The MRI scans show a diastematomyelia with an associated bony and cartilaginous or fibrous septation at L2-3, along with a low-lying tethered cord adherent at L4. These findings are consistent with a form of congenital dysraphism. Symptoms occur primarily because of stretching of the spinal cord, which is frequently present with this disorder. Detethering and removal of the septations frequently are effective.

Atlas SW (ed). Magnetic Resonance Imaging of the Brain and Spine. 5th ed. Philadelphia: Williams and Wilkins, 2017.



Question #

383 ADULT NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Clinical Aspects of Disease**

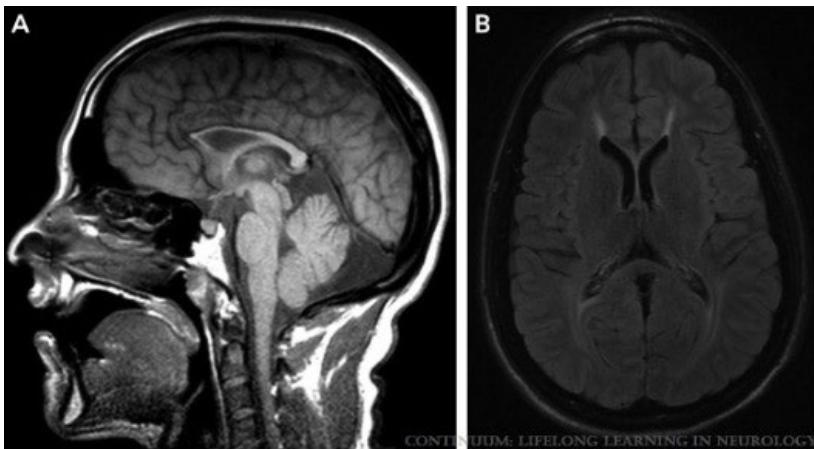
This patient's sagittal T1-weighted MRI scan shows a thin corpus callosum, and the axial FLAIR sequence view shows the ears of the lynx sign. Both findings, together with a clinical picture of progressive spastic paraparesis and onset of intellectual disability during childhood, are characteristic of autosomal recessive complex hereditary spastic paraparesis. Mutation of *SPG11* is the most frequent type of autosomal recessive hereditary spastic paraparesis.

MRI of the spinal cord is used to rule out other causes of spinal cord disorders. Careful review of the MRI scans may reveal volumetric reduction of the cervical and thoracic cord, which often escape the visual analysis.

The other disorders listed are not associated with thinning of the corpus callosum. In addition, adrenomyeloneuropathy and Pelizaeus-Merzbacher disease are leukodystrophies that show white matter abnormalities on FLAIR sequence imaging.

Fink JK. Hereditary myelopathies. *Continuum Lifelong Learning Neurol*. 2021 Feb;27(1):185–204.

da Graça FF, de Rezende TJR, Vasconcellos LFR, et al. Neuroimaging in hereditary spastic paraplegias: current use and future perspectives. *Front Neurol*. 2019 Jan 16;9:1117.



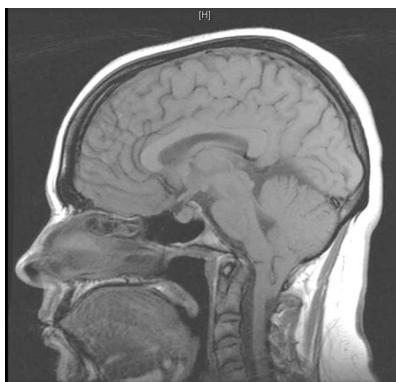
Question #

27 ADULT NEUROLOGY**CORE KNOWLEDGE****Neuroimaging**

The MRI scan shows descent of the cerebellar tonsils beneath the foramen magnum, characteristic of a Chiari type I malformation. The pituitary sella is normal. Sagittal sinus venous thrombosis can appear hyperintense on a noncontrast T1-weighted MRI scan, but this finding is not present here.

The Dandy–Walker malformation refers to agenesis or hypoplasia of the cerebellar vermis, cystic dilation of the fourth ventricle, and enlargement of the posterior fossa; these findings are not present on the scan. The visible portions of the third and fourth ventricle appear normal, without evidence of obstructive hydrocephalus.

Singh K, Mechtler LL, Klein JP. Imaging of spinal cord disorders. *Continuum Lifelong Learning Neurol*. 2016 Oct;22(5):1595–1612.

**42 ADULT NEUROLOGY****CORE KNOWLEDGE****Treatment/Management**

Carbamazepine or oxcarbazepine have the highest levels of evidence for pain control in trigeminal neuralgia while baclofen and lamotrigine may be considered useful second-line agents. The symptoms are less consistent with temporal arteritis which would typically be treated with prednisone.

Gronseth G, Cruccu G, Alksne J, et al. Practice parameter: the diagnostic evaluation and treatment of trigeminal neuralgia (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology and the European Federation of Neurological Societies. *Neurology*. 2008 Oct 7;71(15):1183–1190. Reaffirmed April 2024.

Robertson C. Cranial neuralgias. *Continuum Lifelong Learning Neurol*. 2021 Jun 1;27(3):665–685.

Question #

50 ADULT NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Diagnostic Procedures**

This patient has hemicrania continua, a strictly unilateral continuous headache disorder featuring exacerbations of pain accompanied by ipsilateral parasympathetic activation. Responsiveness to indomethacin is part of the diagnostic criteria.

Further neuroimaging is not likely to demonstrate a referable abnormality. Cluster headache, another trigeminal autonomic cephalgia, responds to high-flow oxygen and SC sumatriptan acutely.

Goadsby PJ. Indomethacin-responsive headache disorders. *Continuum Lifelong Learning Neurol.* 2024 Apr;30(2):488-497.

75 ADULT NEUROLOGY**Clinical Aspects of Disease**

Complex regional pain syndrome typically is associated with an injury as a trigger in which peripheral neuropathic and vasomotor symptoms develop and are not confined to the distribution of one peripheral nerve territory. Using the Budapest diagnostic criteria, patients must have symptoms and signs of each of the following: 1) hyperesthesia and/or allodynia; 2) temperature asymmetry and/or skin color changes; 3) edema and/or sweating changes; and 4) decreased range of motion and/or motor dysfunction (weakness, dystonia, tremor) and/or hair, nail, or skin changes.

Ferraro MC, O'Connell NE, Sommer C, et al. Complex regional pain syndrome: advances in epidemiology, pathophysiology, diagnosis, and treatment. *Lancet Neurol.* 2024 May;23(5):522-533.

96 ADULT NEUROLOGY**CORE KNOWLEDGE****Treatment/Management**

First-line treatments for diabetic polyneuropathy may include tricyclic antidepressants, serotonin norepinephrine reuptake inhibitors (SNRIs), gabapentinoids, and sodium channel blockers. Tricyclic antidepressants may aggravate urinary retention, making duloxetine a better choice for this patient. Opiates should be avoided due their high risk of dependence.

Price R, Smith D, Franklin G, et al. Oral and topical treatment of painful diabetic polyneuropathy: practice guideline update summary. Report of the AAN Guideline Subcommittee. *Neurology.* 2022 Jan 4;98(1):31-43.

Question #

112 NO SPECIFIED PATIENT AGE**Clinical Aspects of Disease**

This patient's attacks have the characteristic features of trigeminal autonomic cephalgias, which include cluster headache, paroxysmal hemicrania, hemicrania continua, and short-lasting unilateral neuralgiform headaches.

Short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT) and short-lasting unilateral neuralgiform headache attacks with cranial autonomic symptoms (SUNA) may be a single entity. All are unilateral and have autonomic symptoms ipsilateral to the headache such as conjunctival injection or lacrimation, nasal congestion or rhinorrhea, eyelid edema, forehead and facial sweating, and miosis or ptosis. The duration and frequency of headaches in these cephalgias overlap. However, only paroxysmal hemicrania and hemicrania continua respond to indomethacin.

Trigeminal neuralgia consists of an electric shooting pain usually lasting less than 2 minutes in the distribution of the trigeminal nerve. Nervus intermedius neuralgia is similar to trigeminal neuralgia except that the pain is primarily in the auditory canal.

Burish M. Cluster headache, SUNCT, and SUNA. *Continuum Lifelong Learning Neurol*. 2024 Apr;30(2):391-410.

Nahas SJ. Cranial neuralgias. *Continuum Lifelong Learning Neurol*. 2024 Apr;30(2):473-487.

Goadsby PJ. Indomethacin-responsive headache disorders. *Continuum Lifelong Learning Neurol*. 2024 Apr;30(2):488-497.

114 PEDIATRIC NEUROLOGY**Clinical Aspects of Disease**

New daily persistent headache is defined by the onset of a continuous headache for at least 3 months in the absence of any primary or secondary cause of headache. Nearly one third of patients experience this syndrome in association with an infection.

Robbins M. New daily persistent headache. *Continuum Lifelong Learning Neurol*. 2024 Apr;30(2):425-437.

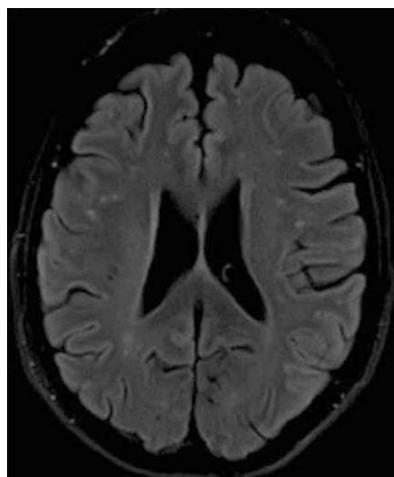
Question #

140 ADULT NEUROLOGY**CORE KNOWLEDGE****Neuroimaging**

A sizeable proportion of individuals with migraine will have scattered white matter hyperintensities on brain MRI. They are typically subcortical and frontal predominant.

Zhang W, Cheng Z, Fu F, et al. Prevalence and clinical characteristics of white matter hyperintensities in migraine: a meta-analysis. *Neuroimage Clin.* 2023;37:103312.

Image: Schramm SH, Tenhagen I, Jokisch M, et al. Migraine or any headaches and white matter hyperintensities and their progression in women and men. *J Headache Pain.* 2024 May 15;25(1):78.

**161 ADULT NEUROLOGY****CORE KNOWLEDGE****Treatment/Management**

This patient presents with cluster headaches. Galcanezumab, a monoclonal antibody against calcitonin gene-related peptide, and verapamil are the preferred agents for preventive treatment.

Ergotamine is an acute treatment. Atenolol has little CNS penetration and is not recommended for headache prevention; imipramine, a tricyclic antidepressant, is more appropriate for migraine prophylaxis.

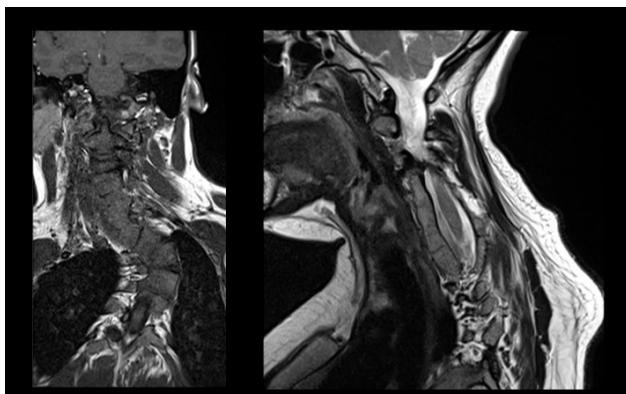
Goadsby PJ. Trigeminal autonomic cephalgias. *Continuum Lifelong Learning Neurol.* 2012 Aug;18(4):883-895.

Question #

185 ADULT NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Neuroimaging**

Incomplete segmentation of the cervical spine is classified as Klippel–Feil syndrome. This patient's MRI scans demonstrate hypoplastic to absent intervertebral disks and hypoplastic adjacent vertebral bodies at multiple levels. The incomplete segmentation is also demonstrated in the coronal view. These changes are congenital and can be seen in both an autosomal dominant or recessive pattern. The patient also has marked scoliosis.

Grimme JD, Costillo M. Congenital anomalies of the spine. Neuroimaging Clin N Am. 2007;17:1-16.

**211 NO SPECIFIED PATIENT AGE****CORE KNOWLEDGE****Treatment/Management**

A migraine attack persisting for longer than 3 days defines status migrainosus. Dihydroergotamine (DHE) 0.5 to 1.0 mg is an effective agent for terminating a migraine attack when administered intravenously, but it is necessary to pretreat with an IV antiemetic to block further drug-induced nausea. Nausea is less likely to complicate therapy with DHE when administered IM or SC.

The combination of prochlorperazine and DHE has been demonstrated to be effective in the treatment of status migrainosus. DHE is contraindicated when triptans have been used within the previous 24 hours.

While sumatriptan is an excellent acute migraine therapy, triptans overall are not likely to be effective so late into an attack, when central sensitization of sensory structures has taken place.

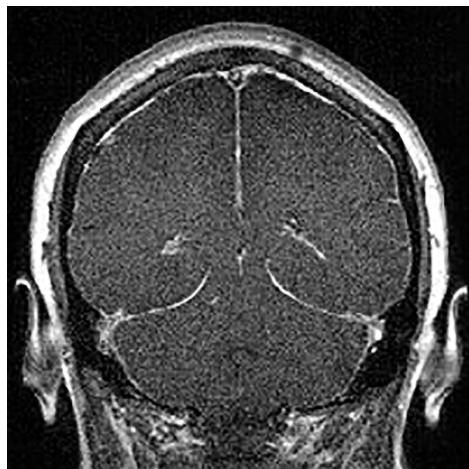
Orr SL, Friedman BW, Christie S, et al. Management of adults with acute migraine in the emergency department: the American Headache Society evidence assessment of parenteral pharmacotherapies. Headache. 2016 Jun;56(6):911–940.

Question #

248 ADULT NEUROLOGY**CORE KNOWLEDGE****Clinical Aspects of Disease**

Clinically, this patient's symptoms are most consistent with spontaneous intracranial hypotension. The MRI scan shows diffuse dural enhancement typical for this disorder. In this case, the hypotension most likely resulted from a tear in the spinal dura.

Green MW. Secondary headaches. *Continuum Lifelong Learning Neurol*. 2012 Aug;18(4):783–795.

**268 ADULT NEUROLOGY****SUBSPECIALTY KNOWLEDGE****Clinical Aspects of Disease**

SUNCT/SUNA (under the umbrella diagnosis SUNHA) is a relatively rare trigeminal autonomic cephalgia (TAC) marked by short-lasting attacks of lateralized severe head pain associated with prominent cranial autonomic features and often triggered by cutaneous stimuli.

Chronic paroxysmal hemicrania (CPH) is more common in women and is characterized by unilateral brief headaches that occur multiple times a day. The pain is usually localized around the eye, temple, and forehead and is often associated with autonomic symptoms, including lacrimation, ptosis, rhinorrhea, and facial flushing. CPH is exquisitely sensitive to indomethacin.

Goadsby PJ, Cittadini E, Cohen AS. Trigeminal autonomic cephalgias: paroxysmal hemicrania, SUNCT/SUNA, and hemicrania continua. *Semin Neurol* 2010;30(2):186–191.

Silberstein SD, Lipton RB, Dodick DW (eds). Wolff's Headache and Other Head Pain. 8th ed. New York: Oxford University Press; 2008.

Question #

287 ADULT NEUROLOGY**CORE KNOWLEDGE****Treatment/Management**

This patient has migraine without aura that has progressed to chronic migraine in the setting of acute medication overuse. This disorder is defined as a headache >15 days/month, plus regular medication overuse for at least 3 months of one or more analgesic drugs, ergotamine, triptans, and/or opioids. The standard of care is initiating a migraine preventive therapy while weaning the implicated acute treatment in medication overuse.

Starting a triptan would be reasonable but not as an action in isolation. Stopping the current combination analgesic alone is not as effective compared to initiating preventive therapy along with discontinuing the analgesic. Oxycodone should be avoided due to risk of dependence.

Rizzoli P. Medication-overuse headache. *Continuum Lifelong Learning Neurol*. 2024 Apr;30(2):379–390.

320 ADULT NEUROLOGY**CORE KNOWLEDGE****Treatment/Management**

This patient has a unilateral headache with autonomic symptoms. The duration of pain is most consistent with a cluster headache attack. Cluster headache responds to oxygen, typically 100% via nonrebreathing mask at 10 to 15 L/min for 20 minutes. In some patients, oxygen is completely effective at aborting an attack if taken when the pain is at maximum intensity, whereas in others, the attack is only delayed for minutes to hours rather than completely alleviated.

Sumatriptan and dihydroergotamine are effective in cluster headache attacks but carry risk for patients with coronary artery disease. Verapamil is effective for prophylaxis but not for a cluster headache attack acutely. Propranolol is effective in the prevention of migraine but not cluster headache. Indomethacin is the treatment of choice for paroxysmal hemicrania, which is shorter in duration than cluster headache and more common in women.

Nahas SJ. Cluster headache and other trigeminal autonomic cephalgias. *Continuum Lifelong Learning Neurol*. 2021 Jun;27(3):633–651.

Question #

345 PEDIATRIC NEUROLOGY**CORE KNOWLEDGE****Clinical Aspects of Disease**

Headache, increasing head circumference, nausea, and vomiting are common manifestations of obstructive hydrocephalus. Aqueductal stenosis, while congenital, may be asymptomatic or lead to an insidious presentation and is the most common cause of congenital hydrocephalus. Head size that is >97th percentile in a 3-year-old child supports this condition has been longstanding.

Headaches in patients with brain tumors are of variable intensity. Morning vomiting is suggestive of hydrocephalus and truncal ataxia of a midline posterior fossa tumor.

Swaiman AF, Ashwal S, Ferriero DM, et al (eds). Swaiman's Pediatric Neurology. Principles and Practice. 6th ed. Philadelphia: Elsevier; 2017.

365 ADULT NEUROLOGY**CORE KNOWLEDGE****Treatment/Management**

This patient's headaches, by description, are consistent with tension-type headaches. Though no medication is absolutely free of maternal and fetal safety concerns, acetaminophen is the first-line medication for tension headaches in pregnancy.

NSAIDs are generally avoided in pregnancy, though these may have a safer window limited to the second trimester only. Butalbital and codeine are not first-line medications for tension-type headache attacks in pregnancy or at other times. Though it may be relatively safe for intermittent use during pregnancy, sumatriptan use should be restricted to migraine or cluster headache.

Pavlovic JM. Headache in women. Continuum Lifelong Learning Neurol. 2021 Jun;27(3):686–702.

Question #

367 ADULT NEUROLOGY**Neuroscience and Mechanism of Disease**

This patient experienced a lacunar infarct leading to hemibody sensory loss, which localizes to the right thalamus in the ventroposterolateral (body sensory) nucleus. A stroke in this location is the most common risk factor for central post-stroke pain syndrome.

The cingulate gyrus is involved in pain modulation. The lateral medulla contains ipsilateral trigeminal and contralateral spinothalamic projections, and the parietal lobe is the primary somatosensory cortex.

Rosner J, de Andrade DC, Davis KD, et al. Central neuropathic pain. Nat Rev Dis Primers. 2023 Dec 21;9(1):73.

389 ADULT NEUROLOGY**CORE KNOWLEDGE****Treatment/Management**

Calcitonin gene-related peptide (CGRP) antagonists are a class of medications that specifically treat migraine. Eptinezumab, fremanezumab, and galcanezumab are monoclonal antibodies targeting CGRP to prevent migraine. Erenumab is a monoclonal antibody against the CGRP receptor and also used to prevent migraine. Ubrogepant is a CGRP receptor antagonist and of the options listed, the only one used for the acute treatment of migraine attacks.

Edvinsson L, Haanes KA, Warfvinge K, et al. CRGP as the target of new migraine therapies —successful translation from bench to clinic. Nat Rev Neurol. 2018 Jun;14(6):338–350.

Question #

17 PEDIATRIC NEUROLOGY**Clinical Aspects of Disease**

Both paroxysmal kinesigenic and nonkinesigenic dyskinesia frequently present in early childhood and are differentiated by whether the attack is precipitated by motor activity. These disorders are frequently misdiagnosed as epilepsy or tics. Sporadic attacks rule out Sydenham chorea, and this patient does not meet the criteria for Tourette syndrome. Juvenile Huntington disease usually presents with bradykinesia and rigidity. Self-limited epilepsy of childhood with centrotemporal spikes (SeLECTS) would be expected to demonstrate abnormalities on EEG.

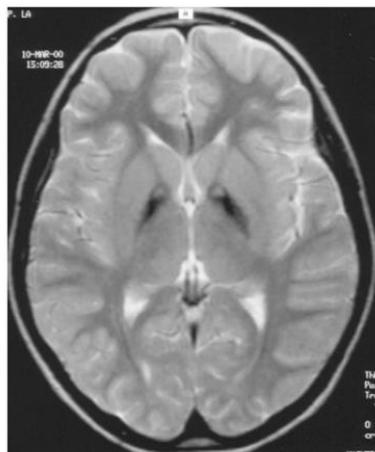
Swaiman AF, Ashwal S, Ferriero DM, et al (eds). Swaiman's Pediatric Neurology. Principles and Practice. 6th ed. Philadelphia: Elsevier; 2017.

23 PEDIATRIC NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Neuroimaging**

The MRI scan demonstrates a characteristic "eye of the tiger" sign with low T2 signal centered in a high T2 signal area. The characteristic dystonic movements in pantothenate-kinase-2 associated neurodegeneration (PKAN2) may follow an initial period of apparent spasticity. Oromandibular dystonia is prominent. In children, Huntington disease presents with prominent dystonic features rather than chorea, but the MRI findings usually show caudate atrophy. Although girls with Rett syndrome will lose purposeful movements of their hands and have progressive gait disturbance, dystonia is not a prominent feature. Patients with dopa-responsive dystonia often have early findings suggestive of spasticity, progressing to dystonia, but typically have normal MRI findings.

Swaiman AF, Ashwal S, Ferriero DM, et al (eds). Swaiman's Pediatric Neurology. Principles and Practice. 6th ed. Philadelphia: Elsevier; 2017.

Arzimanoglou A, O'Hare A, Johnston M, et al (eds). Aicardi's Diseases of the Nervous System in Childhood. 4th ed. London: Mac Keith Press; 2018.



Question #

35 ADULT NEUROLOGY**CORE KNOWLEDGE****Treatment/Management**

Primidone and propranolol are indicated for treatment of essential tremor, but because this patient has a history of asthma and congestive heart failure, a beta-blocker such as propranolol is contraindicated. The other medications listed (amantadine, carbidopa/levodopa, propranolol, baclofen) are not indicated for essential tremor.

Louis ED. Tremor. Continuum Lifelong Learning Neurol. 2019 Aug;25(4):959–975.

48 PEDIATRIC NEUROLOGY**CORE KNOWLEDGE****Treatment/Management**

This patient has had two motor tics and one vocal tic for more than a year, features that meet the criteria for a diagnosis of Tourette syndrome. Guanfacine and risperidone can be considered; however, referral to cognitive behavioral intervention for tics (CBIT) is considered first-line management. CBIT can be particularly beneficial for patients with a premonitory urge, as described here.

This patient's presentation is not consistent with functional neurologic disorder with psychogenic tics.

Nilles C, Hartmann A, Roze E, et al. Tourette syndrome and other tic disorders of childhood. Handb Clin Neurol. 2023;196:457–474.

52 ADULT NEUROLOGY**Neuroscience and Mechanism of Disease**

Rasagiline is an inhibitor of centrally active monoamine oxidase-B, resulting in increased half-life of endogenous or exogenous dopamine in the brain. Rasagiline has been demonstrated to reduce off time in Parkinson disease when given in combination with levodopa. As monotherapy in early Parkinson disease, rasagiline delays the time for initiating levodopa therapy.

Zesiewicz TA. Parkinson disease. Continuum Lifelong Learning Neurol. 2019 Aug;25(4):896–918.

Question #

58 ADULT NEUROLOGY**CORE KNOWLEDGE****Clinical Aspects of Disease**

Lance–Adams syndrome is an action-induced myoclonus that may occur after anoxic brain injury. Symptom onset can be delayed by days to weeks following the injury. There can be a mix of positive and negative myoclonus.

Myoclonic status epilepticus can occur following severe anoxic injury in unresponsive patients. Hemiballismus or hemichorea may occur after a stroke or a hyperglycemic or other metabolic episode. Holmes tremor is a mixed rest and action tremor that occurs after midbrain injury, often vascular.

Gupta HV, Caviness JN. Post-hypoxic myoclonus: current concepts, neurophysiology, and treatment. *Tremor Other Hyperkinet Mov (NY)*. 2016 Sep 17;6:409.

67 ADULT NEUROLOGY**CORE KNOWLEDGE****Neuroanatomy**

Ballism is associated with discrete lesions in the subthalamic nucleus. The dyskinesia occurs contralateral to the lesion and is associated with hypotonia. As the hemiballismus improves, the movements are more like chorea. The subthalamic nucleus modulates (suppresses) ipsilateral basal ganglionic activity, which in turn modulates cortical motor outflow to the contralateral effector muscles.

Blumenfeld H. *Neuroanatomy Through Clinical Cases*. 3rd ed. Sunderland: Sinauer Associates; 2021.

71 ADULT NEUROLOGY**CORE KNOWLEDGE****Clinical Aspects of Disease**

This patient has restless legs syndrome, a disorder that can be idiopathic or secondary to medications, systemic conditions such as iron deficiency and renal insufficiency, or neurologic conditions such as peripheral neuropathy and spinal cord disease.

Because the patient has a normal neurologic examination, peripheral neuropathy and spinal cord disorder are unlikely, making assessment of serum vitamin B12 or MRI studies unnecessary.

Garcia-Malo C, Peralta SR, Garcia-Borreguero D. Restless legs syndrome and other common sleep-related movement disorders. *Continuum Lifelong Learning Neurol*. 2020 Aug;26(4):963–987.

Question #

84 ADULT NEUROLOGY**CORE KNOWLEDGE****Treatment/Management**

Suboptimal doses of carbidopa are a frequent cause of nausea and vomiting at the initiation of levodopa therapy. A dose of 75 to 150 mg of carbidopa per day is needed to saturate the peripheral aromatic amino acid decarboxylase enzyme to prevent peripheral side effects of levodopa. Decreasing the levodopa dose may reduce nausea and vomiting; however, it may also result in less symptomatic improvement and thus would not be the optimal choice.

Fang JY. Update on the medical management of Parkinson disease. *Continuum Lifelong Learning Neurol* 2010 Feb;16(1):96–109.

95 ADULT NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Diagnostic Procedures**

Orthostatic tremor is clinically characterized by profound instability or tremulousness in the legs with standing still that is relieved with walking or sitting. EMG reveals a very rapid (14– to 16-Hz) tremor, which can sound like a helicopter on bedside auscultation or EMG testing.

Louis ED. Diagnosis and management of tremor. *Continuum Lifelong Learning Neurol*. 2016 Aug;22(4):1143–1158.

102 PEDIATRIC NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Clinical Aspects of Disease**

This patient has benign paroxysmal torticollis of infancy (BPT), a benign movement disorder. Children typically present in the first 3 months of life with episodes that can last 30 minutes up to several days. During this time, irritability, pallor, nausea, or ataxia can be present, impacting the patient's behavior and/or demeanor. Patients are typically normal between episodes. Family history of migraine and/or hemiplegic migraine is often present. CACNA1A and SCN8A mutations have been associated with BPT but may not represent all cases. Family history of migraines can aid in the diagnosis, and alternate etiologies with MRI and EEG should be assessed.

BPT is often considered a migraine variant. Children with this disorder may be at risk for migraine and migraine variants in childhood and adolescence, such as cyclic vomiting syndrome or abdominal migraines. There is no increased risk for future development of Tourette syndrome, functional neurologic disorder, attention-deficit/hyperactivity disorder, or stereotypies.

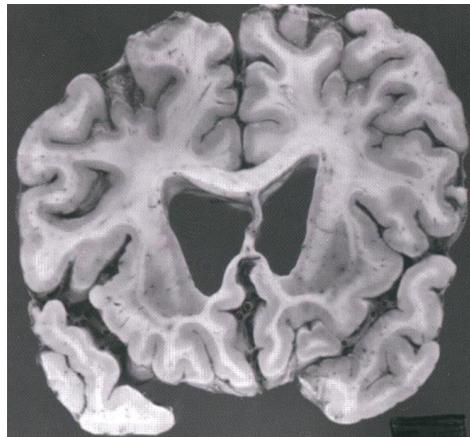
Yates T. Benign paroxysmal torticollis. *Handb Clin Neurol*. 2023;198:241–247.

Question #

117 ADULT NEUROLOGY**Neuroanatomy**

Both the caudate and the cerebral cortex are severely atrophied in this specimen, consistent with a diagnosis of Huntington disease.

Ropper AH, Samuels MA, Klein JP, et al (eds). Adams and Victor's Principles of Neurology. 11th ed. New York: McGraw-Hill Education; 2019.

**131 ADULT NEUROLOGY****SUBSPECIALTY KNOWLEDGE****Neuroscience and Mechanism of Disease**

In multiple-system atrophy, the preganglionic sympathetic neurons are lost in the intermediolateral horns of the spinal cord. However, the postganglionic sympathetic neuron is intact; thus, norepinephrine levels fail to rise when a patient stands, causing disabling orthostatic hypotension. This is why a cardiac scintigraphy MIBG scan is normal in multiple-system atrophy: it measures postganglionic sympathetic neuronal uptake, which is normal in multiple-system atrophy.

Coon EA, Cutsforth-Gregory JK, Benarroch EE. Neuropathology of autonomic dysfunction in synucleinopathies. *Mov Disord*. 2018 Mar;33(3):349–358.

Question #

146 ADULT NEUROLOGY**Clinical Aspects of Disease**

This patient's clinical presentation (slow vertical saccades with normal horizontal saccades, bilateral cogwheel rigidity, and a positive pull test) is consistent with progressive supranuclear palsy–Richardson syndrome (PSP-RS). A decreased midbrain to pons ratio (<0.5) in the sagittal plane seen on MRI is sensitive and specific for PSP. The pull test, also known as the retropulsion test, is a clinical test that measures a patient's ability to recover from a backward pull on the shoulders.

Pantelyat A. Progressive supranuclear palsy and corticobasal syndrome. *Continuum Lifelong Learning Neurol*. 2022 Oct;28(5):1364–1378.

154 ADULT NEUROLOGY**CORE KNOWLEDGE****Clinical Aspects of Disease**

The alpha-synucleinopathies, including Parkinson disease, dementia with Lewy bodies, and multiple-system atrophy, include a prodromal phase that precedes diagnosis by up to 15 years. Symptoms may include olfactory impairment, autonomic dysfunction, REM sleep behavior disorder, and anxiety or depression. Constipation, not diarrhea, is characteristic of the prodromal phase.

Dyskinesias occur late, particularly in patients treated with levodopa, whereas subtle bradykinesia may be present during the prodrome. Impulse control disorder can occur as a complication of treatment with dopaminergic agents.

Chahine LM. Prodromal α -synucleinopathies. *Continuum Lifelong Learning Neurol*. 2022 Oct;28(5):1268–1280.

Question #

175 ADULT NEUROLOGY**Diagnostic Procedures**

Patients with prodromal features of alpha-synucleinopathy should be followed longitudinally to evaluate for development of motor or other features to suggest Parkinson disease (PD), dementia with Lewy bodies, or multiple-system atrophy. Clinical history of dream reenactment confers increased risk (likelihood ratio = 2.3), but polysomnography-confirmed REM sleep behavior disorder confers the highest risk for development (likelihood ratio = 130), and it may be helpful to counsel the patient about risk as well as treatment. Other prodromal features such as constipation, orthostasis, and anosmia (among others) should be probed to obtain a full picture of prodromal risk and inform counseling.

Use of alpha-synuclein seeding assays in the CSF is currently only used in the research setting. DaTscan may be negative in prodromal or early PD, and its clinical use in this context is not yet well understood; therefore, routine use in prodromal PD is not recommended. Brain MRI is nonspecific. The most common PD-related pathogenic variants (*LRRK2*, *GBA*) increase risk but have variable penetrance and therefore would also be unlikely to contribute much at this stage.

Chahine LM. Prodromal α -synucleinopathies. *Continuum Lifelong Learning Neurol*. 2022 Oct;28(5):1268–1280.

Berg D, Postume RB, Adler CH, et al. MDS research criteria for prodromal Parkinson's disease. *Mov Discord*. 2015 Oct;30(12):1600–1611.

179 ADULT NEUROLOGY**Treatment/Management**

This patient has an acute dystonic reaction caused by dopamine receptor blockade by metoclopramide. This adverse effect is most likely to occur in younger patients within the first 48 hours of starting antidopaminergic medications. The appropriate therapy is an anticholinergic agent such as benztropine or diphenhydramine.

Ropper AH, Samuels MA, Klein JP, et al (eds). *Adams and Victor's Principles of Neurology*. 11th ed. New York: McGraw-Hill Education; 2019.

Question #

187 PEDIATRIC NEUROLOGY**CORE KNOWLEDGE****Treatment/Management**

This patient with cerebral palsy due to perinatal stroke presents with localized spasticity of the right arm. Botulinum toxin type A is an FDA-approved treatment for localized/segmental spasticity. Oral baclofen, diazepam, and intrathecal baclofen may be beneficial for generalized spasticity; however, given the localized nature of the patient's spasticity (limited to the right arm), botulinum toxin is preferred. Trihexyphenidyl is used in dystonia.

Quality Standards Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society; Delgado MR, Hirtz D, Aisen M, et al. Practice parameter: pharmacologic treatment of spasticity in children and adolescents with cerebral palsy (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society. *Neurology*. 2010 Jan 26;74(4):336–343. Reaffirmed July 2022.

188 NO SPECIFIED PATIENT AGE**CORE KNOWLEDGE****Neuroanatomy**

The head of the caudate nucleus lies between the lateral ventricle and the anterior limb of the internal capsule. The globus pallidus pars externa lies between the globus pallidus pars interna and the putamen. The putamen lies between the globus pallidus pars externa and the external capsule. The nucleus accumbens represents an area at the base of the forebrain where the caudate and putamen are in continuity. The claustrum is a thin sheet of neurons that lies just deep to the insula between the extreme and external capsules. It is reciprocally connected with wide areas of cortex.

Vanderah TW, Gould DJ (eds). Nolte's The Human Brain. 8th ed. Philadelphia: Elsevier; 2021.

199 ADULT NEUROLOGY**Treatment/Management**

Deep brain stimulation (DBS) is considered in patients with severely disabling motor symptoms despite advanced medical treatment. Of the patient characteristics listed (disabling motor "off state," freezing of gait with falls, tremor controlled with medication, severe cognitive impairment, desire for immediate symptom improvement), a disabling "off" state that occurs more than 20% of the day is a consideration for DBS.

Rawls AE. Surgical therapies for Parkinson disease. *Continuum Lifelong Learning Neurol*. 2022 Oct;28(5):1301–1313.

Chitnis S, Khemani P, Okun MS (eds). Deep Brain Stimulation: A Case-Based Approach. New York, NY: Oxford University Press; 2020.

Question #

203 ADULT NEUROLOGY**Treatment/Management**

Neurologic side effects have been reported in up to 40% of patients treated with amiodarone, at times associated with tremor, ataxia, peripheral neuropathy, malaise or fatigue, sleep disturbances, dizziness, and headaches. Beta-blockers, calcium channel blockers, and digoxin have not been implicated in drug-induced tremors.

Morgan JC, Kurek JA, Davis JL, et al. Insights into pathophysiology from medication-induced tremor. *Tremor Other Hyperkinet Mov (NY)*. 2017 Nov 22;7:442.

214 ADULT NEUROLOGY**Neuropathology**

This patient presents with mixed clinical features of progressive supranuclear palsy and corticobasal degeneration. These syndromes, along with Pick disease and frontotemporal dementia, are tauopathies characterized by abnormal deposits of tau proteins, Pick bodies, and ballooned neurons.

Lewy bodies are seen in synucleinopathies such as idiopathic Parkinson disease and Lewy body dementia. Glial cytoplasmic inclusions are also related to abnormalities in alpha-synuclein and seen in multiple-system atrophy. Neurofibrillary tangles are associated with Alzheimer disease. Bizarre astrocytes are seen in progressive multifocal leukoencephalopathy.

Greene P. Progressive supranuclear palsy, corticobasal degeneration, and multiple system atrophy. *Continuum Lifelong Learning Neurol*. 2019 Aug;25(4):919–935.

230 PEDIATRIC NEUROLOGY**CORE KNOWLEDGE****Clinical Aspects of Disease**

Vocal and motor tics are the hallmark characteristics of Tourette syndrome, and the transient ability to suppress them strongly supports tic disorder over any other abnormal movement. There is a higher incidence of attention-deficit/hyperactivity disorder and obsessive-compulsive disorder in patients with Tourette syndrome.

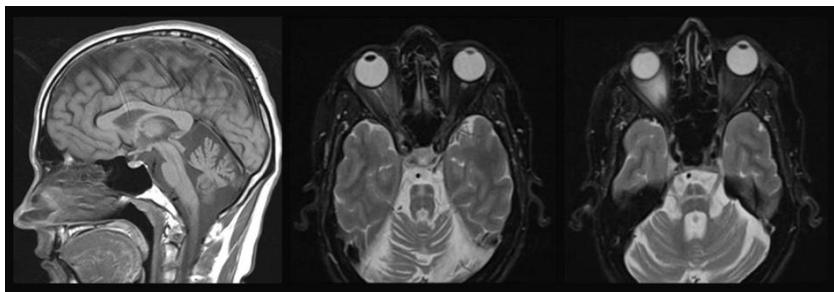
Swaiman AF, Ashwal S, Ferriero DM, et al (eds). *Swaiman's Pediatric Neurology. Principles and Practice*. 6th ed. Philadelphia: Elsevier; 2017.

Question #

237 ADULT NEUROLOGY**Neuroimaging**

The sagittal T1-weighted image shows a small pons and cerebellar atrophy. The axial T2-weighted images show the pons to be reduced in size with the so-called "hot cross buns" sign. This finding is supportive of the diagnosis of multiple-system atrophy

Watanabe H, Riku Y, Hara K, et al. Clinical and imaging features of multiple system atrophy: challenges for an early and clinically definitive diagnosis. *J Mov Disord.* 2018 Sep;11(3):107-120.

**242 NO SPECIFIED PATIENT AGE****Neuroanatomy**

All climbing fibers arise from the contralateral inferior olive nucleus and enter the cerebellum via the inferior cerebellar peduncle. All other afferent fibers to the cerebellum are mossy fibers.

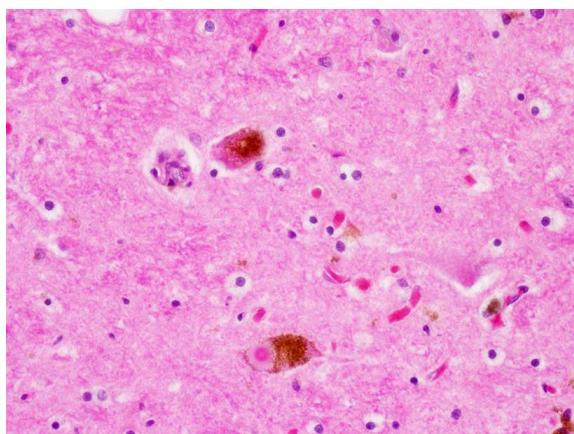
Campbell WW, Barohn RJ (eds). DeJong's The Neurologic Examination. 8th ed. Philadelphia: Wolters Kluwer; 2020.

Question #

252 ADULT NEUROLOGY**Neuropathology**

Parkinson disease is an alpha-synucleinopathy characterized by resting tremors, cogwheel rigidity, and bradykinesia. It may be preceded by a diagnosis of REM sleep behavior disorder. There is loss of the neurons in the grossly pigmented neuronal groups in the substantia nigra and locus ceruleus. Alpha-synuclein immunoreactive Lewy bodies are seen in these neurons histologically.

Ropper AH, Samuels MA, Klein JP, et al (eds). Adams and Victor's Principles of Neurology. 11th ed. New York: McGraw-Hill Education; 2019.

**261 PEDIATRIC NEUROLOGY****CORE KNOWLEDGE****Clinical Aspects of Disease**

Most children (and many adults) engage transiently in repetitive, purposeless movements. These movements have been variously described as motor rhythmias, rhythmic habit patterns, rhythmical stereotypies, habit spasms, mannerisms, and automatisms. The movements described are common in typically developing children, except for hand-wringing and knitting stereotypies, which are frequently seen in Rett syndrome.

Sandweiss AJ, Brandt VL, Zoghbi HY. Advances in understanding of Rett syndrome and MECP2 duplication syndrome: prospects for future therapies. Lancet Neurol. 2020 Aug;19(8):689–698.

Question #

270 ADULT NEUROLOGY**CORE KNOWLEDGE****Treatment/Management**

Deutetrabenazine, a catecholamine-depleting agent of the CNS, is FDA approved for the treatment of chorea in patients with Huntington disease. Its principal adverse effects are depression, suicide ideation, parkinsonism, and sedation. Patients with Huntington disease are at high risk for depression, which must be closely monitored when prescribing deutetrabenazine and similar agents like tetrabenazine and valbenazine. Antipsychotic dopamine-blocking agents such as haloperidol are also used for chorea in Huntington disease.

Ropper AH, Samuels MA, Klein JP, et al (eds). Adams and Victor's Principles of Neurology. 11th ed. New York: McGraw-Hill Education; 2019.

285 ADULT NEUROLOGY**CORE KNOWLEDGE****Treatment/Management**

Restless legs syndrome is characterized by an unpleasant sensation in the extremities that occurs before sleep and is associated with a strong urge to move the limbs. Movement provides temporary relief, but symptoms typically recur when movement stops.

Many patients also experience periodic limb movements during sleep, most commonly in association with iron deficiency, pregnancy, and metabolic dysfunction such as renal failure. The cause is unknown.

Medications reported to be beneficial include dopaminergics (eg, levodopa, bromocriptine, pramipexole, and pergolide), gabapentin and pregabalin, opiates (eg, codeine, propoxyphene), and benzodiazepines (clonazepam, diazepam, triazolam). Anticholinergics and all serotonin reuptake inhibitors except bupropion have been reported to worsen symptoms of restless legs syndrome.

Patel AA, Glaze DG. Sleep disorders. In: Kass JS, Mizrahi EM (eds). Neurology Secrets. 6th ed. Philadelphia: Elsevier; 2017, pp 324–336.

Question #

317 PEDIATRIC NEUROLOGY**CORE KNOWLEDGE****Clinical Aspects of Disease**

In any young person presenting with dystonia, a trial of levodopa must be considered to assess whether dystonia is responsive to medical therapy. Dopa-responsive dystonia (Segawa syndrome) presents in childhood as a progressive dystonia in children without a history of cerebral palsy or cognitive delay. It typically starts in a foot and progresses to become generalized. The most common inheritance pattern is autosomal dominant. This syndrome is unique for its robust and sustained response to low doses of levodopa. Its most notable characteristic is a diurnal variation with symptoms usually are more severe toward the end of the day and improved in the morning.

Jinnah HA. The dystonias. *Continuum Lifelong Learning Neurol*. 2019 Aug;25(4):976–1000.

Ostrem JL, Galifanakis KB. Overview of common movement disorders. *Continuum Lifelong Learning Neurol* 2010;16(1):13–48.

322 ADULT NEUROLOGY**Clinical Aspects of Disease**

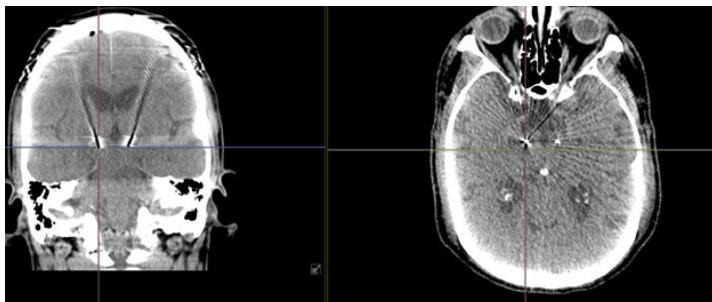
A red flag finding suggesting dystonia over essential tremor is unidirectional head tremor. Essential tremor is usually symmetric in distribution, whereas dystonia is often unilateral and isolated or segmental (involving two or more contiguous body parts). Essential tremor is also characterized by postural and kinetic tremor, whereas dystonia is more characteristically jerky and irregular. Vocal tremor is common in essential tremor. Patients with essential tremor frequently have a positive family history.

Stephen CD. The dystonias. *Continuum Lifelong Learning Neurol*. 2022 Oct;28(5):1435–1475.

329 ADULT NEUROLOGY**Diagnostic Procedures**

The CT scans show bilateral deep brain stimulation leads in the subthalamic nucleus, which is the target for Parkinson disease.

Aum DJ, Tierney TS. Deep brain stimulation: foundations and future trends. *Front Biosci (Landmark Ed)*. 2018 Jan;23(1):162–182.



Question #

337 PEDIATRIC NEUROLOGY**Clinical Aspects of Disease**

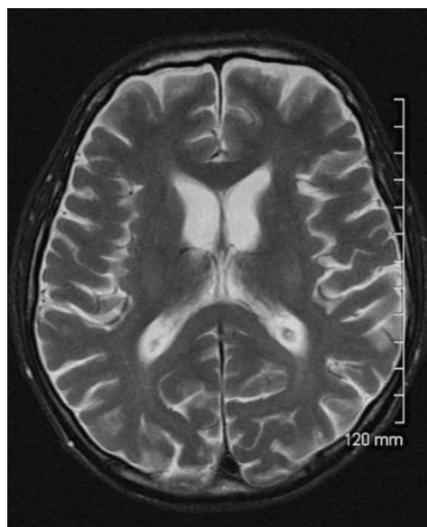
The neurologic manifestations in the father and son (excessive blinking, gait difficulty, excessive involuntary limb movements, cognitive impairment), along with MRI findings of bilateral caudate atrophy, are consistent with Huntington disease.

With the genetic phenomenon of anticipation, this patient most likely has juvenile-onset Huntington disease in which impaired saccadic eye movements often manifest early. Frequent eye blinking and head thrust are usually seen in patients with Huntington disease to compensate for the saccadic dysfunction. The triad of cognitive, psychiatric, and movement disorders, as seen in the father, are characteristic in Huntington disease.

Mestre TA. Chorea. Continuum Lifelong Learning Neurol. 2016 Aug;22(4):1186–1207.

Xing S, Chen L, Chen X, et al. Excessive blinking as an initial manifestation of juvenile Huntington's disease. Neurol Sci. 2008;29:275–277.

Termsarasab P, Thammongkolchai T, Rucker JC, et al. The diagnostic value of saccades in movement disorder patients: a practical guide and review. J Clin Mov Disord. 2015;2:14.



Question #

348 ADULT NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Diagnostic Procedures**

This patient's presentation with cerebellar ataxia, sensory neuropathy, and vestibulopathy is suggestive of CANVAS (cerebellar ataxia, neuropathy, vestibular areflexia) syndrome. This neurodegenerative syndrome was first identified in 2011 and accounts for about 20% of what was previously considered idiopathic late-onset cerebellar ataxia.

Sensory neuropathy is typically the presenting symptom, with cerebellar and vestibular dysfunction developing later in the course. Most patients have a dry cough that may precede neurologic symptoms by 30 years or more.

In 2019, the genetic etiology of CANVAS syndrome was identified as an expanded AAGGG pentamer (AAGGG)exp in an intron of the replication factor C subunit 1 (*RFC1*) gene. Since this is an intronic variant, it would not be identified on whole exome sequencing.

The duration of disease and vestibular dysfunction would not be consistent with anti-Hu paraneoplastic syndrome. While Friedreich ataxia has cerebellar ataxia and sensory neuropathy, the vestibular dysfunction would not be expected. Similarly, fragile X tremor ataxia syndrome would not be expected to demonstrate prominent vestibular dysfunction.

Shukla S, Gupta K, Singh K, et al. An updated canvas of the RFC1-mediated CANVAS (cerebellar ataxia, neuropathy and vestibular areflexia syndrome). *Mol Neurobiol*. 2025 Jan;62(1):693–707.

358 ADULT NEUROLOGY**CORE KNOWLEDGE****Clinical Aspects of Disease**

Trihexyphenidyl is an anticholinergic medication that can be considered for tremor in Parkinson disease in younger patients with tremor-predominant disease who have minimal or no bradykinesia or rigidity, which would not respond to this medication and generally warrants levodopa therapy if disabling. Trihexyphenidyl is generally avoided in older adults due to risk of cognitive side effects. Other anticholinergic side effects can include urinary retention, constipation, and dry mouth.

Thaler A, Alcalay RN. Diagnosis and medical management of Parkinson disease. *Continuum Lifelong Learning Neurol*. 2022 Oct;28(5):1281–1300.

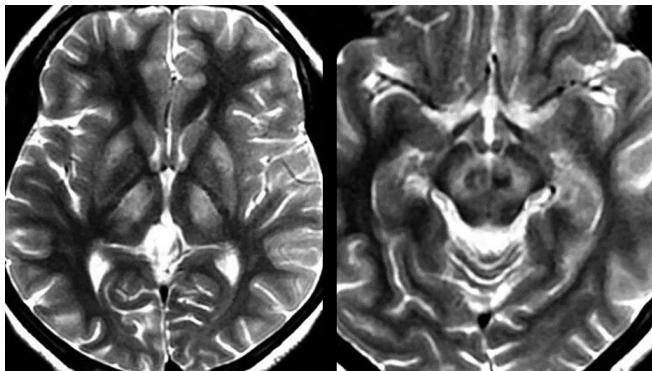
Question #

363 ADULT NEUROLOGY**Neuroimaging**

The MRI findings shown are consistent with Wilson disease. There is symmetric high-signal intensity involvement of the putamen and thalamus bilaterally. The globus pallidus is also involved (but not exclusively) as it is in many patients with carbon monoxide poisoning. The heads of the caudate nuclei appear normal, and there is no significant overall atrophy of the brain. These findings tend to exclude Huntington disease, and the high signal intensity within the globus pallidus and putamen is atypical for Parkinson disease. The NBIA's tend to affect the globus pallidus (with a small central T2 hyperintensity surrounded by T2 hypointensity in PKAN, for example — the classic eye of the tiger sign).

Ropper AH, Samuels MA, Klein JP, et al (eds). Adams and Victor's Principles of Neurology. 11th ed. New York: McGraw-Hill Education; 2019.

Image credit: Shivakumar R. Thomas SV. Teaching NeuroImages: face of the giant panda. MRI correlates of Wilson disease. Neurology. 2009 Mar;72(11):e50.

**369 ADULT NEUROLOGY****CORE KNOWLEDGE****Neuroanatomy**

This patient's large-amplitude involuntary movement of the proximal left arm and leg is consistent with left hemiballismus. Acute onset of this disorder suggests an infarction. The most common localization is the contralateral subthalamic nucleus. The most common causes are ischemic stroke, hemorrhage, and nonketotic hyperglycemia.

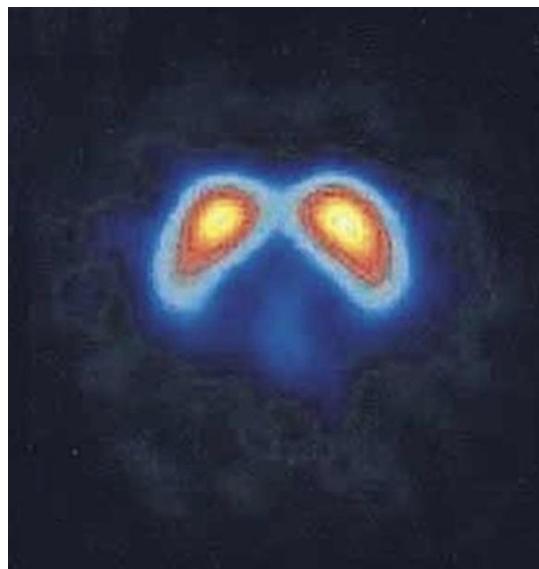
Hawley JS, Weiner WJ. Hemiballismus: current concepts and review. *Parkinsonism Relat Disord*. 2012 Feb;18(2):125–129.

Question #

385 ADULT NEUROLOGY**CORE KNOWLEDGE****Clinical Aspects of Disease**

This patient's dopamine transporter SPECT scan shows symmetric striatal uptake of the tracer in a "comma-shaped" pattern, which is normal. In patients with drug-induced parkinsonism, the scan is normal (unless the patient has concurrent neurodegenerative parkinsonism), whereas in parkinsonism due to a neurodegenerative etiology, symmetric or asymmetric reduced tracer uptake would be observed.

Maiti B, Perlmutter JS. Imaging in movement disorders. *Continuum Lifelong Learning Neurol*. 2023 Feb;29(1):194–218.



Question #

11 PEDIATRIC NEUROLOGY**Diagnostic Procedures**

Myelin oligodendrocyte protein-associated disease (MOGAD) is a distinct syndrome that commonly presents with acute disseminated encephalomyelitis (ADEM), optic neuritis, or transverse myelitis. About 50% of children <11 years of age with ADEM or optic neuritis are MOG-antibody positive. Optic disc edema is seen in many cases of MOG-associated optic neuritis. While optic neuritis can be suggestive of neuromyelitis optica spectrum disorder, this patient's clinical picture is not consistent with ADEM, which is more likely to be associated with MOG antibodies.

CSF oligoclonal bands are infrequently present in patients with ADEM and MOGAD. While NMDA antibodies can be present in patients with MOGAD, the clinical picture in this case is not a good fit for anti-NMDA receptor antibody encephalitis.

T2 hyperintense lesions perpendicular to the lateral ventricles (Dawson fingers) are characteristic of multiple sclerosis, not ADEM or MOGAD.

Banwell B, Bennett JL, Marignier R, et al. Diagnosis of myelin oligodendrocyte glycoprotein antibody-associated disease: International MOGAD Panel proposed criteria. Lancet Neurol. 2023;22(3):268–282.

Question

20 ADULT NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Clinical Aspects of Disease**

Acute disseminated encephalomyelitis (ADEM) is a monophasic syndrome that is usually preceded by an upper respiratory or gastrointestinal infection with a 2- to 30-day latency period. ADEM is thought to be immune-mediated. The most commonly associated viruses are measles, paramyxovirus, varicella zoster, rubella, and Epstein-Barr virus. Children and young adults are most commonly affected.

Onset is often rapid and is characterized by meningeal signs, headache, seizures, altered mental status, and long tract signs. The associated neurologic deficits vary and may include hemiplegia, paraplegia, sensory loss, vision loss, and sphincter dysfunction. Most patients are treated with steroids and begin to recover within 2 to 4 weeks.

Multiple sclerosis typically does not result in encephalopathy and would not have such a fulminant presentation. Encephalopathy is common in Susac syndrome, but paraparesis and loss of sphincter control would be unusual; this syndrome rarely affects the spinal cord.

Bickerstaff encephalitis can be associated with a viral trigger, though herpes simplex or varicella zoster viruses are the most common etiologies. Patients with Bickerstaff encephalitis often have ophthalmoparesis as well.

While transverse myelitis can be a presenting feature of neuropsychiatric lupus erythematosus, it is not common. Onset is often gradual, with behavioral and/or personality changes.

Filippi M, Rocca MA. White Matter Diseases. An Update for Neurologists. Cham, Switzerland: Springer Nature; 2020, pp 109–125.

Question #

22 NO SPECIFIED PATIENT AGE**CORE KNOWLEDGE****Neuroscience and Mechanism of Disease**

The water channel aquaporin-4 is found on the end-feet of astrocytes. IgG antibodies to aquaporin-4 (AQP4-IgG) are pathogenic in neuromyelitis optica spectrum disorders (NMOSD), which are considered to be an autoimmune astrocytopathy.

AQP4-IgG levels are higher in serum than in CSF because they are made in the extrathecal space. If NMOSD is a diagnostic consideration, serum rather than CSF titers of AQP4-IgG should be assessed using a cell-based assay.

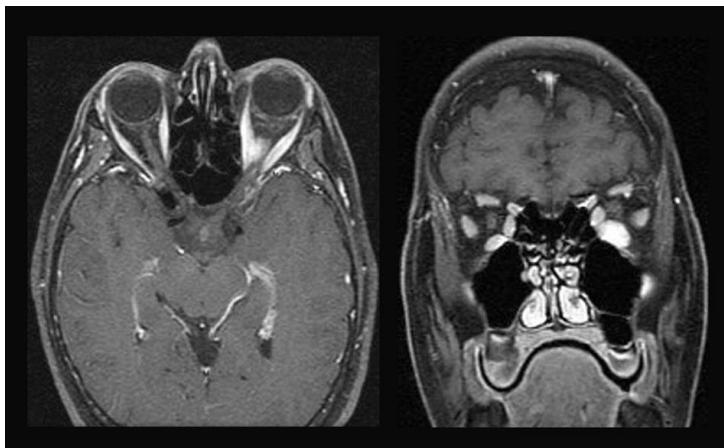
Costello F. Neuromyelitis optica spectrum disorders. *Continuum Lifelong Learning Neurol*. 2022 Aug;28(4):1131–1170.

Rees JH, Rempe T, Tuna IS, et al. Neuromyelitis optica spectrum disorders and myelin oligodendrocyte glycoprotein antibody-associated disease. *Magn Reson Imaging Clin N Am*. 2024;32(2):233–251.

33 ADULT NEUROLOGY**Neuroimaging**

Thyroid-associated ophthalmopathy (Grave ophthalmopathy) is an autoimmune inflammatory condition of the orbit associated with hyper- or hypothyroidism. The typical order of predilection for involvement of the extraocular muscles is inferior > medial > superior > lateral > oblique. These MRI scans demonstrate enlargement of several extraocular muscles, especially the left inferior rectus.

Blaser S, Illner A, Castillo M, et al (eds). *Pocket Radiologist: PedsNeuro Top 100 Diagnoses*. Salt Lake City: Amirsyst; 2003.



Question #

38 NO SPECIFIED PATIENT AGE**CORE KNOWLEDGE****Neuroscience and Mechanism of Disease**

Baclofen is the only therapeutic agent in use for spasticity that mediates its effects directly via activation of GABA-B receptors. The receptors are located in the brain both pre- and postsynaptically where they are coupled to calcium and potassium channels. This results in presynaptic inhibition of release of transmitters such as glutamate.

Bowery NG. GABA-B receptor: a site of therapeutic benefit. *Curr Opin Pharmacol.* 2006 Feb;6(1):37-43.

56 ADULT NEUROLOGY**CORE KNOWLEDGE****Clinical Aspects of Disease**

Neurosarcoidosis, involving the peripheral nervous system or CNS, is seen in 5% of patients with sarcoidosis. Granulomas frequently involve the meninges, hypothalamus, and pituitary gland. Cranial nerve VII (facial), either unilaterally or bilaterally, is most frequently affected. Involvement can be anywhere along the course of the facial nerve.

Tavee JO, Stern BJ. Neurosarcoidosis. *Continuum Lifelong Learning Neurol.* 2014 Jun;20(3):545-559.

Amato AA, Russell JA (eds). *Neuromuscular Disorders.* 2nd ed. New York: McGraw Hill Medical; 2016.

Question #

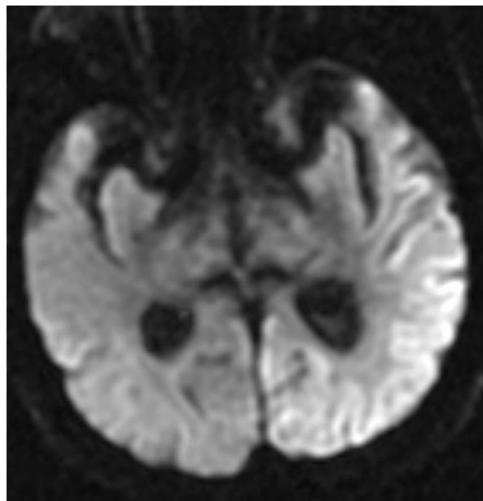
78 ADULT NEUROLOGY**Neuroimaging**

This patient's imaging findings are consistent with sporadic Creutzfeldt–Jakob disease, a progressive neurodegenerative disorder resulting from misfolded prion proteins. His MRI scan shows restricted diffusion involving the left occipital and left lateral temporal cortices.

Hypoxic brain injury typically causes symmetric abnormalities. MELAS does not have to be limited to the cortex and typically causes cortical swelling, which is not seen in this MRI. MRI scans in many paraneoplastic syndromes causing limbic encephalitis are subtly abnormal, with increased T2 hyperintensity in the medial temporal structures.

Status epilepticus in the setting of a paraneoplastic limbic encephalitis can cause cortical restricted diffusion and should be considered in the differential of Creutzfeldt–Jakob disease. Thiamine deficiency does not cause cortical restricted diffusion but instead medial thalamic, mammillary body, and periaqueductal gray T2 hyperintensity.

Bizzi A, Pascuzzo R, Blevins J, et al. Evaluation of a new criterion for detecting prion disease with diffusion magnetic resonance imaging. *JAMA Neurol.* 2020 Sep 1;77(9): 1141-1149.



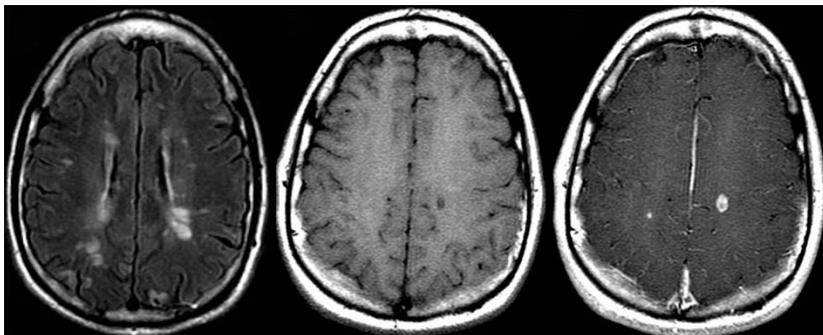
Question #

91 ADULT NEUROLOGY**CORE KNOWLEDGE****Clinical Aspects of Disease**

This patient's imaging studies show multiple T2-hyperintense lesions, along with two acute enhancing lesions. This appearance is most consistent with multiple sclerosis and is not typical for myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) or neurosarcoidosis.

Neuromyelitis optica has a predilection for the hypothalamus and area postrema. Acute demyelinating encephalomyelitis is characterized by larger confluent lesions.

Greenberg JO (ed). Neuroimaging: A Companion to Adams and Victor's Principles of Neurology. 2nd ed. New York: McGraw-Hill, 1999.

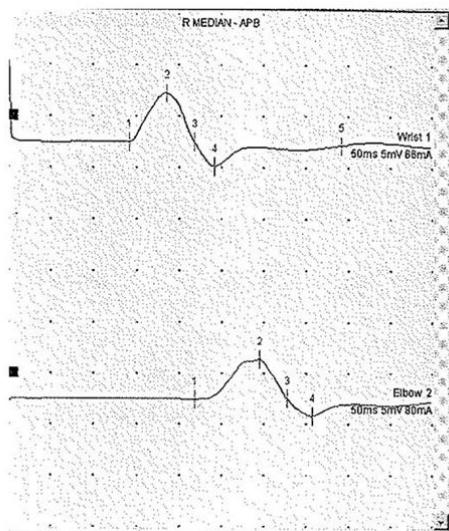


Question #

107 ADULT NEUROLOGY**CORE KNOWLEDGE****Diagnostic Procedures**

Relatively preserved amplitudes in distal segments, in conjunction with prolonged latencies and reduced conduction velocities, suggest a primarily demyelinating cause. Temporal dispersion and conduction blocks are hallmarks of an acquired demyelinating neuropathy, not congenital demyelinating neuropathies such as Charcot–Marie–Tooth disease.

Rubin DI (ed). Clinical Neurophysiology. 5th ed. New York: Oxford University Press; 2021.

**122 ADULT NEUROLOGY****SUBSPECIALTY KNOWLEDGE****Neuropathology**

Using tap water in a neti pot can expose individuals to waterborne organisms not typically found in treated water sources. Free-living amoebae, such as *Naegleria fowleri*, thrive in warm freshwater and can colonize the nasal mucosa, eventually leading to a severe brain infection known as primary amoebic meningoencephalitis.

This condition often presents with hemorrhagic meningoencephalitis, particularly after practices such as nasal irrigation with contaminated water, making this the most likely cause given the patient's history of rhinosinusitis.

Ellison DW, Love S (eds). Neuropathology: A Reference Text of CNS Pathology. 3rd ed. San Francisco: Elsevier; 2013.

Cope JR, Ratard RC, Hill VR, et al. The first association of a primary amebic meningoencephalitis death with culturable *Naegleria fowleri* in tap water from a US treated public drinking water system. Clin Infect Dis. 2015 Apr 15;60(8)e36–e42.

Question

135 ADULT NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Clinical Aspects of Disease**

According to the 2023 diagnostic criteria for myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD), the presence of positive MOG antibodies alone, especially when titers are low or unavailable, is not sufficient to confirm the diagnosis. In addition to negative results on aquaporin-4 antibody testing, clinical or radiologic features supporting MOGAD are required to strengthen the diagnosis. A longitudinally extensive myelitis is the most specific feature of MOGAD.

Optic neuritis can be seen, but it typically is a long (>50%) segment optic neuropathy. Periventricular and juxtacortical hyperintensities and oligoclonal bands are more specific for multiple sclerosis than MOGAD. A CSF pleocytosis can be seen in MOGAD, but it is not as specific nor is a supporting clinical or radiographic feature listed in the criteria.

Banwell B, Bennett JL, Marignier R, et al. Diagnosis of myelin oligodendrocyte glycoprotein antibody-associated disease: International MOGAD Panel proposed criteria. Lancet Neurol. 2023 Mar;22(3):268-282.

Varley JA, Champsas D, Prossor T, et al. Validation of the 2023 International Diagnostic Criteria for MOGAD in a selected cohort of adults and children. Neurology. 2024 Jul 9;103(1):e209321.

147 ADULT NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Treatment/Management**

Contraception is generally recommended to prevent teratogenicity in women with multiple sclerosis (MS) taking disease-modifying agents. Teratogenicity has been observed in animal studies of cladribine, and this drug can be transmitted in male seminal fluid. Male patients with MS should be counseled on their reproductive plans before initiation of treatment with this medication.

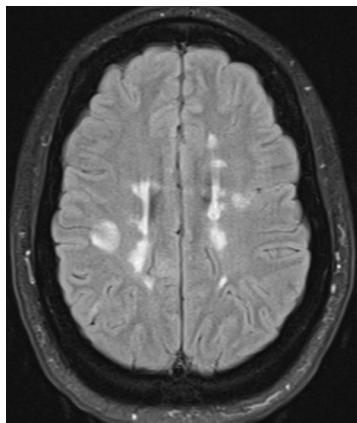
Safi NV, Krieger S. Men with multiple sclerosis. Pract Neurol. 2021 Feb;37:37-40.

Question #

156 ADULT NEUROLOGY**Clinical Aspects of Disease**

Radiologically isolated syndrome, sometimes called preclinical multiple sclerosis (MS), is a recent concept used to describe MRI findings suggestive of MS in the absence of any clinical event consistent with the disease. Its significance lies in the fact that several series have reported that up to one third of patients with this syndrome will develop a clinical attack consistent with MS, and most will show radiographic progression of the disease within a short time.

Lebrun-Frenay C, Kantarci O, Siva A, et al. Radiologically isolated syndrome. Lancet Neurol. 2023;22(11):1075-1086.

**167 ADULT NEUROLOGY****Treatment/Management**

Siponimod interacts with sphingosine-1-phosphate receptor (S1PR) subtypes. Potential side effects include bradydysrhythmias, macular edema, increased hepatic transaminases, increased blood pressure, and a mild decrease in 1-second forced expiratory volume.

Due to cardiac risk, S1PR modulators such as siponimod are contraindicated in patients with sinus bradycardia or first- or second-degree (Mobitz type I) atrioventricular (AV) block. The other disease-modifying therapies listed (alemtuzumab, dimethyl fumarate, natalizumab, and teriflunomide) do not pose significant cardiac risk.

Zhao Z, Lv Y, Gu ZC, et al. Risk for cardiovascular adverse events associated with sphingosine-1-phosphate receptor modulators in patients with multiple sclerosis: insights from a pooled analysis of 15 randomised controlled trials. *Front Immunol.* 2021 Dec;12:795574.

Jones DE. Early relapsing multiple sclerosis. *Continuum Lifelong Learning Neurol.* 2016 Jun;22(3):744-760.

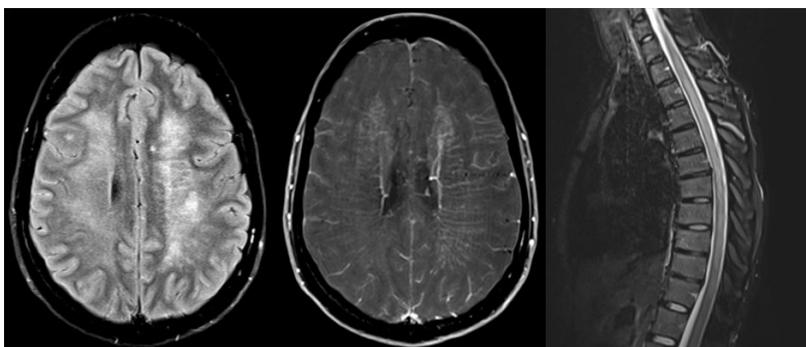
Question #

177 ADULT NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Neuroscience and Mechanism of Disease**

This patient's comprehension difficulties and sensory level likely correspond to the multifocal FLAIR abnormalities seen in the brain MRI scans and the longitudinally extensive cord lesion. While all the etiologies listed could be associated with a longitudinally extensive spinal cord lesion, the radial perivascular enhancement extending from the ventricles noted on the brain MRI scans is typical of GFAP.

Brain lesions in neuromyelitis optica can be large and confluent but do not feature the radial enhancement pattern shown here. Anti-Hu and anti-CRMP5 are not associated with multifocal FLAIR abnormalities with a radial enhancement pattern. NF155 features central and peripheral demyelination but is not associated with a radial enhancement pattern.

Tewkesbury G, Song JW, Perrone CM. Magnetic resonance imaging of autoimmune GFAP astrocytopathy. Ann Neurol. 2021 Oct;90(4):691-692.



Question #

192 ADULT NEUROLOGY**CORE KNOWLEDGE****Diagnostic Procedures**

Optic neuritis can be a presenting feature of other demyelinating diseases as well as multiple sclerosis. The severity of this patient's optic neuritis and poor recovery despite treatment with steroids should raise concern for neuromyelitis optica, which can be diagnosed with positive results on aquaporin-4 antibody testing.

JC virus resulting in progressive multifocal leukoencephalopathy would present with progressive motor, language, or cerebellar dysfunction instead of optic neuropathy. While optical coherence tomography can be helpful in assessing the course of optic nerve edema and/or subsequent scarring, it is not likely to identify the underlying etiology. The suspicion for an underlying malignancy would be low due to the acute onset of the patient's deficits, thereby making CSF cytology less likely to be diagnostic. Brainstem auditory evoked potentials can reveal CNS dysfunction, but there are no referable symptoms to warrant the testing.

Borisow N, Mori M, Kuwabara S, et al. Diagnosis and treatment of NMO spectrum disorder and MOG-encephalomyelitis. *Front Neurol.* 2018 Oct 23;9:888.

197 PEDIATRIC NEUROLOGY**CORE KNOWLEDGE****Neuroanatomy**

This patient has acute flaccid myelitis (AFM), a polio-like illness affecting the anterior horn of the spinal cord. Presentation is typically characterized by acute onset of flaccid weakness of one limb with loss of deep tendon reflexes but preserved sensation, as expected in a disorder affecting lower motor neurons in isolation. AFM is associated with enterovirus infection (particularly enterovirus D68) and has occurred in outbreaks with an every other year pattern since 2012.

Bhattacharyya S, Bradshaw MJ. Infections of the spine and spinal cord. *Continuum Lifelong Learning Neurol.* 2021 Aug;27(4):887-920.

207 NO SPECIFIED PATIENT AGE**Neuroscience and Mechanism of Disease**

Anti-Yo antibodies cause destruction of the Purkinje cells in the cerebellum. The other cells listed (Golgi, granule, basket, stellate) are located in the cerebellum but are not affected by anti-Yo antibodies.

Binks S, Uy C, Honnorat J, et al. Paraneoplastic neurological syndromes: a practical approach to diagnosis and management. *Pract Neurol.* 2022 Feb;22(1):19-31.

Question #

213 NO SPECIFIED PATIENT AGE**Treatment/Management**

There is a risk of progressive multifocal leukoencephalopathy in patients with multiple sclerosis (MS) who have previously been exposed to the JC virus and are being treated with natalizumab therapy, especially with therapy duration of >2 years.

This risk often results in a discussion about discontinuing natalizumab therapy. In this context, it is important that physicians and patients be aware severe MS exacerbations have been reported following discontinuation of natalizumab therapy. Similarly, severe MS exacerbations following discontinuation of fingolimod therapy have also been reported.

Sempere AP, Berenguer-Ruiz L, Feliu-Rey E. Rebound of disease activity during pregnancy after withdrawal of fingolimod. Eur J Neurol. 2013; 20(8):e109–e110.

Havla JB, Pellkofer HL, Meinl I, et al. Rebound of disease activity after withdrawal of fingolimod (FTY720) treatment. Arch Neurol. 2012;69(2):262–264.

West TW, Cree BAC. Natalizumab dosage suspension: are we helping or hurting? Ann Neurol. 2010;68(3):395–399.

Kerbrat A, Le Page E, Leray E, et al. Natalizumab and drug holiday in clinical practice: an observational study in very active relapsing remitting multiple sclerosis patients. J Neurol Sci. 2011;308(1-2):98–102.

219 ADULT NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Clinical Aspects of Disease**

Sjögren syndrome can be associated with either a distal symmetric polyneuropathy or a sensory ganglionopathy (sensory neuronopathy), which is a non-length-dependent loss of sensation. A sensory ganglionopathy can also be seen in association with anti-Hu paraneoplastic syndrome, vitamin B6 toxicity, and following platinum-based chemotherapies.

Goldstein J. Neurological complications of rheumatic disease. Continuum Lifelong Learning Neurol. 2014 Jun;20(3):657–669.

Question #

225 PEDIATRIC NEUROLOGY**Neuroimaging**

MRI characteristics of ADEM include deep gray matter and cortical involvement, bilateral diffuse lesions, poorly defined margins, and large globular lesions. T2/FLAIR lesions that spare the deep gray matter are confined to the juxtacortical white matter or corpus callosum, located perpendicular to the long axis of the corpus callosum. Lesions that have a periventricular pattern are characteristic of multiple sclerosis.

Krupp LB, Tardieu M, Amato MP, et al. International Pediatric Multiple Sclerosis Study Group criteria for pediatric multiple sclerosis and immune-mediated central nervous system demyelinating disorders: revisions to the 2007 definitions. *Mult Scler*. 2013 Sep;19(10):1261-1267.

Pohl D, Alper G, Van Haren K, et al. Acute disseminated encephalomyelitis: updates on an inflammatory CNS syndrome. *Neurology*. 2016 Aug 30;87(9 Suppl 2):S38-S45.

229 NO SPECIFIED PATIENT AGE**SUBSPECIALTY KNOWLEDGE****Treatment/Management**

Neuromyelitis optica (NMO) is an inflammatory demyelinating disorder of the CNS characterized by episodes of optic neuritis, longitudinally extensive myelitis, and brainstem/diencephalic dysfunction.

Approximately 70% to 80% of patients have serum antibodies to aquaporin-4, a water channel found on astrocytes. This autoantibody is thought to be pathogenic for NMO and NMO spectrum disorders (NMOSD).

The goal of long-term treatment of NMO and NMOSD is to prevent relapse. Agents used include corticosteroids, immunosuppressants (azathioprine, mycophenolate), and rituximab, inebilizumab, eculizumab, and satralizumab.

The disease-modifying agents for multiple sclerosis have not demonstrated effectiveness for NMO/NMOSD. In particular, both interferon beta and natalizumab have been associated with increased disease activity in NMO/NMOSD.

Pittock SJ, Lennon VA, McKeon A, et al. Eculizumab in AQP4-IgG-positive relapsing neuromyelitis spectrum disorders: an open-label study. *Lancet Neurol*. 2013;2:554-562.

Wingerchuk DM, Weinshenker BG. Acute disseminated encephalomyelitis, transverse myelitis, and neuromyelitis optica. *Continuum Lifelong Learning Neurol*. 2013 Aug;19(4):944-967.

Question #

250 ADULT NEUROLOGY

Clinical Aspects of Disease

This patient has a sensory neuronopathy on EMG and a cervical spine tractopathy affecting the dorsal columns, findings most consistent with an anti-Hu paraneoplastic syndrome, likely stemming from the patient's underlying adenocarcinoma.

Though vitamin B12 deficiency could result in a longitudinal dorsal column lesion, it does not cause a sensory neuronopathy but rather a sensory motor neuropathy. Thiamine deficiency would also typically have sensory motor neuropathy, but a longitudinal cord lesion would be unlikely. Neuromyelitis optica could feature a longitudinal cord lesion, though neuropathy is not seen.

Gill AJ, Perez MA, Perrone CM, et al. A case series of PD-1 inhibitor-associated paraneoplastic neurologic syndromes. *J Neuroimmunol*. 2019 Sep 15;334:576980.

256 ADULT NEUROLOGY

Diagnostic Procedures

This patient's slowly progressive stiffness and startle reflex are most consistent with stiff person syndrome. Up to 85% of patients will have anti-glutamic acid decarboxylase (GAD) antibodies in their CSF. Oligoclonal bands are often found as well.

Though SCNA is an autosomal dominant gene linked with Parkinson disease, the CSF and EMG findings described here would be unlikely. SPG4 tests for hereditary spastic paraparesis, but a startle reflex and this patient's EMG findings would be unlikely.

Testing for CASPR2 antibodies seeks to confirm possible neuromyotonia, though encephalitic symptoms would also likely be present. The EMG would show bursts rather than continuous activity.

HLA-B27 would screen for ankylosing spondylitis. While CSF oligoclonal bands can be seen at times in rheumatologic disorders, the hyperreflexia and EMG findings would not be expected.

Newsome SD, Johnson T. Stiff person syndrome spectrum disorders; more than meets the eye. *J Neuroimmunol*. 2022 Aug 15;369:577915.

Question #

266 NO SPECIFIED PATIENT AGE**Treatment/Management**

Dimethyl fumarate is approved for the treatment of relapsing-remitting multiple sclerosis. The pathophysiology of demyelination and axonal loss in this disorder is due in part to neuroinflammatory-mediated oxidative stress.

In preclinical models, dimethyl fumarate reduces toxic oxidative stress through activation of the nuclear factor (erythroid-derived 2)-like 2 (Nrf2) antioxidant response pathway. In addition, dimethyl fumarate may suppress proinflammatory cytokines and proinflammatory pathways in the CNS. Side effects include nausea, diarrhea, and flushing, as well as lymphopenia. Aspirin may reduce flushing associated with dimethyl fumarate by inhibiting the prostaglandin pathway.

Gold R, Kappos L, Arnold DL, et al. Placebo-controlled phase 3 study of oral BG-12 for relapsing multiple sclerosis. *N Engl J Med.* 2012 Sep 20;367(12):1098–1107.

273 ADULT NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Clinical Aspects of Disease**

This patient most likely has multiple sclerosis, with enhancing and nonenhancing lesions seen in typical areas of demyelination (periventricular, infratentorial, spinal cord). Paroxysmal dysarthria-ataxia, stemming from ephaptic transmission, can be a presenting symptom in multiple sclerosis. First-line treatment can be carbamazepine/oxcarbazepine.

Pseudobulbar affect is characterized by unprovoked laughter or crying. The stereotyped nature of the patient's episodes makes functional neurologic disorder less likely. Area postrema syndrome is typically characterized by recurrent hiccups or vomiting. There are no abnormal eye or limb movements to suggest opsoclonus-myoclonus, and this would not be episodic.

Shah S, Klassen BT, Flanagan EP. Teaching Video Neuroimages: Paroxysmal dysarthria-ataxia in multiple sclerosis. *Neurology.* 2021 Apr 27;96(17):e2245–e2246.

Question #

289 ADULT NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Treatment/Management**

In patients with detrusor hyperreflexia without outlet obstruction or urinary retention, anticholinergic medications, including tolterodine, are the most appropriate treatment. If retention occurs, this medication should be combined with intermittent self-catheterization.

Yang CC. Bladder management in multiple sclerosis. *Phys Med Rehabil Clin N Am*. 2013 Nov;24(4):673-686.

293 ADULT NEUROLOGY**Clinical Aspects of Disease**

Opsoclonus-myoclonus syndrome (OMS) is a rare neurologic condition characterized by opsoclonus (rapid, involuntary multivectorial eye movements), myoclonus, ataxia, and often encephalopathy, which can manifest as sleep disturbances and irritability. OMS can be an autoimmune or a paraneoplastic disorder associated with neuroblastoma in children and breast and with small cell lung cancer in adults.

Jitprapaikulsan J, Paul P, Thakolwiboon S, et al. Paraneoplastic neurological syndrome: an evolving story. *Neurooncol Pract*. 2021 Feb 24;8(4):362-374.

299 NO SPECIFIED PATIENT AGE**CORE KNOWLEDGE****Contemporary Issues**

The key feature of a case-control study is that participants are ascertained on the basis of outcome (in this case MS relapses). In this study, two groups of patients with MS taking interferon beta are evaluated: one group experiencing relapses since starting therapy and one group with no relapses since starting therapy.

The direction of inquiry of the research question is from outcome to exposure. The "exposure" here is the presence of neutralizing antibodies. The investigators inquired about the frequency of neutralizing antibodies among the cases (MS patients with relapses) and the controls (MS patients without relapses).

Straus SE, Richardson WS, Glasziou P, Haynes RB (eds). *Evidence-based Medicine: How to Practice and Teach EBM*. 5th ed. Philadelphia: Elsevier; 2019.

Question #

304 ADULT NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Neuroscience and Mechanism of Disease**

This patient's history of 4 months of weakness and numbness and an EMG demonstrating a demyelinating polyneuropathy suggest chronic inflammatory demyelinating polyradiculoneuropathy (CIDP). The differential for CIDP also includes POEMS syndrome and antibody-mediated autoimmune nodal-paranodal neuropathies. The latter should be considered based on the clinical phenotype of distal predominant weakness, sensory ataxia, and a poor response to traditional therapies for CIDP such as IVIg.

Neurofascin 155 (NF155) IgG4 is the most common antibody among the autoimmune nodal-paranodal neuropathies, with a frequency of up to 8% in European cohorts and 20% in East Asian cohorts. Patients with NF155 IgG4 antibodies frequently also have a prominent postural tremor, cerebellar dysfunction such as nystagmus or ataxia, and autonomic dysfunction.

Patients with contactin-1 (CNTN1) or contactin-associated protein (CASPR1) antibodies present with a Guillain-Barré syndrome phenotype or a chronic inflammatory sensory polyradiculoneuropathy. The GQ-1 antibody is associated with the Miller Fisher variant of Guillain-Barré syndrome. Vascular endothelial growth factor (VEGF) level is elevated in patients with POEMS syndrome, but antibodies directed against VEGF are not detected.

Gupta P, Mirman I, Shahar S, et al. Growing spectrum of autoimmune nodopathies. *Curr Neurol Neurosci Rep.* 2023;23(5):201–212.

306 ADULT NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Clinical Aspects of Disease**

An area postrema syndrome, characterized by intractable hiccups, nausea, and vomiting, occurs in up to 43% of patients with neuromyelitis optica spectrum disorder.

Sand IK. Neuromyelitis optica spectrum disorders. *Continuum Lifelong Learning Neurol.* 2016 Jun;22(3):864–896.

Question #

315 PEDIATRIC NEUROLOGY**Clinical Aspects of Disease**

This patient's imaging studies show progressive atrophy of the left frontal lobe, insula, and basal ganglia, including the caudate. Based on his clinical and imaging findings, he meets part B clinical criteria for Rasmussen syndrome.

A diagnosis of Rasmussen syndrome requires all three part A criteria or two of three part B criteria. Part A criteria include the following features: focal seizures, unilateral hemispheric slowing on EEG and unilateral seizure onset, and unilateral hemispheric focal cortical atrophy on MRI with gray or white matter T2/FLAIR signal changes or hyperintense signal or atrophy of the ipsilateral caudate head. Part B criteria include the following features: epilepsia partialis continua or progressive unilateral cortical deficits, progressive unilateral hemispheric focal cortical atrophy, and appropriate histopathology.

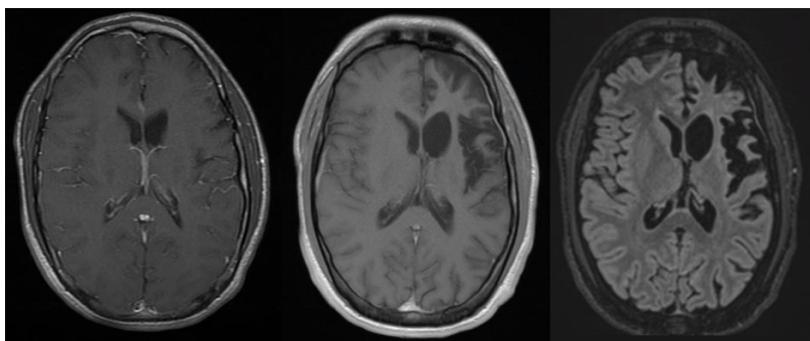
Hemiconvulsion-hemiplegia-epilepsy syndrome presents with focal motor status epilepticus in children younger than age 4 years. This patient's imaging studies do not show hemimegalencephaly and are not consistent with a perinatal infarct. They are also not consistent with Sturge-Weber syndrome as there is no evidence of leptomeningeal enhancement.

Bien CG, Granata T, Antozzi C, et al. Pathogenesis, diagnosis and treatment of Rasmussen encephalitis: a European consensus statement. *Brain*. 2005 Mar;128(Pt 3):454-71.

Zuberi SM, Wirrell E, Yozawitz E, et al. ILAE classification and definition of epilepsy syndromes with onset in neonates and infants: position statement by the ILAE Task Force on Nosology and Definitions. *Epilepsia*. 2022 Jun;63(6):1349-1397.

Specchio N, Wirrell EC, Scheffer IE, et al. International League Against Epilepsy classification and definition of epilepsy syndromes with onset in childhood: position paper by the ILAE Task Force on Nosology and Definitions. *Epilepsia*. 2022 Jun;63(6):1398-1442.

Riney K, Bogacz A, Somerville E, et al. International League Against Epilepsy classification and definition of epilepsy syndromes with onset at a variable age: position statement by the ILAE Task Force on Nosology and Definitions. *Epilepsia*. 2022 Jun;63(6):1443-1474.



Question #

360 ADULT NEUROLOGY**CORE KNOWLEDGE****Neuroscience and Mechanism of Disease**

Systemic sarcoidosis most often involves the lymphoid, respiratory, and cardiac systems. Involvement of heart or lungs can be the cause of patient demise so they are not just unimportant features of the disorder to be considered.

Rao DA, Dellaria PF. Extrapulmonary manifestations of sarcoidosis. *Rheum Dis Clin North Am.* 2013 May;39(2):277-297.

362 ADULT NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Treatment/Management**

Ozanimod has been associated with macular edema. The macula is located in the center of the retina and is responsible for sharp, straight-ahead vision. Fluid buildup causes the macula to swell and thicken. Before switching treatment, the etiology of a patient's visual distortion should be confirmed with a retinal examination by an ophthalmologist. This patient's vision change is less likely to be secondary to optic neuritis because she has no pain with eye movements and does not have an afferent pupillary defect.

Cree BA, Selma JW, Steinman L, et al. Long-term safety and efficacy of ozanimod in relapsing multiple sclerosis: up to 5 years of follow-up in the DAYBREAK open-label extension trial. *Mult Scler.* 2022 Jun;28(12):1944-1962.

Afshar A, Fernández J, Patel R, et al. Cystoid macular edema associated with fingolimod use for multiple sclerosis. *JAMA Ophthal.* 2013;131(1):103-107.

Greenberg BM, Khatri BO, Kramer JF. Current and emerging multiple sclerosis therapeutics. *Continuum Lifelong Learning Neurol.* 2010 Oct;16(5):59-67.

Question #

377 ADULT NEUROLOGY**Clinical Aspects of Disease**

Chimeric antigen receptor (CAR) T-cell therapy is an approved treatment option for diffuse large B-cell lymphoma. With this therapy, a patient's own T cells are genetically modified to express receptors that bind to and eradicate cancerous cells. However, CAR T-cell therapy can result in high levels of systemic inflammation that can disrupt the blood-brain barrier and result in CNS inflammation, a disorder known as immune effector cell-associated neurotoxicity syndrome (ICANS).

ICANS often presents with altered mental status, language difficulties, and seizures. Serum inflammatory markers are typically elevated, and brain MRI scans are often normal. Altered mental status can also be seen with posterior reversible encephalopathy syndrome, progressive multifocal leukoencephalopathy, and anti-mGluR5 encephalitis, but MRI scans are typically abnormal.

Hemophagocytic lymphohistiocytosis can feature elevated serum inflammatory markers but typically demonstrates organomegaly that was not identified on this patient's CT scans.

Stern RC, Stern RM. Immune effector cell associated neurotoxicity syndrome in chimeric antigen receptor-T cell therapy. *Front Neuroimmunol*. 2022 Aug 23;13:879608.

382 ADULT NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Clinical Aspects of Disease**

The spectrum of myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) continues to expand with the manifestation of a cerebral cortical encephalitis. New-onset seizure activity is the most typical symptom. MRI scans often show edematous cortical lesions with leptomeningeal enhancement. This patient's resolved left-sided optic neuropathy is a prior optic neuritis (from which significant or complete recovery can be seen).

Cerebral vasculitis could present with more cortical lesions, though leptomeningeal enhancement would be unusual; more focal deficits and/or stepwise clinical decline would be expected in the setting of sequential infarcts.

GABA-A encephalitis can present with multifocal cortical lesions but typically does not have leptomeningeal enhancement. Anti-CRMP5 paraneoplastic syndrome is linked with a uveo-retinal symptoms, but brain MRI scans are more likely to be normal. Posterior reversible encephalopathy syndrome can result in seizures and cortical blindness, but it typically does not feature leptomeningeal enhancement or optic nerve involvement, and the CSF profile often shows an isolated protein elevation.

Valencia-Sánchez C, Guo Y, Krecke KN, et al. Cerebral cortical encephalitis in myelin oligodendrocyte glycoprotein antibody-associated disease. *Ann Neurol*. 2023 Feb;93(2):297-302.

Question #

390 PEDIATRIC NEUROLOGY**CORE KNOWLEDGE****Neuroscience and Mechanism of Disease**

This patient has metachromatic leukodystrophy (MLD), a disorder caused by deficient activity of lysosomal enzyme arylsulfatase A. In the late infantile form, this disease is characterized by rapid loss of motor function, followed by loss of cognitive function. MRI studies generally reveal T2 signal abnormalities in the frontal and parietal regions with radial stripes (tigroid pattern). This pattern can also be seen in Pelizaeus-Merzbacher disease and globoid cell leukodystrophy. Multiple cranial nerve enhancement is also an MRI finding seen in MLD.

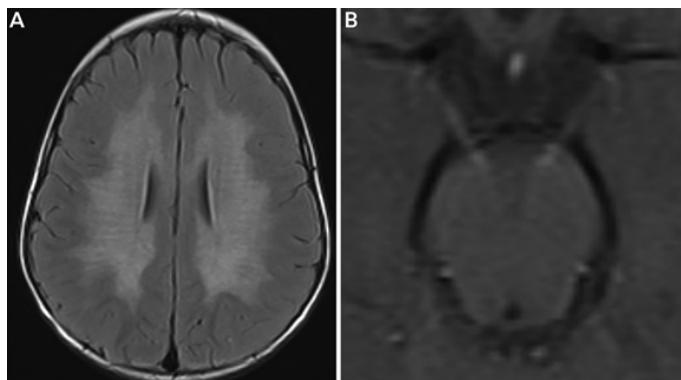
Rett syndrome is caused by mutation in the *MECP2* gene and is characterized by a normal early development followed by slowing in development, loss of motor function, and characteristic hand movements. MRI images are characterized by global atrophy.

Pathologic variants in *GFAP* cause Alexander disease, which generally presents with epilepsy, macrocephaly, developmental delay, and failure to thrive. MRI studies show diffuse symmetric white matter signal abnormalities, predominantly affecting the frontal lobes.

Mutations in *DMD* cause Duchenne muscular dystrophy, which is not associated with central demyelination.

Aspartoacylase deficiency is present in Canavan disease, a disorder characterized by delayed development in the first year of life followed by developmental delay. MRI images show central diffuse hyperintense signal in the cortex and basal ganglia.

Adang L. Leukodystrophies. Continuum Lifelong Learning Neurol. 2022 Aug;28(4): 1194-1216.



Question #

398 ADULT NEUROLOGY**Neuroscience and Mechanism of Disease**

Immune checkpoint inhibitors have been associated with development of paraneoplastic neurologic syndromes. This patient demonstrates clinical symptoms of opsoclonus and ataxia, most suggestive of an anti-Ri/antineuronal nuclear antibody type 2 paraneoplastic syndrome, which is often associated with breast cancer.

Pembrolizumab (a programmed cell death protein 1 inhibitor) is approved for treatment of triple negative breast cancer. Subsequent upregulation of the immune system has permitted a paraneoplastic syndrome to emerge. The other mechanisms listed are used in the treatment of breast cancer (paclitaxel, gemcitabine, carboplatin, doxorubicin) but would not likely result in the clinical presentation.

Gill AJ, Perez MA, Perrone CM, et al. A case series of PD-1 inhibitor-associated paraneoplastic neurologic syndromes. J Neuroimmunol. 2019 Sep 15;334:576980.

Question #

21 ADULT NEUROLOGY**CORE KNOWLEDGE****Clinical Aspects of Disease, Neuroimaging**

This patient has a disk space infection with an associated epidural abscess. The symptom triad of back pain, fever, and neurologic deficit is classic for this disorder. Most infections occur in the thoracolumbar region. Age, diabetes mellitus, and a history of an invasive procedure (coronary angiogram) are risk factors in this patient. Most disk space infections are from *Staphylococcus aureus*.

Ameer MA, Knorr TL, Munakomi S, et al. Spinal epidural abscess. [Updated 2023 Aug 13]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-.

**51 ADULT NEUROLOGY****CORE KNOWLEDGE****Treatment/Management**

This patient's presentation is consistent with Bell palsy. There is class 1 evidence supporting treatment with steroids to improve recovery, but evidence for antiviral treatment is weak. There is no benefit to combination therapy. The upper and lower facial weakness is unlikely to be a stroke.

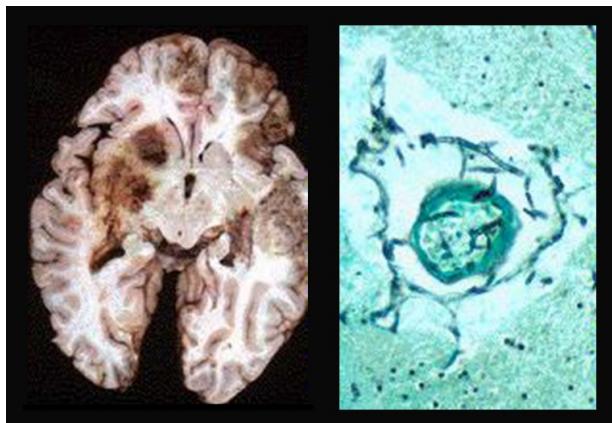
Gronseth G, Peduga R. Evidence-based guideline update: steroids and antivirals for Bell palsy: report of the Guideline Development Subcommittee of the American Academy of Neurology. *Neurology*. 2012 Nov 27;79(22):2209-2213.

Question #

143 ADULT NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Neuropathology**

The gross photograph shows hemorrhages characteristic of vasoinvasive fungi such as Aspergillus. The photomicrograph shows a silver stain, identifying multiple septate fungi with invasion of a blood vessel in the brain, characteristic of *Aspergillus* species. The other organisms listed (toxoplasmosis, cysticercosis, candidiasis, amoebiasis) would not have this typical microscopic appearance or strong predilection for angioinvasive behavior.

Pruitt AA. Central nervous system infections complicating immunosuppression and transplantation. *Continuum Lifelong Learning Neurol*. 2018 Oct;24(5):1370–1396.
INFECT-40716

**184 ADULT NEUROLOGY****Neuroscience and Mechanism of Disease**

West Nile virus is a flavivirus transmitted by mosquitos, predominantly *Culex* and *Aedes albopictus* species, that has spread throughout almost all of North America. While it typically is asymptomatic or presents as a febrile illness, West Nile virus can cause neuroinvasive disease in rare cases. Neurologic manifestations are classically meningitis, encephalitis, or a poliomylitis-like illness affecting the anterior horn cells, as in this patient. Diagnosis is made by serology, IgM antibody-specific ELISA and West Nile virus antigen-specific ELISA.

Spiro P, Dodda V, Sivapalan V, et al. Encephalomyelitis. In: Hall JB, Schmidt GA, Kress JP, et al (eds). *Principles of Critical Care*. 4th ed. New York: McGraw Hill; 2014.

Kuhn JH, Charrel RN, Kuhn JH, et al. In: Jameson J, Fauci AS, Kasper DL, et al (eds). *Harrison's Principles of Internal Medicine*. 20th ed. New York: McGraw Hill; 2018.

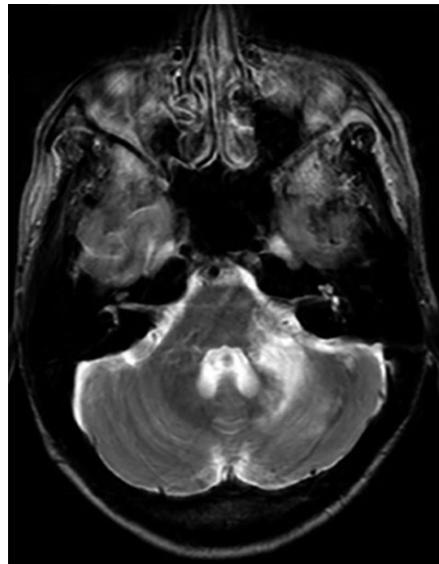
Question #

200 ADULT NEUROLOGY

Clinical Aspects of Disease

This patient has a T2 hyperintensity in the left middle cerebellar peduncle without mass effect or enhancement, consistent with the well-described "shrimp sign" in progressive multifocal leukoencephalopathy.

Adra N, Goodheart AE, Rapalino O, et al. MRI shrimp sign in cerebellar progressive multifocal leukoencephalopathy: description and validation of a novel observation. AJNR Am J Neuroradiol. 2021 Jun;42(6):1073–1079.



Question #

241 PEDIATRIC NEUROLOGY**CORE KNOWLEDGE****Neuroimaging**

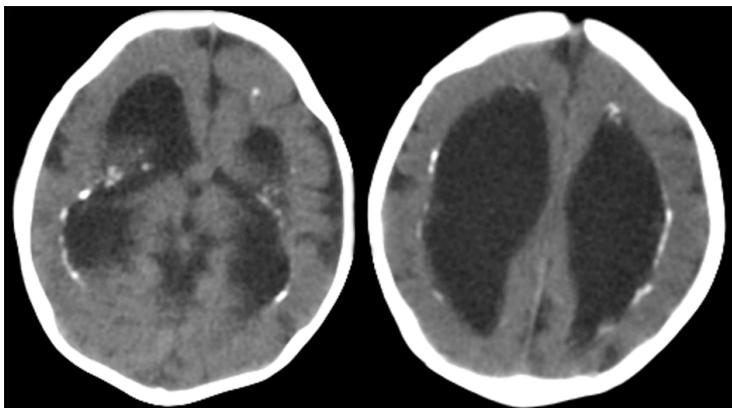
This patient's imaging studies show profound cortical atrophy with ventriculomegaly on an *ex vacuo* basis, with calcifications along the ependymal margin. These findings are frequently seen with congenital cytomegalovirus infections.

Fahr disease is an idiopathic disorder characterized by calcifications involving the basal ganglia, the cerebellar, dentate nuclei, and sometimes the cortical ribbon. These findings are not seen here. No evidence of an obstruction of the ventricular system is seen.

Congenital herpes encephalitis results in encephalomalacia involving the mesial temporal, parasagittal, frontal, and insular cortical regions, which is not the pattern seen here. Mitochondrial cytopathies are not associated with ependymal calcifications, as in this case.

Diogo MC, Glatter S, Binder J, et al. The MRI spectrum of congenital cytomegalovirus infection. *Prenat Diagn*. 2020 Jan;40(1):110–124.

Image credit: Matthew Robbins, MD



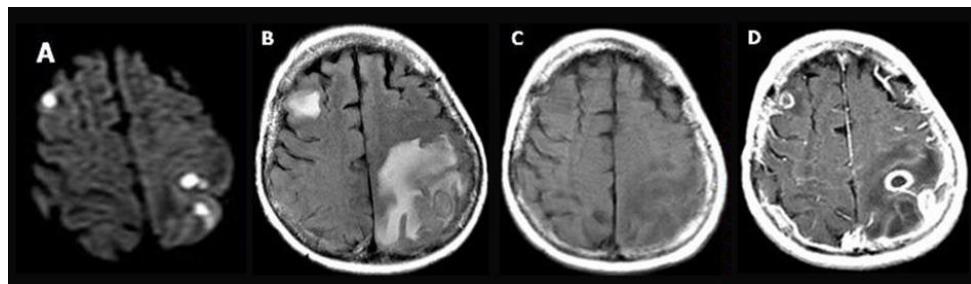
Question #

275 ADULT NEUROLOGY**CORE KNOWLEDGE****Neuroimaging**

This patient's imaging studies show multiple ring-enhancing lesions with adjacent vasogenic edema. The enhancing rings have relatively smooth walls, more commonly seen with infectious masses than with tumors, which more commonly have more irregular and thicker margins. The marked increase in diffusion-weighted signal is more frequently seen with infections compared to tumor.

Acute multiple sclerosis plaques often have open ring configurations, unlike the closed rings seen here. Progressive multifocal encephalopathy typically causes FLAIR signal abnormality without significant enhancement or diffusion restriction. Primary CNS lymphoma can restrict but would have less vasogenic edema and usually demonstrates homogenous enhancement. Immunocompromised patients with lymphoma can demonstrate ring-enhancing lesions.

Greenberg JO (ed). Neuroimaging: A Companion to Adams and Victor's Principles of Neurology. 2nd ed. New York: McGraw-Hill, 1999.

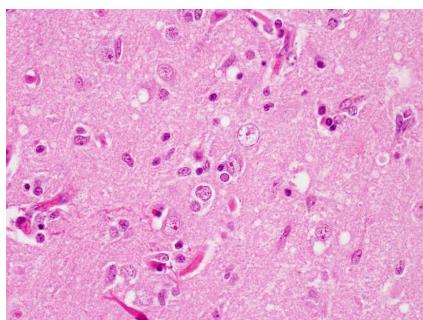


Question #

302 PEDIATRIC NEUROLOGY**Neuropathology**

Subacute sclerosing panencephalitis (SSPE) is caused by defective measles virus replication secondary to natural measles virus infection before age 2 years. Having become rare, SSPE may increase again with the recent decrease in vaccination rates. Intranuclear eosinophilic inclusions and demyelination are seen histologically. Premortem diagnosis can be made by serum or CSF virus-specific IgG.

Yachnis A, Rivera-Zengotita M. High Yield Pathology: Neuropathology. Philadelphia, PA: Elsevier; 2014.

**339 ADULT NEUROLOGY****CORE KNOWLEDGE****Neuroimaging**

The juxtaventricular lesion shown is characteristic of the vesicular stage of neurocysticercosis: a spherical cystic lesion with eccentric calcification (scolex) with no surrounding edema. All other disorders listed (primary CNS malignancy, toxoplasmosis, bacterial abscess, metastasis from a systemic cancer) are likely to have surrounding edema, not this cystic appearance with eccentric calcification.

Raibagkar P, Berkowitz AL. The many faces of neurocysticercosis. J Neurol Sci. 2018 Jul 15; 390:75-76.



Question #

386 NO SPECIFIED PATIENT AGE**CORE KNOWLEDGE****Neuroscience and Mechanism of Disease**

The CSF cryptococcal antigen (CrAg) lateral flow assay is the preferred test for confirming cryptococcal meningitis: it is sensitive, specific, results rapidly, and is widely available. India ink stain is insensitive, culture is sensitive and specific but takes days to return, and PCR is sensitive and specific but not widely available.

Grill MF. Neurologic complications of human immunodeficiency virus. *Continuum Lifelong Learning Neurol*. 2021 Aug;27(4):963–991.

Question #

26 ADULT NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Neurophysiology**

Peripheral nerves are considered to be relatively resistant to radiation injury; however, toxicity related to delayed radiation-induced fibrosis is commonly seen in the brachial plexus and lumbosacral plexus after irradiation for tumors in these regions.

Myokymia is characterized by rhythmic, repetitive, and spontaneous discharges from a motor unit on EMG. Its presence is often seen after radiation injury but not typically with tumor plexopathy. Direct cancerous involvement of the brachial plexus is typically painful and occurs within months of the cancer diagnosis as opposed to years later.

Nolan CP, DeAngelis LM. Neurologic complications of chemotherapy and radiation therapy. *Continuum Lifelong Learning Neurol*. 2015 Apr;2(2):429–451.

32 NO SPECIFIED PATIENT AGE**Neurophysiology**

Large myelinated fibers are measured in clinical nerve conduction studies. Indeed, all routine motor and sensory conduction velocity and latency measurements are obtained from the largest and fastest fibers. Large-diameter fibers have the most myelin and the least electrical resistance, both of which result in faster conduction velocities.

Small myelinated and unmyelinated fibers carry autonomic information (afferent and efferent) and somatic pain and temperature sensations. These fibers are not recorded with standard nerve conduction techniques. Thus, neuropathies that preferentially affect only small fibers will not reveal any abnormalities on nerve conduction studies.

Preston DC, Shapiro BE. Electromyography and Neuromuscular Disorders: Clinical-electrophysiologic Correlations. 4th ed. Philadelphia: Elsevier Saunders; 2020.

Question #

36 ADULT NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Clinical Aspects of Disease**

Sensory loss to pinprick with preservation of vibratory sense and reflexes is consistent with a small fiber neuropathy. These findings are compatible with leprosy, which occurs due to *Mycobacterium leprae*, a neurotropic bacterium. The diagnosis is supported by the distribution of this patient's sensory loss, which includes his extremities, ears, and nose, and the fact that he has emigrated from Brazil, a country endemic for leprosy.

Robinson-Papp J. Infectious neuropathies. *Continuum Lifelong Learning Neurol*. 2012 Feb;18(1):126–138.

Ooi W, Srinivasan J. Leprosy and the peripheral nervous system: basic and clinical aspects. *Muscle Nerve* 2004;30:393–409.

43 NO SPECIFIED PATIENT AGE**Neuroanatomy**

The tibialis anterior, which dorsiflexes and inverts the foot, is innervated by the deep peroneal (fibular) nerve. The peroneus longus is innervated by the superficial peroneal (fibular) nerve. The gastrocnemius plantar flexes the foot and is innervated by the tibial nerve (a branch of the sciatic nerve). The semitendinosus, one of the hamstring muscles, is innervated by the sciatic nerve. The tensor fasciae latae, innervated by the superior gluteal nerve, abducts and medially rotates the thigh. The sartorius muscle inwardly rotates the hip, and flexes the hip and knee and is innervated by the femoral nerve.

Brazis PW, Masdeu JC, Biller J (eds). *Localization in Clinical Neurology*. 8th ed. Philadelphia: Wolters Kluwer; 2022.

Question #

53 NO SPECIFIED PATIENT AGE**Clinical Aspects of Disease**

This patient's presentation of fever, radicular pain, arthralgia, first-degree heart block, and weakness, mononuclear pleocytosis, and nerve root enhancement on imaging studies suggests infectious radiculoneuropathy.

AIDP and CIDP cause acute or subacute weakness and areflexia but usually do not cause fever, and both demonstrate cytoalbuminologic dissociation. Varicella zoster reactivation is usually accompanied by vesicular rash, a finding not present here. In addition, symptom progression over 4 weeks is more indolent than typical for varicella reactivation and suggests Lyme disease. Diabetes mellitus can cause subacute painful root disease but not fever or severe pleocytosis. Of the disorders listed provided, Lyme radiculoneuritis is most likely.

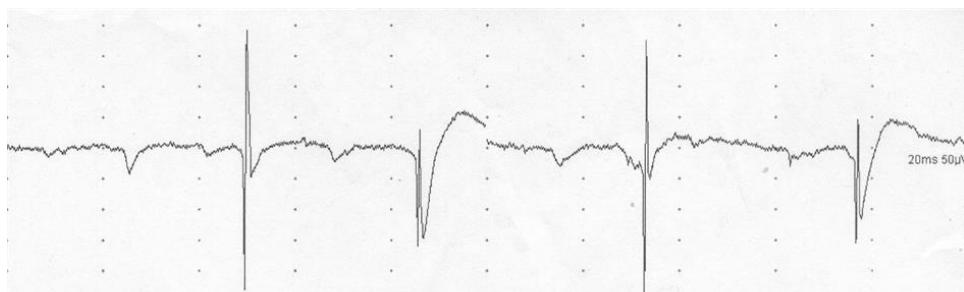
Boegle AK, Narayanaswami P. Infections neuropathies. *Continuum Lifelong Learning Neurol*. 2023 Oct;29(5):1418-1443.

Dabir A, Pawar G. Teaching NeuroImages: Lyme disease presenting as Bannwarth syndrome. *Neurology*. 2018 Oct 9;91(15):e1459-e1460.

62 ADULT NEUROLOGY**CORE KNOWLEDGE****Neurophysiology**

Fibrillations appear in affected muscles approximately 3 to 6 weeks after acute axonal injury. Plexus and nerve lesions affect the sensory nerve conduction studies (postganglionic lesions). Intraspinal lesions such as radiculopathy may have normal nerve conduction studies (preganglionic). Radiculopathy is diagnosed when there is evidence of denervation in muscles supplied by a single nerve root but more than one peripheral nerve. The pronator teres (median) and triceps (radial) share innervation by the C7 nerve root.

Preston DC, Shapiro BE. *Electromyography and Neuromuscular Disorders: Clinical-electrophysiologic Correlations*. 4th ed. Philadelphia: Elsevier Saunders; 2020.



Question #

73 ADULT NEUROLOGY**CORE KNOWLEDGE****Clinical Aspects of Disease**

This patient most likely has brachial neuritis (Parsonage-Turner syndrome). This disorder is more common in young adults and sometimes follows physical exertion or other physical stress, including upper respiratory tract infection, vaccination, surgery, and childbirth. A small percentage of patients have an autosomal dominant inherited form of the disorder.

Typically, brachial plexitis presents with severe pain followed by weakness and atrophy in the upper extremity. This patient's weakness does not localize to any specific portion of the brachial plexus and is more likely multiple motor predominant mononeuropathies. Weakness may occur within 24 hours, but its onset is more commonly delayed 2 weeks or longer. The prognosis for eventual recovery is good. The role of corticosteroids is not certain, although they often provide considerable pain relief.

Bril V, Katzberg HD. Acquired immune axonal neuropathies. *Continuum Lifelong Learning Neurol*. 2014 Oct;20(5):1261-1273.

80 ADULT NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Treatment/Management**

This patient has immune checkpoint-related myositis (ICI-myositis) manifested by proximal weakness and markedly elevated creatine kinase in the setting of treatment with a PD1 antibody for metastatic melanoma. Myocarditis occurs in up to 4% of patients with ICI-myositis and is associated with significant mortality. Thus, prompt screening for myocarditis with serum troponin is important.

The other serum tests (aldolase, carnitine, erythrocyte sedimentation rate, myositis-specific antibodies) do not add diagnostic utility in this setting and are not cost-effective. Erythrocyte sedimentation rate may be elevated but is nonspecific and does not change the diagnosis. Testing for myositis-specific antibodies can be costly and has no established role in the diagnosis of ICI-myositis.

Guidon AC. Lambert-Eaton myasthenic syndrome, botulism and immune checkpoint inhibitor-related myasthenia gravis. *Continuum Lifelong Learning Neurol*. 2019 Dec;25(6):1785-1806.

Hu J-R, Florido R, Lipson EJ, et al. Cardiovascular toxicities associated with immune checkpoint inhibitors. *Cardiovasc Res*. 2019 Apr 15;115(5):854-868.

Question #

92 NO SPECIFIED PATIENT AGE**CORE KNOWLEDGE****Treatment/Management**

According to the 2020 Update of the International Consensus Guideline for Management of Myasthenia Gravis, aminoglycoside, fluoroquinolone, and macrolide should be used with caution, if at all, as these antibiotics may exacerbate myasthenia gravis. The same update advises against using telithromycin, which is a ketolide. These antibiotics exacerbate myasthenia gravis by interfering with neuromuscular transmission presynaptically, postsynaptically, or both. Cephalosporin, penicillin, sulfonamide, and lincosamide (clindamycin) are safe to use in patients with myasthenia gravis.

Narayanaswami P, Sanders DB, Wolfe G, et al. International consensus guidance for management of myasthenia gravis: 2020 update. *Neurology*. 2021;96(3):114–22. Epub 2020/11/05.

Sheikh S, Alvi U, Soliven B, et al. Drugs that induce or cause deterioration of myasthenia gravis: an update. *J Clin Med*. 2021;10(7). Epub 2021/05/01.

101 NO SPECIFIED PATIENT AGE**Neuroanatomy**

The opponens pollicis is innervated by the median nerve and would be involved in a patient with carpal tunnel syndrome. The adductor pollicis, third lumbrical, and palmar interosseous are innervated by the ulnar nerve. The flexor pollicis longus is innervated by the anterior interosseous nerve.

Preston DC, Shapiro BE. Electromyography and Neuromuscular Disorders: Clinical-electrophysiologic Correlations. 4th ed. Philadelphia: Elsevier Saunders; 2020.

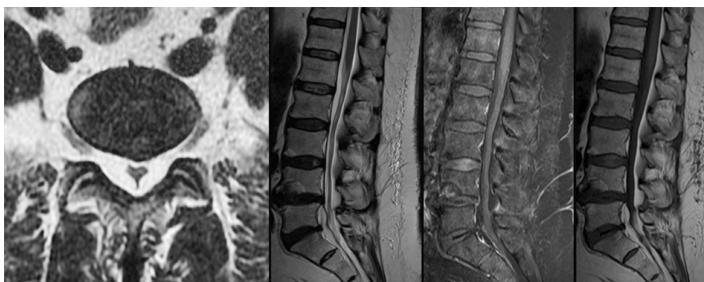
Question #

105 ADULT NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Neuroimaging**

Epidural lipomatosis is the preferred response. The images show significant fat posterior to thecal sac and the fat suppression postcontrast image shows that the signal of the epidural mass suppresses. Epidural hemorrhage has variable signal intensity but would not suppress on fat suppression sequences. Dural arteriovenous fistula would show vascular flow voids and not uniform thickening of the fat.

Leptomeningeal carcinomatosis would demonstrate thick, irregular nerve root enhancement. The vertebral bodies are unremarkable, without hyperintensity suggestive of hemangioma.

Yasuda T, Suzuki K, Kawaguchi Y, et al. Clinical and imaging characteristics in patients undergoing surgery for lumbar epidural lipomatosis. *BMC Musculoskelet Disord.* 2018 Mar;19(1):66.

**111 ADULT NEUROLOGY****CORE KNOWLEDGE****Diagnostic Procedures**

This patient has the hallmark signs of an inflammatory myopathy with proximal weakness, normal sensation and reflexes, and markedly elevated creatine kinase. Muscle biopsy is the best way to confirm and characterize inflammatory myopathies. Although EMG/nerve conduction studies and skeletal muscle MRI help support the diagnosis, neither is specific for any one type of inflammatory myopathy.

Interstitial lung disease and dysphagia can be associated with inflammatory myopathies but are not specific. Acetylcholine receptor-binding antibodies are used to confirm myasthenia gravis, an unlikely diagnosis here given the patient's examination findings and markedly elevated serum creatine kinase.

Amato AA, Greenberg SA. Inflammatory myopathies. *Continuum Lifelong Learning Neurol.* 2013 Dec;19(6):1615-1633.

Question #

118 PEDIATRIC NEUROLOGY**Neurophysiology**

Botulinum toxin inhibits release of acetylcholine vesicles from the presynaptic terminal, resulting in failure of the muscle fiber to fire. When this occurs in many muscle fibers, the compound muscle potential amplitude (CMAP) is reduced.

Voltage-gated calcium channel inhibition occurs in Lambert-Eaton myasthenic syndrome. The number of acetylcholine receptors is reduced in myasthenia gravis as a result of immune-mediated destruction. Hyperpolarization of the presynaptic nerve terminal and necrosis of the postsynaptic terminal are not recognized causes of neuromuscular disease.

Rossetto O, Pirazzini M, Fabris F, et al. Botulinum neurotoxins: mechanism of action. Handb Exp Pharmacol. 2021;263:35–47.

136 ADULT NEUROLOGY**CORE KNOWLEDGE****Clinical Aspects of Disease**

Inclusion body myositis is a slowly progressive inflammatory disorder in older individuals (male predominant). Clinical features include early weakness and atrophy of select muscles: quadriceps, flexors of the forearms, and ankle dorsiflexors. There are other associated laboratory and muscle biopsy findings.

Motor neuron disease is unlikely to run such a slowly progressive course and is associated with other examination abnormalities such as reflex changes. Polymyositis is generally more fulminant, painful, and symmetric. Central core disease is congenital with fairly mild progression over the life span. Both types of myotonic dystrophy are autosomal dominant, typically present earlier in life, and have many systemic manifestations.

Amato AA, Greenberg SA. Inflammatory myopathies. Continuum Lifelong Learning Neurol. 2013 Dec;19 (6):1615–1633.

139 ADULT NEUROLOGY**CORE KNOWLEDGE****Clinical Aspects of Disease**

Isolated visible muscle twitching for several years with no other concurrent symptoms and an EMG without evidence of denervation is most consistent with benign fasciculation syndrome.

Sansone VA. Episodic muscle disorders. Continuum Lifelong Learning Neurol. 2019 Dec;25(6):1696–1711.

Question #

150 PEDIATRIC NEUROLOGY**CORE KNOWLEDGE****Neuroscience and Mechanism of Disease**

This patient most likely has Duchenne muscular dystrophy, which is characterized by an X-linked recessive inheritance pattern and a pathogenic variant of the *DMD* gene located on Xp21.2.

Wicklund MP. The muscular dystrophies. *Continuum Lifelong Learning Neurol*. 2013 Dec;19(6):1535–1570.

153 ADULT NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Treatment/Management**

TTR amyloidosis is a multiple-system disorder that involves small nerve fibers early in the disease course, often with severe autonomic dysfunction. The goal of treatment includes disease-modifying therapy to stabilize misfolding of mutant TTR (TTR stabilizers) or reduce the levels of TTR.

Patisiran is an siRNA that targets a sequence of mRNA on TTR, targeting it for mRNA-associated destruction. It significantly reduces TTR levels and slows neurologic worsening.

Diflunisal is an NSAID that works by stabilizing TTR through the binding of T4 sites on the tetrameric protein and decreasing fibril formation. Tafamidis is a thyroxine-like small ligand inhibitor that stabilizes mutant TTR tetramers, inhibiting dissociation into monomers.

Renal injury is not a feature of TTR amyloidosis; therefore, renal transplant has no role in therapy. The liver is the main producer of amyloid, and liver transplant works by removing the source of ATTR. Early liver transplant in patients with ATTR Val30Met results in better survival at 10 years.

Kapoor M, Rossor AM, Laura M, et al. Clinical presentation, diagnosis, and treatment of TTR amyloidosis. *J Neuromuscular Dis*. 2019;6(2):189–199.

158 ADULT NEUROLOGY**CORE KNOWLEDGE****Diagnostic Procedures**

Initial evaluation for distal symmetric polyneuropathy includes physical examination and serum laboratory studies for common causes such as vitamin B12 metabolites, serum electrophoresis with immunofixation, and blood glucose. Additional serum and electrophysiologic testing can be considered following these initial studies or in atypical cases.

England JD, Franklin G, Gjorvad G, et al. Quality improvement in neurology: distal symmetric polyneuropathy quality measures. *Neurology*. 2014 May 13;82(19):1745–1748.

Question #

168 ADULT NEUROLOGY**CORE KNOWLEDGE****Neuroscience and Mechanism of Disease**

The symptom complex of ataxia, ophthalmoparesis, and areflexia is consistent with the Miller–Fisher variant of Guillain–Barré syndrome; the anti–GQ1b antibody is present in 85% to 90% of patients.

Purkinje cell antibody is associated with paraneoplastic cerebellar ataxia. Glutamic acid decarboxylase antibody is associated with stiff–person syndrome. Myelin–associated glycoprotein antibody is seen with distal acquired demyelinating sensory neuropathy, and N-type calcium channel antibody is associated with Lambert–Eaton myasthenic syndrome.

Teener JW. Miller Fisher's syndrome. Semin Neurol. 2012 Nov;32(5):512–516.

178 ADULT NEUROLOGY**CORE KNOWLEDGE****Neuroanatomy**

Shoulder abduction is performed through the combined action of the supraspinatus muscle (supplied by the suprascapular nerve) and the deltoid (supplied by the axillary nerve).

Preston DC, Shapiro BE. Electromyography and Neuromuscular Disorders: Clinical-electrophysiologic Correlations. 4th ed. Philadelphia: Elsevier Saunders; 2020.

186 ADULT NEUROLOGY**CORE KNOWLEDGE****Diagnostic Procedures**

This patient's presentation of multiple symptoms from different organ systems is concerning for an infiltrative process such as amyloidosis (eg, renal dysfunction, autonomic dysfunction, liver and spleen enlargement, skin changes, and bone marrow failure). Tissue biopsy is indicated for definitive diagnosis and to help guide treatment. Although EMG/nerve conduction studies are useful in documenting the presence and type of peripheral neuropathy, these studies are not helpful in making the diagnosis. Serum autoimmune/paraneoplastic panel is not likely to make a diagnosis in this clinical situation.

Palladini G, Milani P, Merlini G. Management of AL amyloidosis in 2020. Blood. 2020 Dec 3;136(23):2620–2627.

Ryšavá R. AL amyloidosis: advances in diagnostics and treatment. Nephrol Dial Transplant. 2019 Sep 1;34(9):1460–1466.

Question #

194 ADULT NEUROLOGY**CORE KNOWLEDGE****Clinical Aspects of Disease**

Saddle anesthesia, sphincter loss, and loss of ankle reflexes after a fall suggest a process involving the conus medullaris or cauda equina. The absence of knee reflexes is not consistent with a conus medullaris lesion, as the L2/3 cell bodies are above the conus medullaris. Instead, the absent knee reflexes suggests a cauda equina process at L3/4. Of the disorders listed, the most likely diagnosis is a midline disk herniation with compression of the cauda equina.

Intramedullary hematoma almost universally presents with excruciating pain. The neurologic deficit, which occurs suddenly, correlates to the location of the hematoma.

Retroperitoneal hemorrhages are most often secondary to trauma within the abdominal cavity and consist of abdominal and flank bruising. Although AIDP can be associated with initial sensory changes, ascending weakness is typically a prominent symptom. Subdural hematoma would not be expected to produce bilateral foot sensory symptoms and autonomic deficits unless it is large and located bilaterally, in which case many other symptoms would be likely seen.

Jankovic J, Mazzotta JC, Pomeroy SL, et al (eds) Bradley and Daroff's Neurology in Clinical Practice. 7th ed. Philadelphia: Elsevier; 2016.

Olivero C, Wang H, Hanigan WC, et al. Cauda equina syndrome (CES) from lumbar disc herniations. J Spinal Disord Tech. 2009 May;22(3):202–206.

201 ADULT NEUROLOGY**CORE KNOWLEDGE****Neuroanatomy**

The S1 nerve root subserves sensation from the sole and the lateral three toes, as well as the ankle jerk reflex and ankle plantar flexion (along with S2). Involvement of L4 would produce weak ankle dorsiflexion, whereas L5 involvement would produce weak ankle eversion (and hip extension). Peroneal neuropathy would produce weak ankle dorsiflexion and eversion with numbness on the dorsal foot and lateral foreleg. A cauda equina syndrome would produce diffuse lower extremity weakness, numbness, and areflexia.

Brazis PW, Masdeu JC, Biller J (eds). Localization in Clinical Neurology. 8th ed. Philadelphia: Wolters Kluwer; 2022.

Question #

212 ADULT NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Clinical Aspects of Disease**

Cardiac surgery is now typically performed through a median sternotomy. Approximately 5% of patients who undergo this procedure experience brachial plexus injury due to direct compression of the lower trunk. Most lesions affect the lower trunk or C8/T1 nerve roots.

Ferrante MA. Brachial plexopathies. *Continuum Lifelong Learning Neurol*. 2014 Oct;20(5):1323-1342.

218 NO SPECIFIED PATIENT AGE**CORE KNOWLEDGE****Diagnostic Procedures**

This patient has acute-onset right foot drop and numbness over the lateral aspect of the leg and the top of the foot from a perineal neuropathy. One week later, needle EMG would be expected to show no abnormal spontaneous activity and normal motor unit morphology but reduced recruitment. Motor unit recruitment is reduced at the time of axonal injury. Spontaneous activity develops 2 to 3 weeks after the axonal injury and resolves with collateral reinnervation. Motor unit amplitude increases with collateral reinnervation, which begins around 3 months after axonal injury.

A subacute (<3 months) axonal injury would be expected to show abnormal spontaneous activity, normal motor unit morphology, and reduced recruitment. A chronic axonal process (>6 months) with collateral reinnervation would be expected to show no abnormal spontaneous activity, increased motor unit action potential amplitude, and reduced recruitment. If the degree of axonal loss is so severe that complete collateral reinnervation is not possible or the axonal process is ongoing, abnormal spontaneous activity, increased motor unit action potential amplitude, and reduced recruitment would be expected.

No abnormal spontaneous activity, normal motor unit morphology, and full recruitment would be expected in a normal muscle. Abnormal spontaneous activity, decreased motor unit amplitude, and early recruitment describe an EMG pattern that can be seen in myopathic lesions.

Uncini A, Santoro L. The electrophysiology of axonal neuropathies: more than just evidence of axonal loss. *Clin Neurophysiol*. 2020 Oct;131(10):2367-2374.

Question #

234 ADULT NEUROLOGY**CORE KNOWLEDGE****Treatment/Management**

This patient's presentation is consistent with myasthenia gravis (MG), which can worsen in the first trimester of pregnancy or postpartum. MG can be managed safely and successfully in these patients.

Pyridostigmine is safe in doses up to 600 mg/day. Corticosteroids are safe during pregnancy and form the mainstay of treatment. IVIg and plasma exchange are both safe and most useful for treatment of exacerbations.

Mycophenolate mofetil, an important form of treatment for patients without childbearing potential, is an FDA category D drug that can cause miscarriage and has been associated with fetal malformation. It is contraindicated during pregnancy and thus not prescribed in women of childbearing age.

Ciafaloni, E. Myasthenia gravis and congenital myasthenic syndromes. *Continuum Lifelong Learning Neurol.* 2019 Dec;25(6):1767-1784.

Question #

257 NO SPECIFIED PATIENT AGE

Diagnostic Procedures

This patient presents with a rapidly evolving thoracic myelopathy. The imaging study demonstrates flow voids on the surface of the lower thoracic spinal cord, suggestive of a dural arteriovenous fistula. Spinal angiography should be ordered next. In this patient, the angiogram demonstrated an L2 origin artery of Adamkiewicz feeding a spinal dural fistula. The other studies listed (cerebral angiography, brain MRI, lumbar puncture, serum testing for aquaporin-4 antibodies) are unnecessary and thus not cost-effective.

JadHAV AP. Vascular myelopathies. Continuum Lifelong Learning Neurol. 2024 Feb;30(1):160–179.



269 NO SPECIFIED PATIENT AGE

Neuropathology

Wallerian degeneration is the response of the distal part of an axon to transection of the nerve. The neuronal cell body may undergo central chromatolysis but does not die. Onion bulb formation occurs with repeated episodes of demyelination followed by remyelination. Denervated muscle cells will demonstrate fiber-type grouping.

Ellison DW, Love S (eds). *Neuropathology: A Reference Text of CNS Pathology*. 3rd ed. San Francisco: Elsevier; 2013.

Question #

277 PEDIATRIC NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Clinical Aspects of Disease**

Spinal muscular atrophy type I (Werdnig–Hoffmann disease) presents in the first year with weakness, often progressing to death or need for assisted ventilation within a year if untreated. Extraocular muscles and small muscles of the hands are typically spared. Fasciculations are typically visible in the tongue and occasionally in the small muscles of the hands.

Arzimanoglou A, O'Hare A, Johnston M, et al (eds). Aicardi's Diseases of the Nervous System in Childhood. 4th ed. London: Mac Keith Press; 2018.

284 PEDIATRIC NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Clinical Aspects of Disease**

Acid maltase deficiency (Pompe disease) is a lysosomal glycogen storage disease that affects practically all tissues and results from a defect of 1,4-glucosidase (acid maltase). Hypotonia, failure to thrive, and decreased reflexes develop during the first few months of life.

Cardiomegaly is prominent in infantile forms, which more commonly present with pulmonary insufficiency. Unlike other glycogenoses, the liver is normal in size or only slightly enlarged, and there are no abnormalities of glucose homeostasis. PAS-positive glycogen is seen in membrane-bound vacuoles in muscle, hepatocytes, and Schwann cells, but no abnormalities are seen in myelin sheaths.

Cardiomegaly would be rare in the remaining choices (Duchenne muscular dystrophy, spinal muscular atrophy type 1, myotonic dystrophy, neonatal myasthenia gravis). Areflexia would be unusual in myotonic dystrophy. Spinal muscular atrophy presents with profound hypotonia, absent deep tendon reflexes, and tongue fasciculations; the heart is unaffected.

Swaiman AF, Ashwal S, Ferriero DM, et al (eds). Swaiman's Pediatric Neurology. Principles and Practice. 6th ed. Philadelphia: Elsevier; 2017.

Question #

294 NO SPECIFIED PATIENT AGE**CORE KNOWLEDGE****Clinical Aspects of Disease**

Myotonic dystrophy is the most common muscular dystrophy of adults. It is a trinucleotide repeat disorder that has an autosomal dominant inheritance pattern. Therefore, clinical worsening (anticipation) can be seen with successive generations, as illustrated here. Of the options listed (facioscapulohumeral dystrophy, limb girdle muscular dystrophy, mitochondrial myopathy, myotonic dystrophy, and thyroid myopathy), only myotonic dystrophy exhibits both distal weakness and percussion myotonia. Facial weakness and early cardiac death are also seen.

Wicklund MP. The muscular dystrophies. *Continuum Lifelong Learning Neurol*. 2013 Dec;19(6):1535–1570.

301 ADULT NEUROLOGY**CORE KNOWLEDGE****Clinical Aspects of Disease**

The femoral nerve innervates muscles involved in hip flexion and knee extension, and its sensory territory includes the territory of the saphenous nerve below the knee. It is one of the most common nerves to be injured during childbirth.

The obturator nerve also can be injured during childbirth, but it supplies muscles that adduct the thigh. Peroneal nerve injury would cause foot drop and weakness of ankle eversion with numbness on the lateral leg and foot dorsum. Tibial nerve injury would cause weakness of ankle plantar flexion and an absent Achilles reflex. Sciatic nerve injury would cause weakness of all muscles in the leg and the hamstrings, as well as an absent Achilles reflex.

Kimura J, Strakowski JA (eds). *Electrodiagnosis in Diseases of Nerve and Muscle: Principles and Practice*. 5th ed. New York: Oxford University Press; 2025.

Question #

312 ADULT NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Clinical Aspects of Disease**

This patient has Fabry disease, an X-linked disorder caused by mutation of the alpha-galactosidase A (*GLA*) gene. Patients typically present in the second or third decade of life with painful small fiber peripheral neuropathy, renal dysfunction, and angiokeratoma of the skin. There is an associated increased incidence of ischemic stroke, usually presenting by the third decade and initially often due to small vessel disease. Subsequently, both large and small vessel strokes can occur due to a vasculopathy.

The apolipoprotein E4 allele (*APOE4*) confers an increased risk of Alzheimer disease and microtubule-associated protein tau (*MAPT*) with tau dementias. The *NOTCH3* gene is associated with CADASIL, and the transthyretin (*TTR*) gene with the small fiber peripheral neuropathies and hemorrhagic CNS vasculopathies of familial amyloidosis.

Schiffmann R. Fabry disease. *Handb Clin Neurol*. 2015;132:231–248.

316 ADULT NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Neuroimaging**

This patient's presentation is typical of Hirayama disease, which most commonly presents in young males as slowly progressive unilateral weakness and atrophy of the hand muscles. Originally classified as a focal motor neuron disease, it is now recognized to be a focal cervical myelopathy. The first autopsied case identified anterior-posterior flattening of the lower cervical cord associated with ischemic and atrophic changes of the anterior horn cells.

Dynamic cervical MRI is now the diagnostic test of choice. MRI performed during neck flexion demonstrates forward displacement of the posterior wall of the lower cervical dural sac, which is the hallmark and primary pathogenetic mechanism of the disease.

London ZN. A structured approach to the diagnosis of peripheral nervous system disorder. *Continuum Lifelong Learning Neurol*. 2020 Oct;26(5):1130–1160.

Huang YL, Chen C-J. Hirayama disease. *Neuroimaging Clin N Am*. 2011 Nov;21(4):939–50, ix–x.

Question #

327 NO SPECIFIED PATIENT AGE**CORE KNOWLEDGE****Neuroanatomy**

Fasciculation potentials result from spontaneous discharges of a whole or possibly part of a motor unit. The generator source of nearly all fasciculations has a motor axonal origin. Fasciculation potentials, although typically associated with diseases of anterior horn cells, are also seen in radiculopathy, entrapment neuropathy, and muscular pain-fasciculation syndrome.

Preston DC, Shapiro BE (eds). Electromyography and Neuromuscular Disorders: Clinical-electrophysiologic Correlations. 4th ed. Philadelphia: Elsevier Saunders; 2020.

338 ADULT NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Treatment/Management**

Eculizumab is an FDA-approved treatment for seropositive generalized myasthenia gravis. A complement inhibitor, eculizumab increases the risk of meningococcal infections. The prescriber must enroll in a risk evaluation and mitigation strategy (REMS) program, and the patient must receive both types of meningococcal vaccine at least 2 weeks before the first dose of eculizumab.

Quantitative immunoglobulins are sometimes measured before treatment with IVIg to identify patients with IgA deficiency, as they may have an anaphylactic reaction to IVIg. Screening for the JC virus antibody is required before and during treatment with natalizumab for multiple sclerosis. Hepatitis B and C screening is recommended before treatment with rituximab. Checking varicella immune status and/or vaccinating for varicella is desirable (but not mandatory) in patients older than age 50 years.

Malpica L, van Duin D, Moll S. Preventing infectious complications when treating nonmalignant immune-mediated hematologic disorders. Am J Hematol. 2019;94:1396-1412.

Question #

344 ADULT NEUROLOGY**CORE KNOWLEDGE****Clinical Aspects of Disease**

This sudden-onset of paraparesis suggests a spinal cord infarction. Examination reveals evidence of corticospinal, spinothalamic, and autonomic dysfunction with sparing of the dorsal columns, which is in the distribution of the anterior spinal artery.

Although this infarction is limited to a vascular distribution, spinal cord infarctions frequently cross vascular distributions. In the classic description of a spinal cord infarction, the nadir of weakness occurs within 4 hours, though in a subset of patients weakness can occur over 4 to 48 hours and is more difficult to distinguish from transverse myelitis.

Guillain–Barré syndrome is a consideration, although acute onset of paraplegia with back pain and complete sparing of the upper extremities is more consistent with spinal cord pathology. In demyelinating forms of Guillain–Barré syndrome, vibration and joint position sense would be affected. This patient does not have risk factors for epidural hematoma.

Brazis PW, Masdeu JC, Biller J (eds). Localization in Clinical Neurology. 8th ed. Philadelphia: Wolters Kluwer; 2022.

349 ADULT NEUROLOGY**CORE KNOWLEDGE****Clinical Aspects of Disease**

This patient has a cervical central spinal cord syndrome with characteristic "cape-like" sensory loss due to spinothalamic tract involvement, dissociated spinothalamic and posterior column dysfunction, and segmental sensory and motor neuron dysfunction. A cord syrinx is the most likely etiology. Ependymomas, which are the most common intramedullary tumor of the spinal cord, often have an associated syrinx.

Spinal arteriovenous fistulae are rare in the cervical region and usually do not produce a central cord syndrome. The progressive course over several months makes demyelinating disease unlikely. Copper deficiency typically affects the posterior and lateral columns of the spinal cord and is painless. Cervical disk herniation with extramedullary cord compression is unlikely to produce a central cord syndrome.

Brazis PW, Masdeu JC, Biller J (eds). Localization in Clinical Neurology. 8th ed. Philadelphia: Wolters Kluwer; 2022.

Question #

353 PEDIATRIC NEUROLOGY**CORE KNOWLEDGE****Treatment/Management**

Corticosteroids have been shown to prolong ambulation in patients with Duchenne muscular dystrophy (DMD). The effect is to induce small amounts of dystrophin, not as an anti-inflammatory treatment, so other dosing strategies are not helpful. Intravenous gentamicin has been proposed for one of the rare point mutations causing DMD. L-carnitine, creatine, valproic acid, and coenzyme Q10 have been used for various muscle disorders but have no proven efficacy in DMD.

Swaiman AF, Ashwal S, Ferriero DM, et al (eds). Swaiman's Pediatric Neurology. Principles and Practice. 6th ed. Philadelphia: Elsevier, 2017.

Gloss D, Moxley RT, Ashwal S, et al. Practice guideline update summary: corticosteroid treatment in Duchenne dystrophy. Report of the Guideline Development Subcommittee of the American Academy of Neurology. Neurology Feb 2; 2016;86(5):465–472. Reaffirmed January 2022.

359 NO SPECIFIED PATIENT AGE**SUBSPECIALTY KNOWLEDGE****Neurophysiology**

In acquired demyelinating polyneuropathy, varied demyelination of individual motor nerve fibers causes their potentials to arrive at the muscle at different times. This results in a CMAP that is prolonged in duration, low in amplitude, and irregular in shape. This is termed pathologic temporal dispersion. Nerve conduction studies in acquired demyelinating polyneuropathy can also cause a reduction in proximal CMAP amplitude when compared to distal CMAP amplitude without an increase in duration. This process is known as conduction block.

Delay at the neuromuscular junction occurs in myasthenia gravis and Lambert-Eaton myasthenic syndrome but does not affect the CMAP duration, though it may affect amplitude. Hyperpolarization of muscle membrane and elevated stimulation threshold do not affect the CMAP. Low temperature increases, not decreases, CMAP amplitude.

Preston DC, Shapiro BE. Electromyography and Neuromuscular Disorders: Clinical-electrophysiologic Correlations. 4th ed. Philadelphia: Elsevier Saunders; 2020.

Question #

364 NO SPECIFIED PATIENT AGE**SUBSPECIALTY KNOWLEDGE****Neuroanatomy**

The anterior interosseous nerve is a motor branch of the median nerve after it passes between the two heads of the pronator teres. The anterior interosseous nerve innervates the flexor pollicis longus, flexor digitorum profundus to the index and middle fingers, and pronator quadratus. A lesion of this nerve impairs an individual's ability to make an OK sign with the thumb and index finger, producing instead a pinching of the thumb and index finger.

Brazis PW, Masdeu JC, Biller J. Localization in Clinical Neurology. 7th ed. Philadelphia: Lippincott Williams and Wilkins; 2017.

370 PEDIATRIC NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Clinical Aspects of Disease**

The myopathic form of carnitine palmitoyltransferase II (CPT II) deficiency is the most common disorder of lipid metabolism involving skeletal muscle. It is also the most common cause of hereditary rhabdomyolysis. CPT II transports acylcarnitine across the mitochondrial membrane for fatty oxidation.

Almannai M, Alfadhel M, El-Hattab AW. Carnitine inborn errors of metabolism. *Molecules*. 2019 Sep 6;24(18):3251.

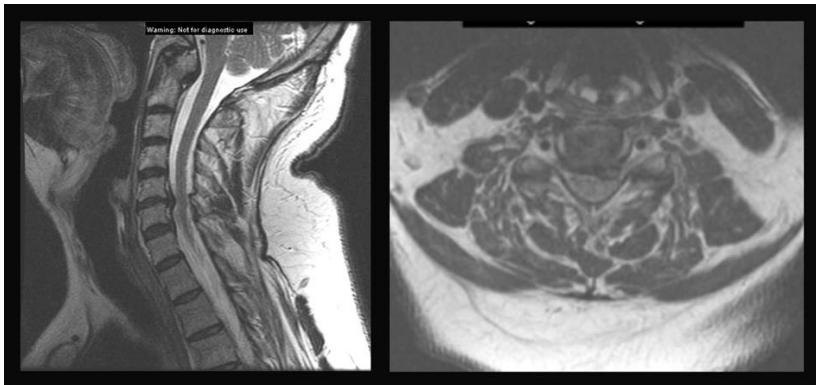
Saponaro C, Gaggini M, Carli F, et al. The subtle balance between lipolysis and lipogenesis: a critical point in metabolic homeostasis. *Nutrients*. 2015 Nov 13;7(11):9453-9474.

Question #

391 ADULT NEUROLOGY**CORE KNOWLEDGE****Neuroimaging**

The elevated dura is visible as a thin hypointense line on the sagittal T2-weighted MRI scan. This extradural localization makes intradural compression by metastasis or osteophyte incorrect. The herniation lesion is centered at the disk and is isointense to the disk. Abscess, lymphoma, and metastasis would not be localized in the disk.

Diehn FE, Krecke KN. Neuroimaging of spinal cord and cauda equina disorders. Continuum Lifelong Learning Neurol. 2021 Feb;27(1):225–263.



Question #

392 PEDIATRIC NEUROLOGY**Contemporary Issues**

In some states, pregnancy may be terminated at any time during gestation. However, once an infant is born, it has the rights afforded to all people. While parents serve as surrogate decision makers, treatment decisions must be directed by the best interests of the child.

Clinicians must assess, to the best of their abilities, an infant's prognosis with and without certain interventions. If the infant is likely to survive and the risk of unacceptably severe morbidity is low, withholding indicating interventions is not appropriate. In the situation described, if all medical/surgical care is pursued, this infant is likely to survive and perhaps have mild to moderate disability. If nutrition is withheld, or if the infant does not undergo an indicated neurosurgical intervention, suffering and death are likely. The rights of an infant to receive this care supersede parental rights.

At this time, there is no indication that the infant in this scenario will need to be placed in protective custody. A discussion between the health care team and the parents is needed first to ensure the parents understand the prognosis and why medical intervention/nutrition cannot be withheld.

American College of Obstetricians and Gynecologists. Committee on Obstetric Practice, Committee on Ethics. ACOG Committee Opinion Number 786 Perinatal Palliative Care. Pediatrics. 2019 Dec;144(6):e20193146.

de Vos MA, Seeber AA, Gevers SKM, et al. Parents who wish no further treatment for their child. J Med Ethics. 2015 Feb;41(2):195–200.

American Academy of Pediatrics Committee on Fetus and Newborn; Bell EF. Noninitiation or withdrawal of intensive care for high-risk newborns. Pediatrics. 2007 Feb;119(2):401–403.

Racine E, Shevell MI. Ethics in neonatal neurology: When is enough, enough? Pediatr Neurol. 2009 Mar;40(3):147–155.

Question #

15 ADULT NEUROLOGY**CORE KNOWLEDGE****Neuroimaging**

Osteoblastic metastases, most commonly seen in prostate cancer, demonstrate hypointense vertebral body lesions on both T1- and T2-weighted imaging, as seen here. Lytic vertebral body metastases as seen in lung cancer, melanoma, and renal cell carcinoma, are T2 isointense or hyperintense and will enhance with contrast.

Hemangiomas typically have a hyperintense appearance on noncontrast T1-weighted views, along with a honeycomb appearance. Spondylosis is another name for degenerative disk disease, which is not a pertinent finding on these images. Radiation-induced changes would cause diffusely hyperintense signal on noncontrast T1-weighted views. There is no loss of height at any level to suggest fracture.

Salzman KL, Jhaveri MD, Ross JS (eds). ExpertDDx: Brain and Spine. 3rd ed. Philadelphia: Elsevier; 2023.



Question #

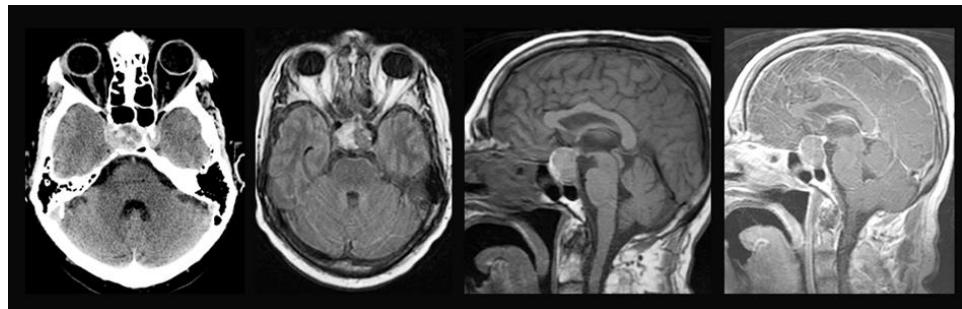
29 ADULT NEUROLOGY**Neuroimaging**

These imaging studies demonstrate increased density within the pituitary fossa extending to the cavernous sinuses bilaterally with an expansile lesion, seen on the FLAIR and T1 views as areas of both increased and decreased signal. An ovoid mass throughout the suprasellar cistern is compressing the optic chiasm. It appears as a large pituitary mass, likely a pituitary macroadenoma. The noncontrast view shows a perimeter of increased T1-weighted signal.

A compilation of these features is consistent with hemorrhagic transformation (pituitary apoplexy of a pituitary tumor mass). A pituitary tumor of this size can be expected to result in bitemporal hemianopia. However, in the absence of hemorrhagic transformation, the tumor's presence would not be expected to result in impaired arousal as described here.

A colloid cyst would not be expected in this location and generally arises as an intraventricular lesion adjacent to the foramen of Monro in the third ventricle. A metastatic lesion within the sella would be in the differential of a tumor mass; however, again, it would not be the best clinical explanation for this patient's clinical presentation of sudden coma.

Jhaveri MD, Salzman KL, Osborn AG (eds). Diagnostic Imaging: Brain. 4th ed. Philadelphia: Elsevier; 2016.



Question #

85 ADULT NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Neuroimaging**

This T1-weighted MRI scan shows a mixed-signal destructive mass involving the clivus and nasopharynx extending to the spinal canal. The lesion is consistent with a clivus chordoma. The ventral pontine surface is compressed.

Primary tumors such as chordomas and cartilaginous tumors of the skull base are rare. Chordomas arise from remnants of the embryonic notochord, which is a mesodermal derivative. Cranial chordomas are most common in the third and fourth decades of life, with men affected more often than women. Cartilaginous tumors occur between 20 and 60 years of age. They are extradural, with over half arising in or adjacent to the body of the sphenoid bone.

Radiologically, the normal high-signal marrow cavity of the clivus is replaced by a lower signal intensity tumor. Large areas of calcification may be seen as void phenomena.

Radiographically, distinguishing among chordomas, chondrosarcomas, and chondromas may be impossible. Meningiomas are isointense to the brain before contrast. This patient has an extrapontine lesion; the brainstem is not involved. The pituitary gland is normal. Parapharyngeal abscesses are usually smoothly contoured.

Ham JS, Huss RG, Benson JE, et al. MRI imaging of the skull base. *J Comput Assist Tomogr*. 1984;8:944-952.

McGinnis BD, Brady TJ, New PF, et al. MR imaging of tumors of the posterior fossa. *J Comput Assist Tomogr*. 1984;7:575-584.



Question #

120 NO SPECIFIED PATIENT AGE**Neuroanatomy**

Germ cell tumors most frequently occur in midline structures, especially the pineal. They are histologically similar to their counterparts in the ovaries and testes.

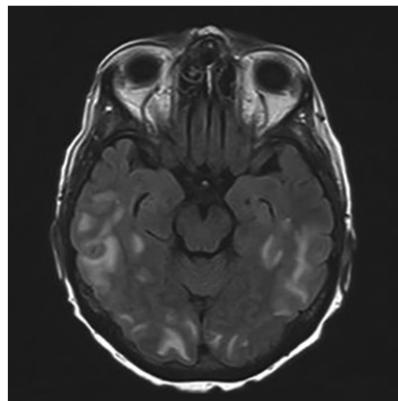
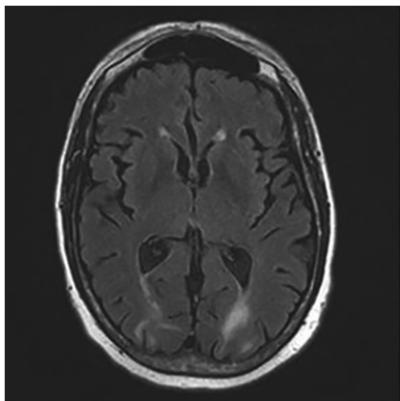
WHO Classification of Tumours Editorial Board. WHO Classification of Tumours of the Central Nervous System. 5th ed. Lyon, France: International Agency for Research on Cancer; 2021.

182 ADULT NEUROLOGY**CORE KNOWLEDGE****Clinical Aspects of Disease**

This patient presents with a seizure and cortical blindness, findings consistent with a posterior reversible encephalopathy syndrome while on bevacizumab. Bevacizumab is also associated with an increased incidence of stroke, intracranial hemorrhage, and optic neuropathy. The presentation of seizure, somnolence, and normal pupillary responses is most consistent with reversible posterior leukoencephalopathy.

DeAngelis LM, Posner JB. Neurologic Complications of Cancer. 2nd ed. New York: Oxford University Press; 2009.

Image credit: Singhal AB. Posterior reversible encephalopathy syndrome and reversible cerebral vasoconstriction syndrome as syndromes of cerebrovascular dysregulation. Continuum Lifelong Learning Neurol. 2021 Oct;27(5):1301-1320.



Question #

217 PEDIATRIC NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Diagnostic Procedures**

The neoplasm likely represents a diffuse midline glioma, H3 K27M-mutant, formerly referred to as a diffuse intrinsic pontine glioma (DIPG). These gliomas have a poor prognosis regardless of histologic features, and finding a mutation in *H3F3A* would warrant a grade IV designation and aggressive therapy.

Mutations in the other genes listed (*IDH*, *PTEN*, *TSC1*, *VHL*) are characteristic of familial tumor syndromes and demonstrate germline rather than somatic mutations; these are not associated with diffuse midline gliomas.

WHO Classification of Tumours Editorial Board. WHO Classification of Tumours of the Central Nervous System. 5th ed. Lyon, France: International Agency for Research on Cancer; 2021.

280 PEDIATRIC NEUROLOGY**Clinical Aspects of Disease**

Gangliogliomas most commonly occur in the frontal and temporal lobes and are cortically based. They are rarely encountered in the brainstem, cerebellum, or suprasellar regions. Craniopharyngioma is primarily suprasellar in 95% of patients. Germ cell tumors occur most commonly in the pineal region; they can be in suprasellar regions in up to 30% of patients.

Choroid plexus papillomas are the most common of the intraventricular tumors. Myxopapillary ependymoma always involves the filum terminale and distal cord and is located in the extramedullary intradural space.

Supratentorial cortical-based tumors represent 25% to 40% of all pediatric brain tumors and are typically derived from glial or neuronal tissue (eg, astrocytoma, ganglioglioma, gangliocytoma, DNET, neurocytoma). These tumors are often slow growing, low-grade tumors. About 50% of patients present with increased intracranial pressure and about 40% present with seizures. The first presenting neurologic abnormality can be seizure activity. About 60% of tumors originate in the posterior fossa, (eg, pilocytic astrocytoma, medulloblastoma, ependymoma). The most frequent presenting symptoms are nausea, vomiting, headache, ataxia, papilledema, abnormal eye movements, and torticollis.

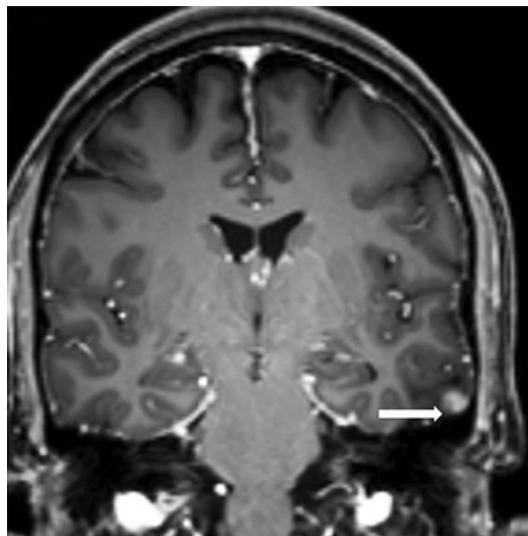
(continues)

Question

More than 10% of tumors in children are located in the brainstem. Ocular symptoms, cranial nerve palsies, tremors, and parkinsonian symptoms are common presenting features. Cerebellopontine angle tumors present with focal sensorineural hearing loss, tinnitus, and vertigo. Tumors of the pineal gland can present with Parinaud syndrome and can produce upgaze paralysis, pseudo-Argyll Robertson pupil, and convergence nystagmus.

More than 10% of tumors in children are located in the brain stem. Ocular symptoms, cranial nerve palsies, tremors and parkinsonian symptoms are common presenting features. Cerebropontine angle tumors present with focal sensorineural hearing loss, tinnitus, and vertigo. Tumors of the pineal gland can present with Parinaud syndrome and they produce upgaze paralysis, pseudo-Argyll Robertson pupil and convergence nystagmus.

Keating RF, Goodrich JT, Pacher RJ (eds). Tumors of the Pediatric Central Nervous System. 2nd ed. New York: Thieme; 2013.



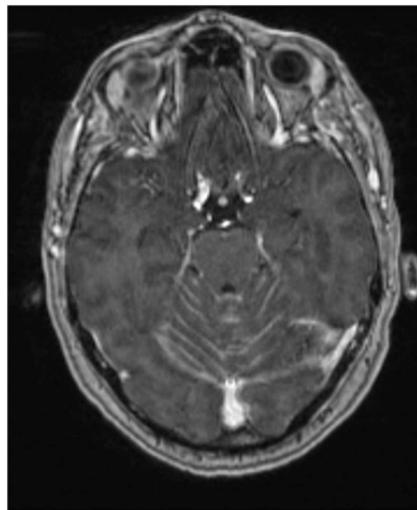
Question #

282 ADULT NEUROLOGY**CORE KNOWLEDGE****Neuroimaging**

This patient's MRI scan demonstrates contrast enhancement in the cerebellar folia and surrounding the upper pons, characteristic of leptomeningeal carcinomatosis.

The two types of meningeal enhancement are as follows: leptomeningeal (pia and arachnoid), when enhancement of the meninges follows the convolutions of the gyri and/or involved the meninges around the basal cisterns; and pachymeningeal (dura), when the enhancement is thick and linear or nodular along the inner surface of the calvarium, falx, or tentorium without extension into the cortical gyri or basal cistern involvement.

Pruitt A. Epidemiology, treatment, and complications of central nervous system metastases. *Continuum Lifelong Learning Neurol.* 2017 Dec;23(6):1580–1600.



Question #

296 ADULT NEUROLOGY**Clinical Aspects of Disease**

Paraneoplastic syndromes refer to symptoms or signs that develop in response to damage to organs or tissues that are remote from the site of a malignancy. These syndromes generally are rare, affecting only 0.01% of patients with cancer, except for Lambert-Eaton myasthenic syndrome, myasthenia gravis, and polyneuropathy in association with a osteosclerotic plasmacytoma.

Antibodies directed at neural nuclear or cytoplasmic epitopes can be measured in CSF and serum. Identification of these antibodies and their target antigens has improved the ability to make an early diagnosis of malignancy if present in a symptomatic patient.

The presence of antigen-specific cytotoxic T cells and circulating anti-Yo antibodies has been documented in patients with acute and subacute pancerebellar degeneration. These antibodies are directed against the cytoplasm of cerebellar Purkinje cells. Other antibodies have also been implicated in paraneoplastic subacute cerebellar degeneration, including anti-Tr and anti-Hu. Anti-Yo is associated with gynecologic and breast malignancies, whereas anti-Hu is associated with small cell lung cancer and anti-Tr with Hodgkin lymphoma.

Lancaster E. Paraneoplastic disorders. *Continuum Lifelong Learning Neurol*. 2015 Apr;21(2):452-475.

Darnell RB, Posner JB. Paraneoplastic syndromes involving the nervous system. *N Engl J Med*. 2003 Oct;349(16):1543-1554.

Question #

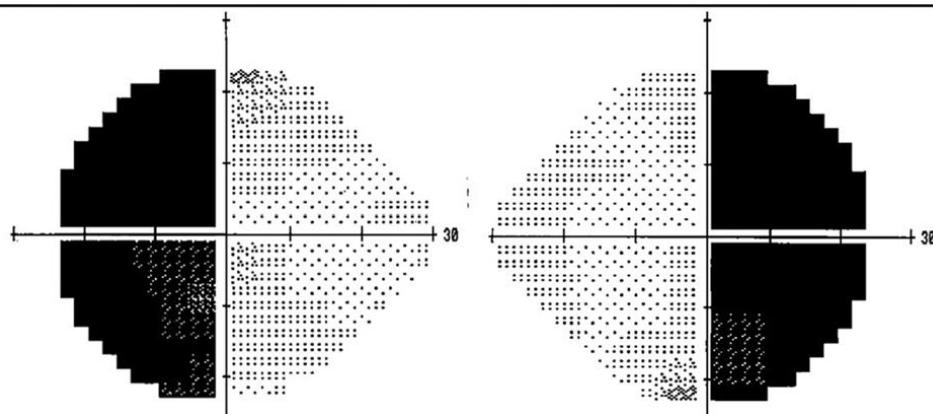
318 NO SPECIFIED PATIENT AGE**Neuroanatomy**

The visual field test shows a partial bitemporal hemianopia, which is characteristic of a lesion compressing the optic chiasm such as a pituitary macroadenoma. An afferent pupillary defect may be observed in the eye that has greater visual field loss.

Ischemic stroke typically involves parietal, temporal, or occipital lobe structures, which should cause a homonymous hemianopia without a relative afferent pupillary defect (RAPD). Idiopathic intracranial hypotension causes constriction of the visual fields and enlarged blind spots but is not associated with RAPD or visual field defects that respect the vertical meridian.

Branch retinal artery occlusion would have monocular visual field loss with an ipsilateral RAPD but would not have the temporal visual field deficit in the contralateral eye. The visual field defects in nonarteritic ischemic optic neuropathy usually respect the horizontal, not vertical, meridian.

Forst DA, Jones PS. Skull base tumors. *Continuum Lifelong Learning*. 2023 Dec;29(6): 1752-1778.



Question #

396 ADULT NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Diagnostic Procedures**

This patient most likely has POEMS (polyneuropathy, organomegaly, endocrinopathy, M-protein, and skin changes) syndrome, a disorder associated with osteosclerotic myeloma. CT of the axial skeleton and long bones is superior to skeletal survey. VEGF level is typically elevated. Muscle or liver biopsy and other hepatitis serologies are not helpful in establishing the diagnosis.

Mauermann ML. Neurologic complication of lymphoma, leukemia and paraproteinemias. Continuum Lifelong Learning Neurol. 2017 Jun;23(3):669–690.

Dispenzieri A, Kyle RA, Lacy MQ, et al. POEMS syndrome: definitions and long-term outcome. Blood. 2003;101(7):2496–2506.

Question

13 ADULT NEUROLOGY**CORE KNOWLEDGE****Clinical Aspects of Disease**

This patient has a pupil-sparing third nerve palsy, most likely related to diabetes mellitus or a small brainstem infarct. A posterior communicating artery aneurysm usually would not spare the pupil. Meningioma often involves cranial nerves IV and VI as well and may be associated with proptosis. A third nerve lesion associated with an extrinsic mass typically would not be pupil-sparing.

Acute onset, isolated involvement of the third nerve, and sparing of the pupil make cavernous sinus meningioma unlikely. Carotid territory infarct would not involve cranial nerve III. Giant cell arteritis could cause a pupil-sparing third nerve palsy, but the erythrocyte sedimentation rate of 35 mm/h is not sufficiently high to raise concern for this disorder. A posterior communicating artery aneurysm causing third nerve palsy involves the pupil.

Smith AG, Singleton JR. Diabetic neuropathy. *Continuum Lifelong Learning Neurol*. 2012 Feb;18(1):60–84.

44 PEDIATRIC NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Treatment/Management**

This patient has more than six café-au-lait spots >0.5 cm and axillary freckling, findings that meet the diagnostic criteria for neurofibromatosis type 1 (NF1). Optic gliomas associated with NF1 are usually detected prior to age 6 years.

Once an optic glioma is discovered, the current recommendation is for eye examinations every 3 to 4 months for the first year after diagnosis and at increasing intervals after a year. In the absence of documented visual abnormalities, observation is usually advised as regression of the tumor is possible.

Enlarging optic gliomas may be treated with chemotherapy (carboplatin and vincristine). Radiation therapy is to be avoided as it has been associated with the development of secondary peripheral nerve sheath tumors within the treatment field.

Schnur RE. Type I neurofibromatosis: a geno-oculo-dermatologic update. *Curr Opin Ophthalmol*. 2012;23(5):364–372.

Question #

70 ADULT NEUROLOGY**CORE KNOWLEDGE****Neuroimaging**

This patient's presentation is consistent with idiopathic intracranial hypertension. Common MRI findings include posterior globe flattening, empty sella turcica, optic disc elevation, dilation and increased tortuosity of the optic nerve sheath, and acquired (not congenital) cerebellar tonsillar descent.

Thurtell MJ. Idiopathic intracranial hypertension. *Continuum Lifelong Learning Neurol*. 2019 Oct;25(5):1289–1309.

93 NO SPECIFIED PATIENT AGE**CORE KNOWLEDGE****Neuroanatomy**

The maxillary division of the trigeminal nerve travels within the wall of the posterior cavernous sinus inferior to cranial nerves III, IV, and VI. It exits the skull base through the foramen rotundum and does not travel within the anterior cavernous sinus, superior orbital fissure, or the orbital apex.

Blumenfeld H. *Neuroanatomy Through Clinical Cases*. 3rd ed. Sunderland: Sinauer Associates; 2021.

99 ADULT NEUROLOGY**Clinical Aspects of Disease**

Pupillary dilation to instillation of 0.5% apraclonidine eyedrops confirms a diagnosis of Horner syndrome. With this patient's history of chiropractic manipulation, arterial dissection should be suspected.

Pupillary dilation to instillation of 1% hydroxyamphetamine suggests a preganglionic lesion; therefore, vertebral artery dissection is more likely than carotid artery dissection.

Neurologic deficits accompanying this patient's left-sided Horner syndrome should be characteristic of those seen in lateral medullary infarction (Wallenberg syndrome), including right-sided hemiparesis and left-sided facial and right limb sensory loss.

Bouffard MA. The pupil. *Continuum Lifelong Learning Neurol*. 2019 Oct;25(5):1194–1214.

Lee S-H, Kim J-M, Schuknecht B, et al. Vestibular and ocular motor properties in lateral medullary stroke critically depend on the level of the medullary lesion. *Front Neurol*. 2020 Jun;5:11:390.

Question #

109 PEDIATRIC NEUROLOGY**CORE KNOWLEDGE****Clinical Aspects of Disease**

Opsoclonus is an abnormal eye movement characterized by spontaneous, arrhythmic, large-amplitude conjugate horizontal and vertical saccades without a saccadic interval. It can have an autoimmune or paraneoplastic etiology. Opsoclonus-myoclonus is a well-known paraneoplastic complication of neuroblastoma in children.

Niederhuber JE, Armitage JO, Doroshw JH, et al (eds). Abeloff's Clinical Oncology. 6th ed. Philadelphia: Elsevier; 2020.

130 ADULT NEUROLOGY**CORE KNOWLEDGE****Neuroanatomy**

This patient presents with a complete horizontal gaze palsy to the right (unable to look to the right with either eye) and internuclear ophthalmoplegia on the right (inability to adduct the right eye on leftward gaze). These findings are consistent with one-and-a-half syndrome due to involvement of the right paramedian pontine reticular formation (PPRF) and/or right cranial nerve VI nucleus (causing ipsilateral impairment of conjugate horizontal gaze) and right medial longitudinal fasciculus (MLF) (causing ipsilateral impaired adduction on contralateral gaze—impaired right adduction on left gaze in this case). The PPRF and cranial nerve VI nucleus and MLF are all located in the dorsal pons.

Berkowitz AL. Extraocular movements and approach to diplopia: cranial nerves 3,4, & 6. In: Berkowitz AL (ed). Lange Clinical Neurology and Neuroanatomy: A Localization-based Approach. 2nd ed. New York: McGraw-Hill; 2022, pp 99–116.

165 ADULT NEUROLOGY**Neurophysiology**

Prolongation of P100 latency on one side results from slowing of conduction in the optic nerve on that side. Acute optic neuritis causes prolongation of P100 latency and is a common cause of monocular vision loss in young adults.

Leocani L, Guerrieri S, Comi G. Visual evoked potentials as a biomarker in multiple sclerosis and associated optic neuritis. *J Neuroophthalmol*. 2018 Sep;38(3):350–357.

Question

193 ADULT NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Neuroscience and Mechanism of Disease**

This patient has posterior cortical atrophy, a neurodegenerative disease characterized by parietal and occipital atrophy. Clinically, patients present with visuospatial and perceptual dysfunction, as well as features of Gerstmann syndrome (acalculia, left-right disorientation, finger agnosia, and agraphia), Balint syndrome (ocular motor apraxia, optic ataxia, and simultanagnosia), and alexia and agraphia. The most common pathology associated with this disorder is low amyloid beta 1–42, consistent with the pathology seen in Alzheimer disease.

Alpha-synuclein protein is associated with Parkinson disease. *MAPT* is a tau gene linked to FTD-tau pathology; alternative splicing of this gene results in different tau isoforms that are associated with Pick disease, progressive supranuclear palsy, corticobasal degeneration, global glial tauopathy, and argyrophilic grain disease.

Progranulin is generally seen with behavioral variant frontotemporal dementia (bvFTD), nonfluent variant frontotemporal dementia (nfvFTD), or corticobasal syndrome. TAR DNA binding protein-43 (TDP-43) is associated with tau-negative frontotemporal dementia and motor neuron disease.

Schott JM, Cruth SJ. Posterior cortical atrophy. *Continuum Lifelong Learning Neurol*. 2019 Feb;25(1):52–75.

209 ADULT NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Treatment/Management**

This patient most likely has episodic ataxia type 2, an autosomal dominant disorder due to a mutation in the *CACNA1A* gene encoding for a calcium channel protein. Episodic ataxia type 2 is characterized by atactic spells lasting hours to days, often with interictal downbeat nystagmus.

Patients may have episodes of isolated ataxia or a broader range of symptoms, such as diplopia, vertigo, and dysarthria, often localizing to the brainstem. Generalized and hemiplegic weakness, migraine, intellectual disability, dystonia, and seizures may also be seen.

Acetazolamide is the recommended treatment, and the response to treatment may even help confirm the diagnosis. The other medications listed (propranolol, topiramate, vitamin E, and magnesium gluconate) have not been shown to be useful in this disorder but can be useful in migraine prevention.

Fife TD. Dizziness in the outpatient care setting. *Continuum Lifelong Learning Neurol*. 2017 Apr;23(2):359–395.

Guterman, EL, Yurgionas, B, Nelson AB. Pearls & oysters: episodic ataxia type 2. *Neurology*. 2016 Jun; 86(23):e239–e241.

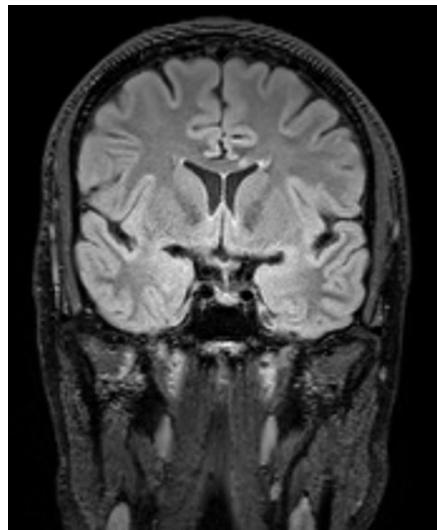
Question #

240 ADULT NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Clinical Aspects of Disease**

Susac syndrome is a medium to small vessel vasculopathy that affects younger and middle-aged persons, with involvement of retinal and auditory artery branches. Whitening of an area of the retina suggests a branch retinal artery occlusion. Migraine with aura is common in Susac syndrome, and hyperintensities in the corpus callosum are typical.

CADASIL less frequently features these clinical symptoms, and FLAIR sequence MRI scans are more likely to show hyperintensities on the temporal poles and external capsules. Multiple sclerosis is rarely associated with hearing loss. Strokes associated with patent foramen ovale are more likely to occur in association with migraine with aura, but retinal and auditory infarcts would be unusual.

Dawe JA, Green AL. Headache in Susac's syndrome. Curr Pain Headache Rep. 2021 Mar 18;25(4):25.



Question #

265 NO SPECIFIED PATIENT AGE**CORE KNOWLEDGE****Neuroanatomy**

This patient's presentation is classic for internuclear ophthalmoplegia, also known as medial longitudinal fasciculus (MLF) syndrome. An MLF lesion typically results in adduction weakness of the ipsilateral eye. Monocular nystagmus of the abducting eye may also be present.

The inferior rectus and inferior oblique muscles, pupil, and eyelid are not involved; therefore, a third cranial nerve palsy is unlikely. Although lesions in the pons can involve the MLF, it passes through the pontine tegmentum rather than the basis pontis.

Myasthenia gravis can mimic an internuclear ophthalmoplegia, but this is rare. The nucleus prepositus hypoglossi is one of the neural integrators for conjugate, horizontal eye movements. A lesion here would cause abnormalities of horizontal gaze holding.

Brazis P, Masdeu J, Biller J (eds). Localization in Clinical Neurology. 8th ed. Lippincott, Williams, Wilkins. 2021.

291 ADULT NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Diagnostic Procedures**

Dehiscence of the superior semicircular canal is a vestibular disorder resulting from a pathologic "third window" into the labyrinth, leading to changed pressure gradients and pressure- and/or sound-induced symptoms and signs, such as vertigo and nystagmus (Tulio phenomenon). None of the other disorders listed features these typical triggers of symptoms and signs. Benign paroxysmal positional vertigo would have vertigo attacks elicited by certain head motions but would not be accompanied by auditory symptoms.

Ishiyama G. Selected otologic disorders causing dizziness. *Continuum Lifelong Learning Neurol*. 2021 Apr 1;27(2):468–490.

Question #

309 NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

Neuroanatomy

Preganglionic sympathetic fibers leave the spinal cord via the ventral roots of T1 and T2 then join the paravertebral sympathetic chain and synapse in the superior cervical ganglion. Postganglionic fibers follow the carotid plexus, eventually reaching the pupillodilator muscle.

Campbell WW, Barohn RJ (eds). DeJong's The Neurologic Examination. 8th ed. Philadelphia: Wolters Kluwer; 2020.

Brazis P, Masdeu J, Biller J (eds). Localization in Clinical Neurology. 8th ed. Lippincott, Williams, Wilkins. 2021.

334 ADULT NEUROLOGY

CORE KNOWLEDGE

Clinical Aspects of Disease

Patients with vestibular neuronitis have a relatively acute onset of continuous vertigo, often in the context of a viral prodrome. There is no hearing loss, which differentiates it from labyrinthitis and Ménière disease. The presence of a positive head impulse test on the right side makes vestibular migraine less likely. The more continuous nature of the symptoms makes vestibular neuronitis more likely than benign paroxysmal peripheral vertigo.

Smith T, Rider J, Cen S, et al. Vestibular neuronitis. [Updated 2023 Mar 11]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-.

379 ADULT NEUROLOGY

CORE KNOWLEDGE

Treatment/Management

This patient has upbeat and torsional nystagmus toward the right shoulder when a right Dix-Hallpike maneuver is performed. This finding is consistent with right-sided postural canal benign paroxysmal positional vertigo (BPPV). The appropriate repositioning treatment is a right Epley maneuver.

The BBQ roll maneuver, also called the Lempert maneuver, is used for horizontal canal BPPV. The deep head hanging maneuver is for the least common type of BPPV, anterior canal BPPV.

Gold DR, Morris L, Kheradmand A, et al. Repositioning maneuvers for benign paroxysmal positional vertigo. *Curr Treat Options Neurol*. 2014 Aug;16(8):307.

Question #

381 ADULT NEUROLOGY**CORE KNOWLEDGE****Neuroanatomy**

Fibers in the inferior aspect of the retina detect vision in the superior quadrants. After synapsing in the lateral geniculate, those fibers enter the temporal lobe as Meyer's loop and project to the occipital lobe. The superior visual fields project to the inferior bank of the contralateral calcarine sulcus.

Campbell WW, Barohn RJ (eds). DeJong's The Neurologic Examination. 8th ed. Philadelphia: Lippincott, Williams & Wilkins; 2019.

Question #

31 NO SPECIFIED PATIENT AGE**CORE KNOWLEDGE****Neuroanatomy**

Descending fibers in the spinal trigeminal tract convey impulses concerned with pain and thermal and tactile sense from the face, forehead, and mucous membranes of the nose and mouth. The spinal trigeminal tract and nucleus (pars caudalis) are the only structures uniquely concerned with the perception of pain and thermal sense.

Blumenfeld H. Neuroanatomy Through Clinical Cases. 3rd ed. Sunderland: Sinauer Associates; 2021.

100 NO SPECIFIED PATIENT AGE**CORE KNOWLEDGE****Neuroanatomy**

The gyrus rectus is medially located on the inferior aspect/orbital surface of the frontal lobe. It lies just medial to the olfactory bulb and tract. The primary auditory cortex is the posterior medial part of the transverse temporal gyrus and typically only manifests as hearing loss when bilateral. Language is primarily mediated by the perisylvian frontal, parietal, and temporal cortices of the dominant hemisphere. Taste localizes to the parainsular portion of the parietal operculum, whereas visual function localizes to the calcarine cortex.

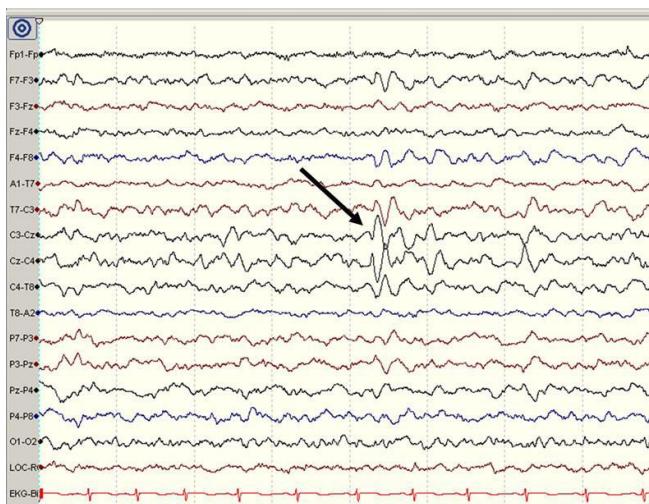
Brazis P, Masdeu J, Biller J (eds). Localization in Clinical Neurology. 8th ed. Lippincott, Williams, Wilkins. 2021.

Question #

106 NO SPECIFIED PATIENT AGE**CORE KNOWLEDGE****Neurophysiology**

The arrow is pointing to a vertex transient, which is a marker of normal sleep. Vertex transients begin to be seen about 6 weeks after delivery and can be seen through all stages of sleep, though they are most clearly associated with stages 1 and 2 NREM sleep.

Schomer D, Lopez de Silva F (eds). Niedermeyer's Electroencephalography: Basic Principles, Clinical Applications, and Related Fields. 7th ed. New York: Oxford University Press; 2018.

**144 NO SPECIFIED PATIENT AGE****Contemporary Issues**

Only random error can be reduced by increasing sample size. The other three types or error listed (ascertainment bias, confounding error, misclassification bias, selection bias) are all examples of systematic error (or bias). If there is a systematic problem with the data being collected, then increasing the sample size will only result in the collection of more data with the same systematic problem.

Guyatt G, Rennie D, Meade MO, et al (eds). Users' Guides to the Medical Literature: A Manual for Evidence-Based Clinical Practice, 3rd ed. McGraw-Hill Education; 2015. Accessed June 18, 2024. <https://jamaevidence.mhmedical.com/content.aspx?bookid=847§ionid=69030714>"

Question #

159 NO SPECIFIED PATIENT AGE**Contemporary Issues**

The Open Payments Program (also referred to as the Physician Payments Sunshine Act) is a national disclosure program that promotes transparency and accountability in the health care system. Section 6002 of the Affordable Care Act (ACA) of 2010 requires medical product manufacturers to disclose to the Centers for Medicare & Medicaid Services (CMS) any payments or transfers of value made to physicians or teaching hospitals. It also requires certain manufacturers and group purchasing organizations to disclose any physician ownership or investment interests held in those companies.

Centers for Medicare & Medicaid Services. What is the Open Payments Program? <https://www.cms.gov/priorities/key-initiatives/open-payments>. Updated October 2024. Accessed December 2024.

171 NO SPECIFIED PATIENT AGE**CORE KNOWLEDGE****Contemporary Issues**

In a trial of 57 patients receiving a study drug, the study drug was effective in 43% of patients (95% CI 30% to 55%). Since the 95% CI includes 50%, we cannot be confident to state that the majority of patients will or will not benefit from the drug. The efficacy may be as low as 30% and as high as 55%. No information about a comparison to the placebo arm is given.

Tu SP, Chen A, Chen A, et al. Clinical trials: understanding and perceptions of female Chinese-American cancer patients. *Cancer*. 2005 Dec 15;104(12 Suppl):2999–3005.

223 NO SPECIFIED PATIENT AGE**Contemporary Issues**

Disclosure of patient information that can lead to identification of the patient, including on social media platforms, is a violation of the Health Insurance Portability and Accountability Act (HIPAA).

US Department of Health and Human Services. Summary of the HIPAA Privacy Rule. <https://www.hhs.gov/hipaa/for-professionals/privacy/laws-regulations/index.html>. Reviewed October 19, 2022. Accessed December 2024.

Question #

227 NO SPECIFIED PATIENT AGE**CORE KNOWLEDGE****Contemporary Issues**

The essential feature of a cohort study is that subjects are ascertained/identified for inclusion in the study based on the presence or absence of an exposure. The direction of inquiry is then from exposure to outcome. The investigator seeks to answer the question whether a particular outcome is more or less frequent among two groups – those with and those without the exposure.

Straus SE, Richardson WS, Glasziou P, Haynes RB (eds). Evidence-based Medicine: How to Practice and Teach EBM. 5th ed. Philadelphia: Elsevier; 2019.

232 ADULT NEUROLOGY**Contemporary Issues**

Sharing patient medical records is necessary for multiple reasons, including to ensure continuity of care between medical providers. Written permission to share records is required to ensure that patient privacy is protected and that only authorized people have access to their sensitive health information.

US Department of Health and Human Services. HIPAA enforcement. <https://www.hhs.gov/hipaa/for-professionals/compliance-enforcement/index.html>. Published July 2017. Accessed November 2024.

Question #

244 NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

Contemporary Issues

A confounder is a factor that confounds or "mixes up" the association between the exposure and outcome variables of interest. Researchers are typically interested in determining whether there is an association between a particular exposure (eg, a new form of treatment) and some outcome (eg, morbidity, mortality). A confounder is some extraneous variable that interferes with the assessment of the association between exposure and outcome. A good example is the association between thymectomy and outcome in patients with myasthenia gravis. If younger patients with milder disease undergo thymectomy, but older patients with more severe disease do not, then age and disease severity may confound elucidation of the relationship between thymectomy and outcome.

Confounding occurs when characteristics influencing the development of the disease are unequally distributed between groups with the putative causal factor and without the causal factor. Under these circumstances, it is difficult to determine if any differences in the risk of developing the disease are due to the confounding factors or the putative causal factor. The threat described in other options is random error, classification bias, and selection bias.

Caparrotta TM, Dear JW, Colhoun HM, Webb DJ. Pharmacoepidemiology: Using randomised control trials and observational studies in clinical decision-making. Br J Clin Pharmacol. 2019 Sep;85(9):1907-1924.

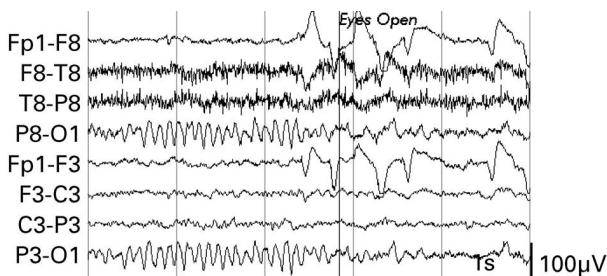
271 NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

Neurophysiology

The background activity is a posteriorly dominant alpha rhythm at 9 to 9.5 Hz, which is normal waking occipital activity. The normal occipital background rhythm disappears on eye opening, which is shown in the EEG tracing.

Ebersole JS, Husain AM, Nordli DR (eds). Current Practice of Clinical Electroencephalography. 4th ed. Philadelphia: Wolters Kluwer Health; 2014.



Question #

278 NO SPECIFIED PATIENT AGE**Contemporary Issues**

The Stark Law "prohibits a physician from making referrals for certain designated health services (DHS) payable by Medicare to an entity with which he or she (or an immediate family member) has a financial relationship (ownership, investment, or compensation), unless an exception applies." With regards to a financial relationship, this is defined as "a direct or indirect ownership or investment interest" or "a direct or indirect compensation arrangement." "Radiology and certain other imaging services" are listed as prohibited designated health services.

Centers for Medicare & Medicaid Services. Physician self-referral. https://www.cms.gov/Medicare/Fraud-and-Abuse/PhysicianSelfReferral/index.html?redirect=/physicianselfreferral/11_list_of_codes.asp. Updated September 2024. Accessed December 2024.

332 NO SPECIFIED PATIENT AGE**CORE KNOWLEDGE****Neuroanatomy**

The structure indicated by the arrow is the trochlear (cranial nerve IV) nerve, which completely decussates before it exits from the dorsal aspect of the brainstem at the level of the inferior colliculus. It is the only cranial nerve to exit the brainstem posteriorly. After it exits the brainstem, the trochlear nerve innervates the superior oblique muscle, resulting in depression and intorsion of the ipsilateral eye.

Blumenfeld H. Neuroanatomy Through Clinical Cases. 3rd ed. Sunderland: Sinauer Associates; 2021.



Question #

371 NO SPECIFIED PATIENT AGE**CORE KNOWLEDGE****Neuroanatomy**

Both the direct and indirect motor frontal–subcortical pathways include the striatum (caudate and putamen), globus pallidus internus, and VA and VL nuclei of the thalamus. The indirect pathway also includes the globus pallidus externus and subthalamic nucleus. The indirect pathway of the frontal–subcortical circuits provides a “braking effect” on the direct pathway via inhibitory outflow from the subthalamic nucleus.

Campbell WW, Barohn RJ (eds). DeJong's The Neurologic Examination. 8th ed. Philadelphia: Wolters Kluwer; 2020.

376 NO SPECIFIED PATIENT AGE**Contemporary Issues**

Medical errors occur frequently and currently are thought to result from systems errors. The American Academy of Neurology Patient Safety Committee has published patient safety tips, as well as a link to the 2006 Patient Safety Colloquium syllabus, on the AAN website. The syllabus addresses many of the issues presented here.

The AAN, the American Medical Association, and other specialty medical associations urge disclosing errors to patients under most circumstances, and recommend including both an apology and a promise to investigate the causes of the error. The purpose of disclosure is not to place blame on individuals, but rather to inform the patient of the events. Errors should be disclosed by persons with the greatest experience, and those with responsibility for the patient's care—in this case, the attending physician. Although in this situation the patient was not harmed, additional laboratory tests and an extra hospital day are serious consequences that justify a disclosure.

It is inappropriate to ask a resident to make an error disclosure alone, although it would be appropriate for the resident to be present with the attending physician when the error is disclosed. It also is unrealistic to expect any health care professional will never make an error; rather, it is important to acknowledge that we all commit errors and are obligated to investigate errors to prevent future recurrence. Failure to disclose an error for fear of malpractice lawsuit is inappropriate, as it constitutes concealment.

Webb A. Response to medical errors. *Continuum Lifelong Learning Neurol*. 2017 Jun;23(3):872–876.

Question #

9 ADULT NEUROLOGY**CORE KNOWLEDGE****Treatment/Management**

Clozapine has the highest risk of hemopoietic reactions among most second-generation antipsychotics. Agranulocytosis, defined by an absolute neutrophil count of $<500/\text{mm}^3$, has been estimated to occur in association with clozapine use at a cumulative incidence of about 1.3% at 1 year. Thus, all patients need to be registered and WBC counts followed regularly if this drug is prescribed. This amount of risk is not seen with any of the other antipsychotic medications listed here.

Haloperidol and risperidone have the potential to cause many adverse effects, including parkinsonism, hypotension, sexual dysfunction, and QT interval prolongation, but not hemopoietic reactions. Aripiprazole is associated with an increased risk of akathisia and withdrawal dyskinesias but not pancytopenia. Olanzapine is associated with an increased risk of weight gain and metabolic syndrome, but not hemopoietic reactions.

Solmi M, Murru A, Pacchiarotti I, et al. Safety, tolerability, and risks associated with first and second generation antipsychotics: a state of the art clinical review. *Ther Clin Risk Management*. 2017 Jun 29;13:757-777.

39 ADULT NEUROLOGY**CORE KNOWLEDGE****Clinical Aspects of Disease**

Factitious disorder is defined as a syndrome of intentional production of psychological or physical symptoms in the absence of external incentives but in the presence of a psychological need to assume the sick role. When there are external incentives for the behavior, then malingering is likely.

Amnestic disorder is characterized by difficulty learning new things. Symptoms from somatic symptom disorder are not intentionally produced. Somatic symptom disorder refers to excessive thoughts feelings or behaviors related to somatic symptoms that are not due to any physical disorder.

American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 5th Edition. Arlington, VA: American Psychiatric Association; 2013.

Carnahan KT, Jha A. Factitious disorder. [Updated 2023 Jan 2]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-.

Question #

65 ADULT NEUROLOGY**CORE KNOWLEDGE****Clinical Aspects of Disease**

Patients with a history of depression are at higher risk for poststroke depression (PSD). About 30% of patients with stroke develop PSD. Onset is highest within the first year and has been associated with degree of physical disability, stroke severity, prior depression, and cognitive impairment. PSD has also been associated with lack of social support and poststroke anxiety. Sex, older age, stroke subtype, living alone, prior stroke or history of diabetes, and baseline education level have not been shown to be consistently associated with PSD.

Towfighi A, Ovbiagele B, El Husseini N, et al; American Heart Association Stroke Council; Council on Cardiovascular and Stroke Nursing; and Council on Quality of Care and Outcomes Research. Poststroke depression: a scientific statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2017 Feb;48(2):e30–e43.

82 NO SPECIFIED PATIENT AGE**CORE KNOWLEDGE****Neuroscience and Mechanism of Disease**

Serotonin is a modulatory neurotransmitter in which low levels are associated with depression. A decrease in norepinephrine activity is associated with some forms of depression and an increase is linked to mania. Deficits in GABA, acetylcholine, histamine or glutamate are not associated with depression.

Sekhon S, Gupta V. Mood disorder. [Updated 2023 May 8]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-.

116 NO SPECIFIED PATIENT AGE**Contemporary Issues**

Speak to a violent patient in a nonthreatening manner and avoid provocative physical gestures. Excessive firmness or demands may provoke additional violence. Physical force should be left to security personnel, who should be involved as soon as possible when a situation escalates to the point of violence. Crowds can exacerbate a feeling of being threatened so the scene should be cleared promptly. Prolonged, direct eye contact also should be avoided.

Harwood RH. How to deal with violent and aggressive patients in acute medical settings. *J R Coll Physicians Edinb*. 2017 Jun;47(2):94–101.

Question #

128 NO SPECIFIED PATIENT AGE**Neuroanatomy**

The mesolimbic dopamine circuit is the main pathway involved in intoxication and addiction. The first step in this pathway involves release of dopamine from the ventral tegmental nucleus.

The amygdala, nucleus accumbens, anterior cingulate cortex, and lateral hypothalamus are later steps in this pathway and are involved after the initial release of dopamine from the ventral tegmental area.

Volkow ND, Michaelides M, Baler R. The neuroscience of drug reward and addiction. *Physiol Rev.* 2019;99(4):2115–2140.

149 ADULT NEUROLOGY**CORE KNOWLEDGE****Clinical Aspects of Disease**

Somatic symptom disorder is characterized by excessive thoughts, feelings, or behaviors related to somatic symptoms. Any one somatic symptom may not be continuously present, but the state of being symptomatic typically lasts at least 6 months. Patients have one or more symptoms that are distressing and cause disruptions in daily life.

After appropriate investigation, each of the symptoms cannot be fully explained by a known condition or are in excess of what would be expected from the history, physical examination, or laboratory findings. The symptoms are not intentionally feigned or produced (as in factitious disorder or malingering).

Borderline personality disorder is associated with a high degree of depression, and the essential feature of histrionic personality disorder is an excessive pattern of emotionality and attention-seeking behavior. These individuals are lively, dramatic, enthusiastic, and flirtatious. They may be inappropriately sexually provocative, express strong emotions with an impressionistic style, and be easily influenced by others.

Obsessive-compulsive disorder is characterized by recurrent and persistent thoughts and urges that are intrusive and unwanted. These thoughts can cause marked anxiety or distress but not physical symptoms.

American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 5th Edition. Arlington, VA: American Psychiatric Association; 2013.

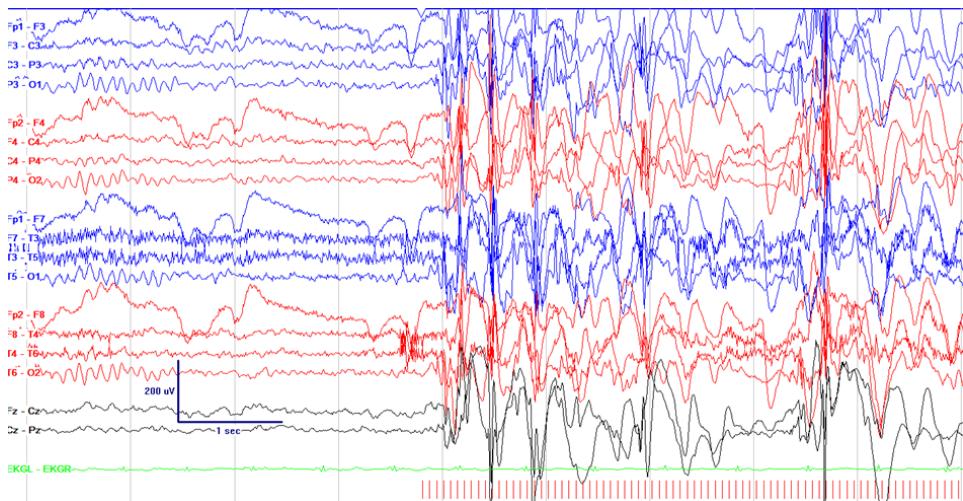
D'Souza R and Hooten W. Somatic sensory disorder [Updated 2023 Mar 13]. In: [Internet]. StatPearls. Treasure Island (FL): StatPearls Publishing; 2024 Jan-.

Question #

19 PEDIATRIC NEUROLOGY**CORE KNOWLEDGE****Neurophysiology**

Juvenile myoclonic epilepsy is characterized by generalized polyspike wave discharges. These findings are often elicited by photic stimulation. Studies demonstrate that photoparoxysmal discharges—polyspike wave discharges evoked by photic stimulation—that outlast stimuli are often associated with epilepsy, whereas those that do not outlast stimuli can be seen in asymptomatic individuals.

Schomer D, Lopez de Silva F (eds). Niedermeyer's Electroencephalography: Basic Principles, Clinical Applications, and Related Fields. 7th ed. New York: Oxford University Press; 2018.



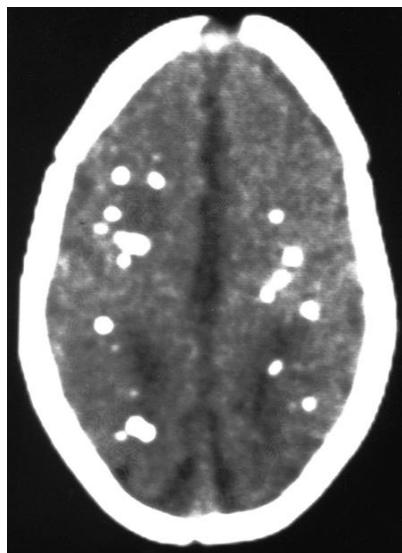
Question #

204 PEDIATRIC NEUROLOGY**CORE KNOWLEDGE****Neuroimaging**

This CT scan shows multiple parenchymal calcifications with mild atrophy, a finding characteristic of a host of infections, including toxoplasmosis, rubella, cytomegalovirus, and herpes.

Calcification seen in Sturge–Weber syndrome is typically cortical and gyriform. Although lipomas may calcify, they are extra-axial, usually single, and appear hypodense on CT scans. This patient's scan does not show malformations of the sulci or ventricles to suggest schizencephaly. Other than calcifications, there are no features on this study to suggest cavernomas.

Patel P. Congenital infections of the nervous system. *Continuum Lifelong Learning Neurol.* 2021 Aug;27(4):1105–1126.



Question #

3 ADULT NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Treatment/Management**

This patient's clinical presentation and electrophysiologic study results are consistent with Lambert-Eaton myasthenic syndrome (LEMS). In LEMS, antibodies to the presynaptic calcium channel inhibit calcium influx into the nerve terminal. Because calcium is needed for acetylcholine release, blockage of the calcium channels inhibits acetylcholine release, causing neuromuscular junction failure and weakness.

Amifampridine is a potassium channel blocker that prolongs the presynaptic potential, improving acetylcholine release. In 2018, amifampridine became the first FDA-approved treatment for LEMS.

Subcutaneous immunoglobulin is FDA approved for the treatment of CIDP. Salbutamol is used off-label for some forms of congenital myasthenia gravis. Deflazacort is a FDA-approved treatment for Duchenne muscular dystrophy. Pyridostigmine may offer limited benefit in LEMS but is FDA approved only for myasthenia gravis and for prophylaxis against the lethal effects of Soman nerve agent poisoning.

Oh SJ, Shcherbakova N, Kostera-Pruszczak A, et al. Amifampridine phosphate (Firdapse®) is effective and safe in a phase 3 clinical trial in LEMS. *Muscle Nerve*. 2016 May;53(5):717-725.

12 ADULT NEUROLOGY**CORE KNOWLEDGE****Neurophysiology**

This patient's signs and symptoms are typical for a selective small fiber neuropathy. Skin biopsy quantifies epidural nerve density with high sensitivity. Autonomic fibers are involved early in small fiber neuropathies. Nerve conduction studies evaluate large sensory and motor fibers, not small fibers. EMG and muscle biopsy assess large (motor) fiber function as well. Somatosensory evoked potentials record large fiber and dorsal column neural activity.

Alport AR, Sander HW. Clinical approach to peripheral neuropathy: anatomic localization and diagnostic testing. *Continuum Lifelong Learning Neurol*. 2012 Feb;18(1):13-38.

Question #

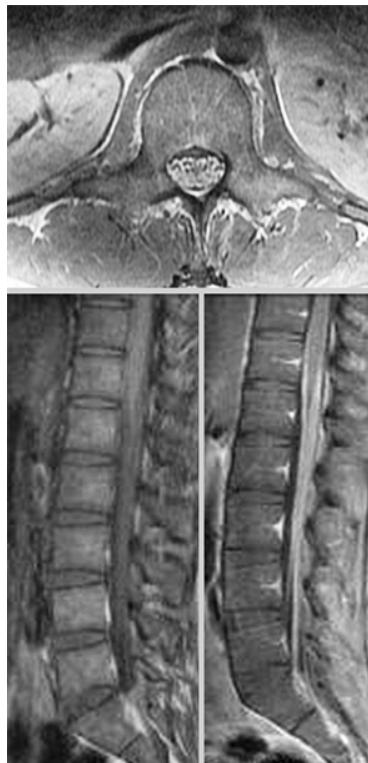
16 ADULT NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Neuroimaging**

This patient's clinical history and imaging studies are most consistent with chronic inflammatory demyelinating polyradiculitis (CIDP). On MRI scans, both acute inflammatory polyradiculoneuropathy and CIDP are frequently associated with leptomeningeal thickening and enhancement, as seen here. These studies show marked enhancement of the thecal sac and cauda equina, with the findings diffuse, not nodular. The 2-year history of weakness is not consistent with carcinomatosis or leptomeningeal seeding from a ependymoma.

Cysticercosis can be associated with dural enhancement; cyst formations would be expected but are not seen in this study. Tuberculosis and sarcoid can produce dural or leptomeningeal enhancement; however, a relapsing course without treatment would be inconsistent with CIDP.

Srinivasan J, Chaves C, Scott B, Small JE (eds). Netter's Neurology. 3rd ed. San Francisco: Elsevier; 2019.

Small JE, Schaefer PW, Sarma A, Bunch P (eds). Neuroradiology: Key Differential Diagnoses and Clinical Questions. 2nd ed. San Francisco: Elsevier; 2023.



Question #

157 ADULT NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Treatment/Management**

Anterograde amnesia is the most common adverse event after initial electroconvulsive therapy (ECT) and may take 2 to 4 weeks to resolve. Retrograde amnesia or gaps in autobiographical memory develop more slowly and after the course of several treatments. Acute confusional states and global amnesia are rare adverse events after ECT. Unprovoked seizures are not seen after ECT.

Espinosa RT, Kellner CH. Electroconvulsive therapy. N Engl J Med. 2022 Feb 16;386(7): 667-672.

173 NO SPECIFIED PATIENT AGE**Clinical Aspects of Disease**

According to the *DSM-5*, gender dysphoria is "a marked incongruence between their experienced or expressed gender and the one they were assigned at birth," and it must be accompanied by significant distress or functional impairment. A feeling that there is a discrepancy between one's assigned gender and gender identification is not a mental disorder. If this feeling results in significant distress, however, it meets the criteria for a diagnosis of gender dysphoria.

Dissociative identity disorder is defined as the presence of two or more distinct identities or personality states in which each personality has its own pattern of perceiving, relating to, and thinking about the environment and self.

In body dysmorphic disorder, individuals have a distorted view of their appearance. Social anxiety disorder is characterized by a marked fear or anxiety about one or more social situations. Paraphilic disorders occur when a person has recurrent and intense sexual arousal from deviant fantasies for at least 6 months and has acted on these fantasies.

Cooper K, Russell A, Mandy W, et al. The phenomenology of gender dysphoria: a systematic review and meta-analysis. Clin Psychol Rev. 2020 Aug;80:101875.

American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 5th Edition. Arlington, VA: American Psychiatric Association; 2013.

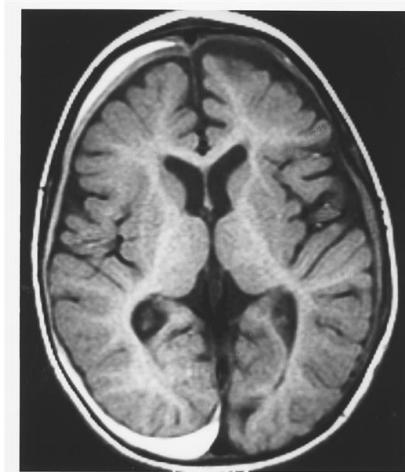
Question #

151 ADULT NEUROLOGY**CORE KNOWLEDGE****Neuroimaging**

The axial T1-weighted image shows an extra-axial hyperintense lesion that lies between the hypointense inner table of the skull and the isointense brain parenchyma. The sulci are displaced and the cortex appears intact. There is a corresponding displacement of the ventricular system. The high signal intensity (T1 shortening) is consistent with a methemoglobin-containing subacute clot in the subdural space.

Epidural hematoma is excluded because the blood collection crosses suture lines. Subdural hygroma and empyema are excluded because the signal is not consistent with CSF or pus. En plaque meningioma is usually iso- to hypointense on noncontrast T1-weighted images, although its appearance could be similar to the image shown had the study been done postcontrast.

Yahyavi-Firouz-Abadi N. Head trauma. In Rohini N, Lin DDM, Yousem DM (eds). Neuroradiology: The Requisites. Philadelphia PA: Elsevier; 2025, pp 122–146.



Question #

183 ADULT NEUROLOGY**CORE KNOWLEDGE****Clinical Aspects of Disease**

Serotonin syndrome is a toxic hyperserotonergic state produced by use of serotonin uptake inhibitors, particularly when used in combination with other serotonergic drugs. The syndrome is characterized by autonomic instability, hyperreflexia, rigidity and delirium. Death may result.

This disorder is difficult to distinguish from the neuroleptic malignant syndrome (NMS) because the symptoms are similar. Serotonin syndrome typically develops over 24 hours, whereas NMS develops over days to weeks. Hypertensive encephalopathy would not be expected to cause either fever or diaphoresis. There are no other symptoms to suggest vasculitis or sinus thrombosis. Malignant hyperthermia usually follows general anesthesia.

Katus LE, Frucht SJ. Management of serotonin syndrome and neuroleptic malignant syndrome. *Curr Treat Options Neurol.* 2016 Sep;18(9):39.

Schaefer SM, Rostami R, Greer DM. Movement disorders in the intensive care unit. *Semin Neurol.* 2016 Dec;36(6):607-614.

216 NO SPECIFIED PATIENT AGE**Neuroanatomy**

Global depression severity is primarily linked to a lesion in the right dorsolateral prefrontal cortex and inferior frontal gyrus. Lesions in the basal ganglia, including the putamen and pallidum, and the orbitofrontal cortex are associated with decreased motivation, which can be seen with depression. Lesions in the left precentral gyrus are associated with anxiety. Lesions in the dorsal thalamus (predominantly right lesions) are associated with emotional symptoms that can be related to depression.

Krick S, Koob JL, Latarnik S, et al. Neuroanatomy of post-stroke depression: the association between symptoms clusters and lesion location. *Brain Comm.* 2023;5(5):facad275.

Question #

243 ADULT NEUROLOGY**CORE KNOWLEDGE****Clinical Aspects of Disease**

Ictal semiology that helps differentiate psychogenic nonepileptic seizures (PNES) from epileptic seizures includes the following: ictal duration >10 minutes, asynchronous limb movements, out-of-phase clonic activity, side-to-side head movements, pelvic thrusting, and eye closure during the ictus. No single pathognomonic sign or symptom, however, is considered sufficient to distinguish PNES from an epileptic event. Risk factors for PNES include the following: female sex, psychiatric comorbidities, and a history of sexual abuse during childhood. Video-EEG is frequently needed to confirm the diagnosis.

Huff JS, Lui F, Murr NI. Psychogenic nonepileptic seizures. [Updated 2024 Feb 25]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-.

258 ADULT NEUROLOGY**Diagnostic Procedures**

Lithium is an FDA-approved treatment for acute mania and for maintenance and prophylaxis of bipolar disorder. It is not metabolized in the liver and is excreted unchanged by the kidneys. The range of toxicity is narrow, with levels >2.5 mEq/L considered a severe toxicity requiring dialysis.

Medications such as NSAIDs, thiazide diuretics, ACE inhibitors, and calcium channel blockers can cause increased lithium levels and should be used with caution. Clinical symptoms of severe toxicity include seizures and often also acute renal failure. Other laboratory changes seen with lithium therapy include an increased thyroid-stimulating hormone level, mildly increased free calcium levels, as well as a mild leukocytosis.

Medic B, Stojanovic M, Stimec B, et al. Lithium: pharmacological and toxicological aspects: the current state of the art. Curr Med Chem. 2020;27(3):337–351.

El-Mallakh RS. Lithium: Actions and Mechanisms. Washington, DC: American Psychiatric Press;1996.

Question #

262 ADULT NEUROLOGY**CORE KNOWLEDGE****Treatment/Management**

Selective serotonin reuptake inhibitors remain the first choice for the overall management of depression and in persons with epilepsy because of their lack of drug interactions with antiseizure medications.

Olanzapine is an atypical antipsychotic medication used only for refractory depression or depression with psychotic features. Bupropion and tricyclic antidepressants should be avoided as they may lower seizure threshold. Ketamine may be used for treatment-resistant depression but would not be a first-line medication for this patient.

Kanner AM, Shankar R, Margraf NG, et al. Mood disorders in adults with epilepsy: a review of unrecognized facts and common misconceptions. Ann Gen Psychiatry. 2024 Mar 4;23(1):11.

290 NO SPECIFIED PATIENT AGE**CORE KNOWLEDGE****Clinical Aspects of Disease**

Functional neurologic disorder is characterized by either altered sensory or voluntary motor function that is not consistent with recognized neurologic or medical conditions. Biological, social, and psychological factors can all contribute to this disorder. Symptoms are frequently associated with an adverse life event or trauma, including a history of childhood sexual or psychosocial abuse. Psychiatric disorders are more common in patients with functional neurologic disorders.

Somatic symptom disorder, illness anxiety disorder and functional neurologic disorder are unconscious, whereas factitious disorder and malingering are intentional. Somatic symptom disorder is diagnosed when one or more somatic symptoms become disproportionately or persistently distressing or lead to disruption in the patient's life. Hypochondriasis is an illness anxiety disorder in which patients become excessively preoccupied with developing/having a medical condition. This term has been removed from the *DSM-5*. Factitious disorder is suspected when patients, intentionally but usually unconsciously, either falsify symptoms or induce injury/disease to themselves for primary gain. Malingering is similar to factitious disorder but is for secondary gain such as monetary compensation, time off, or increased attention.

American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 5th Edition. Arlington, VA: American Psychiatric Association; 2013.

Question #

303 ADULT NEUROLOGY**CORE KNOWLEDGE****Treatment/Management**

All of the selective serotonin reuptake inhibitors (SSRIs) and SNRIs have been reported to have erectile dysfunction as a side effect.

Amitriptyline also causes erectile dysfunction. Bupropion, however, has a low incidence of erectile dysfunction.

Braund TA, Tillman Q, Palmer DM, et al. Antidepressant side effects and their impact on treatment outcome in people with major depressive disorder: an iSPOT-D report. *Transl Psychiatry*. 2021 Aug 4;11(1):417.

Labbate LA, Fava M, Rosenbaum JF, Arana GW (eds). *Handbook of Psychiatric Drug Therapy*. 6th ed. Philadelphia: Lippincott, Wolters Kluwer Lippincott Williams & Wilkins; 2010.

340 ADULT NEUROLOGY**Treatment/Management**

This patient's presentation is consistent with postictal psychosis, a disorder that typically occurs in people with long-standing epilepsy after a cluster of seizures. Initially, the symptoms are episodic but can evolve to interictal (persistent) psychosis.

Treatment typically consists of a benzodiazepine or an antipsychotic medication, which can be used for short periods for symptom control. If symptoms become persistent, chronic treatment with an antipsychotic medication is needed. It is also important to improve seizure control as much as possible.

Devinsky O. Postictal psychosis: common, dangerous, and treatable. *Epilepsy Curr*. 2008 Mar-Apr;8(2):31-34.

Kim JS, Hong S-B, Park K-W, et al. Psychotic symptoms in patients with major neurological Diseases. *J Clin Neurol*. 2024 Mar;20(2):153-165.

352 ADULT NEUROLOGY**Treatment/Management**

Beta-blockers and short-term use of benzodiazepines are the most effective medications to treat symptoms of akathisia. Anticholinergics are effective for drug-induced parkinsonism and may be effective in treating both parkinsonism and akathisia, but adverse effects, including memory loss, and the relatively high doses needed to achieve a clinical response make this class of medication less attractive. Dopamine agonists are used to treat Parkinson disease and restless legs syndrome. NMDA receptor antagonists are used for Alzheimer disease.

Pringsheim T, Gardner D, Addington D, et al. The assessment and treatment of antipsychotic-induced akathisia. *Can J Psychiatry*. 2018 Nov;63(11):719-729.

Question #

395 ADULT NEUROLOGY**CORE KNOWLEDGE****Treatment/Management**

A 2017 meta-analysis of various antipsychotic medications determined that olanzapine caused a significant amount of weight gain compared with other antipsychotics. Quetiapine and risperidone caused intermediate weight gain, and ziprasidone caused the least amount of weight gain.

Puzantian T, Carlat DJ. Medication Fact Book for Psychiatric Practice. 5th ed. Newburyport, MA: Carlat Publishing LLC; 2021.

Dayabandara M, Hanwella R, Ratnatunga S, et. al. Antipsychotic associated weight gain: management strategies and impact on compliance. Neuropsychiatr Dis Treat. 2017 Aug 22;13:2231-2241.

Question #

2 NO SPECIFIED PATIENT AGE**CORE KNOWLEDGE****Neuroscience and Mechanism of Disease**

In humans, where narcolepsy is associated with human leukocyte antigen (HLA) abnormalities, recent studies report that narcolepsy with cataplexy is usually (>90%) caused by the lack of two related brain chemicals, hypocretin-1 and hypocretin-2. The cause of narcolepsy without cataplexy is still under investigation.

More than 90% of patients with narcolepsy-cataplexy carry HLA-DQB1*0602. This marker is more specific and sensitive than the old marker HLA-DR2, and so it is speculated that narcolepsy with cataplexy probably is associated with an autoimmune disorder.

Thorpy MJ. Narcolepsy. *Continuum Lifelong Learning Neurol*. 2007 Jun;13(3):101-114.

37 ADULT NEUROLOGY**CORE KNOWLEDGE****Neuroscience and Mechanism of Disease**

Lewy body dementia, Parkinson disease, and multiple-system atrophy are associated with REM sleep behavior disorder, a syndrome that may present up to decades prior to the onset of the neurodegenerative illness. These disorders are characterized by abnormal deposition of alpha-synuclein in the cytoplasm of neurons and glial cells and are grouped histopathologically as synucleinopathies. The treatment of choice for REM sleep behavior disorder is melatonin or clonazepam.

Auger RR, Boeve BF. Sleep and neurodegenerative disorders. *Continuum Lifelong Learning Neurol* 2007;13:201-224.

Malkani R. REM sleep behavior disorder and other REM parasomnias. *Continuum Lifelong Learning Neurol*. 2023 Aug 1;29(4):1092-1116.

Question #

63 ADULT NEUROLOGY**Treatment/Management**

Narcolepsy is a syndrome characterized by the tetrad of excessive daytime sleepiness (EDS), cataplexy, hypnagogic hallucinations, and sleep paralysis. Primary narcolepsy is now thought to be an autoimmune disorder that typically presents in the second or third decade of life. Its pathogenesis is related to the loss of hypocretin-containing neurons in the lateral and preoptic hypothalamus.

The diagnosis is clinical, with confirmation by polysomnography, multiple sleep latency testing, and CSF analysis showing reduced hypocretin. The most disabling symptoms of narcolepsy are excessive daytime somnolence and cataplexy.

Cataplexy responds to both tricyclic antidepressants and selective serotonin reuptake inhibitors. Excessive daytime somnolence can be treated with CNS stimulants such as modafinil. The only agent approved to treat both excessive daytime somnolence and cataplexy is sodium oxybate, a sodium salt of gamma-hydroxybutyrate and an endogenous inhibitor of GABA, dopamine, and glutamate neurotransmission. It has a short half-life and must be taken in two doses, at bedtime and 3 to 4 hours later.

Morgenthaler TI, Kapur VK, Brown TM, et al. Standards of Practice Committee of the AASM. Practice parameters for the treatment of narcolepsy and other hypersomnias of central origin. *Sleep* 2007;30(12):1705-1711.

Thorpy MJ. Narcolepsy. *Continuum Lifelong Learning Neurol* 2007 Jun;13(3):101-114.

Question #

124 NO SPECIFIED PATIENT AGE**SUBSPECIALTY KNOWLEDGE****Clinical Aspects of Disease**

Fatal familial insomnia (FFI) is a prionopathy with insomnia that progresses to disrupted circadian sleep-wake cycles. In addition to autonomic dysfunction, neurologic findings include cranial neuropathies, hallucinations, ataxia, gait difficulty, and memory loss. Thalamic diffusion on MRI is due to gliosis.

Gerstmann–Sträussler–Scheinker (GSS) syndrome is another prionopathy and, along with FFI, is often RT-QuIC negative. GSS does not feature sleep disruption or dysautonomia.

RT-QuIC is positive in Creutzfeldt–Jakob disease. Diffuse Lewy body disease may present with fluctuation in cognition and alertness and REM sleep behavior disorder, but it does not include progressive disruption of sleep-wake cycles or specific MRI findings. Steroid-responsive encephalopathy associated with autoimmune thyroiditis (SREAT) shows medial temporal lobe FLAIR hyperintensities.

Khan Z, Sankari A, Bollu PC. Fatal familial insomnia. [Updated 2024 Feb 25]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-.

Schmitz M, Villar-Piqué A, Hermann P, et al. Diagnostic accuracy of cerebrospinal fluid biomarkers in genetic prion diseases. *Brain*. 2022 Apr 18;145(2):700–712.

Elder GJ, Lazar AS, Alfonso-Miller P, et al. Sleep disturbances in Lewy body dementia: a systematic review. *Int J Geriatr Psychiatry*. 2022 Oct;37(10):10.1002/gps.5814.

Cracco L, Appleby BS, Gambetti P. Fatal familial insomnia and sporadic fatal insomnia. *Handb Clin Neurol*. 2018;153:271–299.

Question

132 ADULT NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Clinical Aspects of Disease**

This patient's history is consistent with exploding head syndrome, a non-REM parasomnia characterized by hypnagogic hallucinations of either a loud noise or flash of light associated with an abrupt arousal from sleep. Episodes are more likely to occur with sleep deprivation or stress. Once a patient is reassured about the diagnosis, no investigation or treatment is typically required.

Hypnic headaches occur during sleep, often awakening the affected individual. The headache typically lasts 15 minutes and can be prevented with caffeine. Other non-REM parasomnias include sleep walking, sleep terrors, and confusional arousals. Cataplexy is a REM-associated parasomnia. Night terrors is a disorder of young children and occurs from slow wave sleep. Nocturnal frontal lobe epilepsy would not present with either visual or auditory phenomena.

Vaughn BV, D'Cruz O. Parasomnias and other nocturnal events. *Continuum Lifelong Learning Neurol*. 2007 Jun;13(3):225–245.

Goadsby PJ. Unique migraine subtypes, rare headache disorders, and other disturbances. *Continuum Lifelong Learning Neurol*. 2015 Aug;21(4):1032–1040.

164 ADULT NEUROLOGY**CORE KNOWLEDGE****Treatment/Management**

When managing a patient with obstructive sleep apnea, current symptoms, especially daytime sleepiness, apnea-hypopnea index (AHI), and comorbid cardio/cerebrovascular, metabolic, and pulmonary disorders should be taken into consideration.

As indicated by this patient's AHI of 26, he has moderate obstructive sleep apnea and comorbid poorly controlled hypertension with significant daytime sleepiness. Therefore, aggressive management is indicated to decrease the daytime sleepiness and possibly better control his hypertension. Among the steps listed, CPAP, if used appropriately, is 100% effective and thus is the best option for this patient.

Surgery has a success rate of ~50% with a high relapse rate. A dental appliance might be beneficial for mild obstructive sleep apnea. Weight loss should be encouraged in all patients with sleep apnea and a BMI >25; however, weight loss is not helpful in isolation. Use of hypnotic medications alone in patients with moderate to severe obstructive sleep apnea might actually worsen the apnea and thus is not the best option.

Johnson KG. Obstructive sleep apnea. *Continuum Lifelong Learning Neurol*. 2023 Aug 1;29(4):1071–1091.

Question #

228 ADULT NEUROLOGY**CORE KNOWLEDGE****Treatment/Management**

This patient has REM sleep behavior disorder (RBD). Patients with this syndrome can be treated with clonazepam or melatonin. Melatonin is also considered to be a first-line treatment for RBD, as clonazepam may cause excessive daytime somnolence.

Howell MJ. Rapid eye movement sleep behavior disorder and other rapid eye movement parasomnias. *Continuum Lifelong Learning Neurol*. 2020 Aug;26(5):929–945.

Jiménez-Jiménez FJ, Alonso-Navarro H, García-Martín E, et al. Current treatment options for REM sleep behaviour disorder. *J Pers Med*. 2021 Nov 14;11(11):1204.

255 PEDIATRIC NEUROLOGY**Clinical Aspects of Disease**

Kleine-Levin syndrome is a sleep disorder predominant in adolescent males characterized by bouts of excessive sleeping up to 18 hours a day in episodes lasting 7 to 14 days. Associated symptoms include hypersexual behavior, either anorexia or hyperphagia, feelings of depersonalization, and cognitive issues. Hypocretin and orexin levels are reduced during episodes. Treatment is with either lamotrigine or lithium.

Kotagal S. Sleep wake disorders of childhood. *Continuum Lifelong Learning Neurol*. 2017 Apr; 23(4):1132–1150.

259 ADULT NEUROLOGY**Clinical Aspects of Disease**

Confusional arousal and sleep terrors are forms of non-REM parasomnias. These are brief events that occur around the onset of sleep. Confusional arousal is characterized by brief awakenings manifested by confusion; the lack of ambulation differentiates this disorder from sleepwalking. The lack of a fear component differentiates it from sleep terrors. Some individuals with confusional arousals may exhibit sexual behaviors, ranging from masturbation to assault. These events are called sexsommias.

Spector AR. Non-REM sleep parasomnias. *Continuum Lifelong Learning Neurol*. 2023 Aug;29(4):1117–1129.

Question #

272 NO SPECIFIED PATIENT AGE**CORE KNOWLEDGE****Treatment/Management**

Medications that block dopamine, including some psychotropic medications and antiemetics, also exacerbate symptoms of restless legs syndrome. Antidepressants and antihistamines also aggravate symptoms for unknown reasons.

Buchfuhrer, MJ. Strategies for the treatment of restless legs syndrome. Neurotherapeutics. 2012;9(4):776–790.

Walters AS. Restless legs syndrome and periodic limb movements in sleep. Continuum Lifelong Learning Neurol. 2007 Jun;13(3):115–138.

311 ADULT NEUROLOGY**CORE KNOWLEDGE****Neuroscience and Mechanism of Disease**

REM sleep behavior disorder (RBD) is a parasomnia in which, during REM sleep, patients exhibit vocalizations or complex and sometimes violent motor behaviors, essentially acting out their dreams. Normal atonia during REM sleep does not occur.

RBD frequently develops as a prodrome of alpha-synucleinopathies, such as Parkinson disease, Lewy body dementia, and multiple-system atrophy, and may predate the onset of motor signs by years or even decades. Clonazepam and melatonin taken at bedtime can be useful in treating RBD. RBD is now considered a core feature of Lewy body dementia.

Gros P, Videnovic A. Overview of sleep and circadian rhythm disorders in Parkinson disease. Clin Geriatr Med. 2020;36(1):119–130.

McKeith IG, Boeve BF, Dickson DW, et al. Diagnosis and management of dementia with Lewy bodies: Fourth Consensus Report of the DLB Consortium. Neurology. 2017;89: 88–100.

Video credit: Malkani R. REM sleep behavior disorder and other REM parasomnias. Continuum Lifelong Learning Neurol. 2023 Aug;29(4):1092–1116.

Question #

313 ADULT NEUROLOGY**CORE KNOWLEDGE****Treatment/Management**

Insomnia is defined as the combination of difficulty sleeping, lack of sleep, and daytime problems that include fatigue, mood, and behavioral issues. Symptoms need to be present at least three times a week for 3 months to be considered insomnia.

Patients typically have sleep latency of more than 30 minutes, prolonged waking or waking 30 minutes or more before their planned wake time. While numerous medications are available to treat insomnia, behavioral therapies are more effective with minimal adverse effects. These include cognitive behavioral therapy, brief behavioral treatment, and mindfulness therapies.

Kutscher S, Juang C. Insomnia. *Continuum Lifelong Learning Neurol*. 2023 Aug;29(4): 1167-1187.

375 PEDIATRIC NEUROLOGY**CORE KNOWLEDGE****Clinical Aspects of Disease**

The abnormal movements described are consistent with myoclonus during sleep and the transition to sleep but not during wakefulness. The patient has a normal tone exam, Moro reflex, and clonus as allowed for age.

Benign neonatal seizures can start in the first week of life and do not resolve with awakening. Early myoclonic epileptic encephalopathy is associated with burst suppression on EEG; clinically, this would be associated with encephalopathy, not described here, and occur in both sleep and wakefulness. Hyperekplexia, an exaggerated startle response, is not described. Sandifer syndrome refers to abnormal posturing secondary to gastroesophageal reflux.

Facini C, Spagnoli C, Pisani F. Epileptic and non-epileptic paroxysmal motor phenomena in newborns. *J Matern Fetal Neonatal Med*. 2016 Nov;29(22):3652-3659.

Question #

387 ADULT NEUROLOGY**Treatment/Management**

Pramipexole use has the highest prevalence of sleep attacks (50%) compared with ropinirole. Pregabalin and gabapentin are indicated for restless legs syndrome but not Parkinson disease. These medications may cause somnolence or drowsiness but are not associated with sleep attacks. Selegiline is a monoamine oxidase B (MAO-B) and reduces daytime sleepiness.

Yeung EYH, Cavanna AE. Sleep attacks in patients with Parkinson's disease on dopaminergic medications: a systematic review. *Mov Disord Clin Pract.* 2014;1(4):307–316.

Gallazzi M, Mauri M, Bianchi ML, et al. Selegiline reduces daytime sleepiness in patients with Parkinson's disease. *Brain Behav.* 2021 May;11(5):e01880.

393 ADULT NEUROLOGY**CORE KNOWLEDGE****Clinical Aspects of Disease**

This patient's symptoms are consistent with cataplexy, an emotionally induced loss of strength and postural tone. Excessive daytime sleepiness and cataplexy are the most commonly occurring accompaniments of narcolepsy, with hypnagogic hallucinations and sleep paralysis being less common. Other associated symptoms may include vivid dreams, fragmented unrestful nocturnal sleep, automatic behaviors, periodic limb movements of sleep and REM sleep behavior disorder.

Malhotra S, Kushida CA. Primary hypersomnias of central origin. *Continuum Lifelong Learning Neurol.* 2013 Feb;19(1):67–85

Blattner M, Maski K. Central disorders of hypersomnolence. *Continuum Lifelong Learning Neurol.* 2023 Aug 1;29(4):1045–1070.

399 ADULT NEUROLOGY**Neurophysiology**

This patient most likely has REM sleep behavior disorder (RBD) in which there is impairment of REM-induced atonia. Patients appear to physically enact their dreams. The polysomnogram in RBD demonstrates muscle activity by EMG during REM sleep. RBD is more common in patients with degenerative brain diseases, including Parkinson disease.

Frequent arousals and apneic episodes are associated with obstructive sleep apnea. Sleep-onset REM is seen with narcolepsy, and epileptiform activity is associated with a seizure disorder.

Boeve BF REM sleep behavior disorder: Updated review of the core features, the REM sleep behavior disorder-neurodegenerative disease association, evolving concepts, controversies, and future directions. *Ann N Y Acad Sci.* 2010 Jan;1184:15–54.

Question #

5 ADULT NEUROLOGY**CORE KNOWLEDGE****Neuroscience and Mechanism of Disease**

Copper deficiency can produce a clinical syndrome very similar to subacute combined degeneration. Clinical settings in which this occurs include malabsorption, including gastric bypass, or as a consequence of excess zinc ingestion.

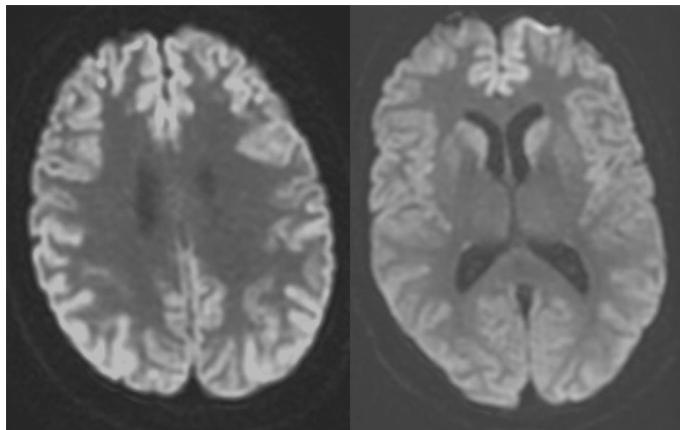
Schwendimann RN. Metabolic and toxic myelopathies. *Continuum Lifelong Learning Neurol.* 2018;24(2):427–440.

28 ADULT NEUROLOGY**CORE KNOWLEDGE****Neuroimaging**

This patient's diffusion-weighted (DWI) MRI scans show diffuse cortical hyperintensity, suggestive of cortical ischemia following cardiopulmonary arrest.

Shear injury typically would be localized and affect white matter structures in the setting of severe rotational injury. Posterior reversible encephalopathy syndrome (PRES) typically is patchy and more commonly in the posterior circulation, and while meningoencephalitis can cause changes on DWI, hyperintensity is usually seen in both in the cortex and extra-axial regions.

Jhaveri MD, Salzman KL, Osborn AG (eds). *Diagnostic Imaging: Brain.* 4th ed. Philadelphia: Elsevier; 2016.



Question #

79 ADULT NEUROLOGY**CORE KNOWLEDGE****Treatment/Management**

Thiamine deficiency can affect the CNS, the peripheral nervous system, and the cardiovascular system. Wernicke encephalopathy related to alcoholism or as a complication following bariatric surgery is common. Clinical features include ocular abnormalities, gait ataxia, and mental status changes. In its most common presentation, only one of these three symptoms is present. Thiamine has been shown to dramatically improve the symptoms of Wernicke encephalopathy, particularly the eye movement abnormalities.

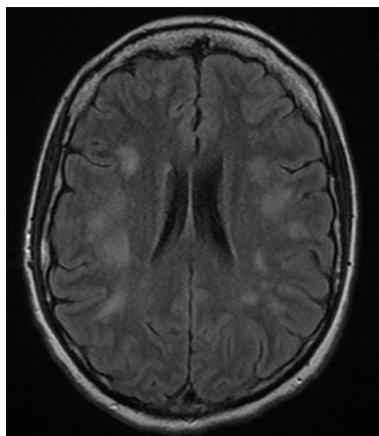
Kumar N. Nutrients and neurology. Continuum Lifelong Learning Neurol. 2017 Jun;23(3):822-861.

88 ADULT NEUROLOGY**Neuroimaging**

Intrathecal methotrexate, which is commonly used in the treatment of acute lymphocytic leukemia, is associated with leukoencephalopathy. While stroke-like symptoms can be seen early in the course of therapy, this patient has likely had these radiographic findings for an extended period. This is further supported by her unrevealing neurologic examination.

CADASIL and SMART present with acute neurologic findings.

Bhojwani D, Sabin ND, Pei D, et al. Methotrexate-induced neurotoxicity and leukoencephalopathy in childhood acute lymphoblastic leukemia. J Clin Oncol. 2014 Mar 20;32(9):949-59.



Question #

121 PEDIATRIC NEUROLOGY**CORE KNOWLEDGE****Clinical Aspects of Disease**

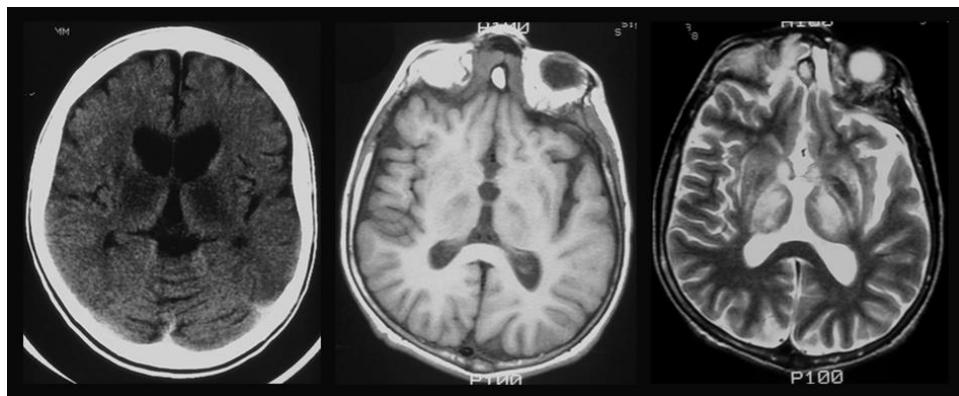
Wilson disease results from accumulation of copper due to a deficiency of ceruloplasmin, its serum transport protein. This disease, also known as hepatolenticular degeneration, affects the liver, brain, and other tissues. MRI findings include T1 hypointensities in the lenticular and caudate nucleus, T2 hyperintensities in the thalamus and pons, white matter hyperintensities, and cerebral and cerebellar atrophy. Age at symptom onset is often in the teenage years.

Adrenoleukodystrophy (ADL) typically affects peritrigonal white matter, not the basal ganglia. ADL has an X-linked inheritance pattern, and females present in adulthood, typically with a myelopathy not cerebral findings.

Wernicke encephalopathy typically occurs with malnutrition, often in the context of alcoholism, and affects periaqueductal structures, the tectum, and medial thalamus.

Canavan disease is a macrocephalic leukodystrophy that diffusely affects white matter, including subcortical U fibers. Krabbe disease is a diffuse leukodystrophy that initially spares the subcortical U fibers, not the distribution seen here. Canavan disease and Krabbe disease present in infancy.

Zhong W, Huang Z, Tang X. A study of brain MRI characteristics and clinical features in 76 cases of Wilson's disease. *J Clin Neurosci*. 2019 Jan;59:167-174.



Question #

134 ADULT NEUROLOGY

Clinical Aspects of Disease

This patient's history of rheumatoid arthritis and clinical presentation is consistent with atlantoaxial subluxation, a serious complication due to damage to the transverse ligament or erosion of the odontoid process. This disorder typically presents with cervical or occipital pain that is worse with movement; it also may produce a progressive high cervical myelopathy and sometimes symptoms of vertebrobasilar insufficiency. Symptoms are not explained solely by the C6–C7 disk herniation given the deltoid involvement, which has C5 innervation, and interossei involvement, which has C8/T1 innervation.

Syringomyelia is associated with Chiari malformation and can cause a central cord syndrome, impairing pain and temperature sensation bilaterally while sparing the dorsal columns.

Epidural abscesses could be considered in patients taking immunosuppressive agents such as methotrexate, but abscesses tend to occur more frequently in the thoracic and lumbar spine, affecting the posterior spine 80% of the time. Patients often have symptoms such as fever and malaise as well.

DeQuattro K, Imboden J. Neurologic manifestations of rheumatoid arthritis. *Rheum Dis Clin North Am.* 2017 Nov;43(4):561–571.

Joaquim AF, Appenzeller S. Cervical spine involvement in rheumatoid arthritis—a systematic review. *Autoimmun Rev.* 2014 Dec;13(12):1195–202.

Question #

172 ADULT NEUROLOGY**Treatment/Management**

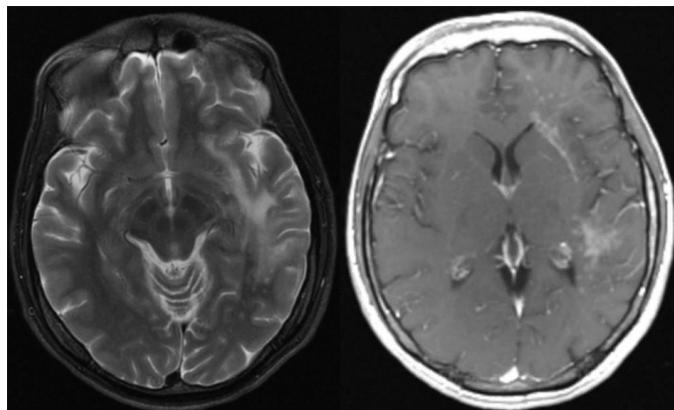
Combination antiretroviral therapy with transient paradoxical worsening of infectious processes is recognized as immune reconstitution inflammatory syndrome (IRIS), a disorder caused by rapid dysregulated restoration of the immune system in patients with HIV.

IRIS often occurs in the setting of infection by intracellular pathogens such as mycobacteria (tuberculous and non-tuberculous), cryptococcus, cytomegalovirus, herpes simplex virus, varicella zoster virus, and JC virus. The inflammatory reaction is usually self-limited but occasionally may be severe enough to result in long-term sequelae and fatal outcomes.

This patient has progressive multifocal leukoencephalopathy (PML) confirmed by positive CSF PCR testing for JC virus.

Smith AB, Smirniotopoulos JG, Rushing EJ. Central nervous system infections associated with human immunodeficiency virus infection: radiologic-pathologic correlation. Radiographics. 2008; 28:2033-2058.

Berger JR, Levy RM, Flomenhoft D, et al. Predictive factors for prolonged survival in acquired immunodeficiency syndrome-associated progressive multifocal leukoencephalopathy. Ann Neurol 1998; 44(3):341-349.



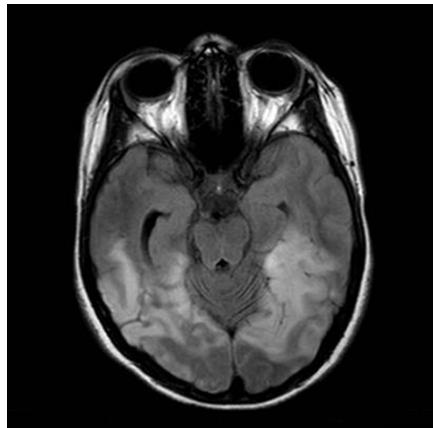
Question #

198 PEDIATRIC NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Clinical Aspects of Disease**

This patient's MRI scan shows extensive bilateral lesions in both gray and white matter, and the MR spectroscopy image demonstrates marked elevation of lactate and decrease in N-acetylaspartate (NAA) in an involved area. These findings are most consistent with mitochondrial encephalopathy with lactic acidosis and stroke-like episodes (MELAS). The course is chronic, and although there is some relapsing/remitting quality, this patient does not return to normal.

Hearing loss is also associated with several of the mutations causing MELAS.

Swaiman AF, Ashwal S, Ferriero DM, et al (eds). Swaiman's Pediatric Neurology. Principles and Practice. 6th ed. Philadelphia: Elsevier, 2017.

**226 ADULT NEUROLOGY****Neuroscience and Mechanism of Disease**

The main site of disposal of manganese in the body is biliary excretion. Patients with biliary atresia, chronic liver disease, or exposure to high doses of manganese during prolonged parenteral nutrition, are prone to develop manganese toxicity. Clinically, it is characterized by parkinsonism and dystonia, neither of which responds to levodopa. T1-weighted MRI scans show hyperintensity in the globus pallidus, striatum, and midbrain. The primary site of damage is the globus pallidus.

Prabhakaran K, Ghosh D, Chapman GD, et al. Molecular mechanism of manganese exposure-induced dopaminergic toxicity. *Brain Res Bull*. 2008 Jul 1;76(4):361-367.

Question #

235 NO SPECIFIED PATIENT AGE**Treatment/Management**

Pseudoephedrine is a stimulant that is often found in decongestants and has a similar structure to amphetamine. Although pseudoephedrine is not as potent as amphetamine, it has been reported that the actions of pseudoephedrine on the CNS via dopamine release resemble to amphetamine. Excessive use of pseudoephedrine can result in dopamine release with resultant dyskinesia.

To rebalance dopamine levels in the striatum, the anticholinergic diphenhydramine is used as an antidote to hyperkinetic movements. Dextromethorphan in large doses can serve as a dopamine receptor blocking agent, which is more likely to cause a dystonia. Guaifenesin is a mucous thinning agent that can have sedating effects but no connection to dyskinesia. Acetaminophen does not impact dyskinesia.

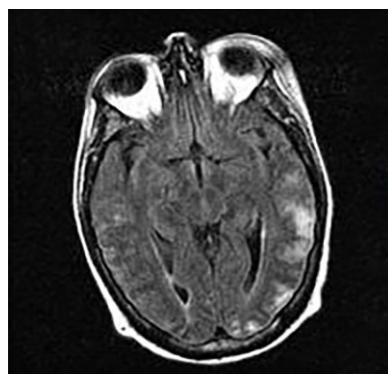
Cornett EM, Novitch M, Kaye AD, et al. Medication-induced tardive dyskinesia: a review and update. *Ochsner J*. 2017 Summer;17(2):162–174.

236 ADULT NEUROLOGY**CORE KNOWLEDGE****Treatment/Management**

The syndrome of posterior reversible encephalopathy (PRES) has been widely associated with hypertension, sepsis, shock, and with cyclosporine use. Patients typically present with a constellation of symptoms, including seizures, encephalopathy/altered mental status, and a variety of visual complaints.

Neuroimaging generally shows symmetric vasogenic edema, predominantly in the posterior parietal and occipital lobes, although it can also be seen in the frontal and temporal lobes. The syndrome, as the name implies, is reversible with treatment of the inciting factors.

Bartynski WS Posterior reversible encephalopathy syndrome, part 1: fundamental imaging and clinical features. *Am J Neuroradiol* 2008;29:1036–1042.



Question #

247 ADULT NEUROLOGY**Treatment/Management**

This patient's presentation is consistent with unintentional carbon monoxide (CO) poisoning. Clinical severity varies greatly, ranging from the most commonly reported symptoms of headache, nausea and dizziness, to altered mental status, seizures, and cardiovascular collapse. Approximately 40% of patients can develop delayed neuropsychiatric sequelae, which can manifest as varying degrees of cognitive impairment, personality changes, movement disorders, as well as progressive coma.

CO poisoning can lead to systemic hypoxic ischemic injuries, as CO is readily absorbed through the alveoli and binds to hemoglobin with an affinity 240 times that of oxygen. Oxygen saturation is often normal as arterial partial pressure of oxygen remains normal. However, the level of carboxyhemoglobin measured in arterial blood is almost always elevated. The classic radiographic finding is bilateral globus pallidus edema, although other patterns consistent with hypoxic ischemic injuries can be seen.

Treatment includes removal of the CO source and delivery of 100% oxygen via a nonrebreathing mask. Patients with signs of severe CO poisoning should be intubated with FiO₂ 100%. While treatment with hyperbaric oxygen remains controversial, most experts agree that patients with severe CO poisoning or patients who are pregnant should be treated expeditiously with hyperbaric oxygen. The theoretical benefit of hyperbaric oxygen is felt to be at decreasing the risk of delayed neuropsychiatric sequelae through reducing ischemia-reperfusion injury.

Cyanide poisoning and CO poisoning are often concomitant in the setting of fire and smoke inhalation and can produce similar appearing brain lesions. Cyanide poisoning is less likely in this patient as there is no reported fire or smoke inhalation. Hydroxocobalamin is the treatment for cyanide poisoning and produces the idiosyncratic transient reddish discoloration of skin and urine.

(continues)

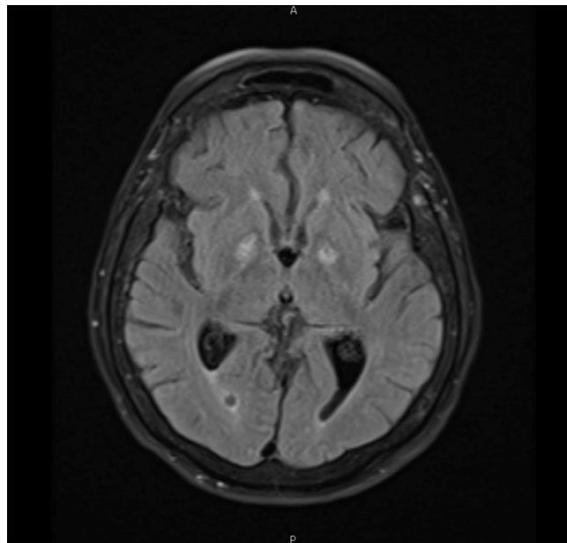
Question

Atropine and pralidoxime are the primary treatments for organophosphate poisoning, which can also present with similar globus pallidus lesions. However, the clinical scenario for organophosphate poisoning is that of the SLUDGE syndrome (salivation, lacrimation, urination, defecation, gastrointestinal distress and emesis).

Fomepizole is the antidote for methanol poisoning, which typically produces an anion gap. Methanol poisoning is less likely given the clinical scenario and normal anion gap.

Penicillamine is a chelating agent often used to bind excess copper found in Wilson disease. This patient's presentation is not consistent with Wilson disease.

Buboltz JB, Robins M. Hyperbaric treatment of carbon monoxide toxicity. 2023 Apr 24. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-.



Question #

253 NO SPECIFIED PATIENT AGE**CORE KNOWLEDGE****Neurophysiology**

Though not a diagnostic finding, generalized beta activity (activity >14 Hz) can be seen as a consequence of drug use, particularly benzodiazepines or barbiturates. Dementia is associated with a slow background. Head trauma, particularly closed head injury, is often associated with a normal background or a mild encephalopathy pattern, though focal features may be seen. Hypoglycemia is associated with generalized slow activity, and epilepsy may be associated with a variety of epileptiform abnormalities.

Schomer D, Lopez de Silva F (eds). Niedermeyer's Electroencephalography: Basic Principles, Clinical Applications, and Related Fields. 7th ed. New York: Oxford University Press; 2018.

281 ADULT NEUROLOGY**Clinical Aspects of Disease**

Botulism causes pupil dilation due to its effect on both muscarinic and nicotinic cholinergic nerve terminals. Other disorders that may acutely produce this constellation of symptoms (eg, myasthenia gravis, Guillain–Barré syndrome, diphtheria) are not typically associated with pupillary abnormalities. Autonomic dysfunction can be seen with Guillain–Barré syndrome and diphtheria but usually not in early stages.

Berkowitz AL. Tetanus, botulism, and diphtheria. *Continuum Lifelong Learning Neurol*. 2018 Oct;24(5):1459–1488.

333 PEDIATRIC NEUROLOGY**Clinical Aspects of Disease**

Lead poisoning is much more common in children than adults and manifests with irritability, listlessness, vomiting and abdominal pain; seizures and drowsiness ensue. Laboratory tests show basophilic stippling of red blood cells and neuroimaging demonstrates cerebral edema.

Prayson RA, Yeaney G (eds). *Neuropathology: Foundations in Diagnostic Pathology Series*. 3rd ed. Philadelphia: Elsevier; 2023.

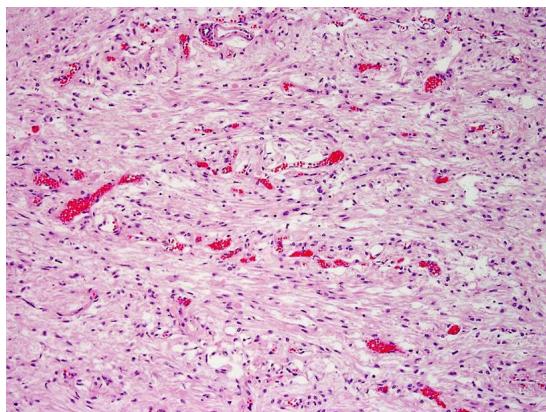
Question #

354 ADULT NEUROLOGY**Neuropathology**

Wernicke encephalopathy is clinically characterized by the triad of eye abnormalities, ataxia, and mental status symptoms. Classically seen in persons with alcohol use disorder, thiamine deficiency can be seen in many malnourished states such as hyperemesis after gastric bypass or hyperemesis during pregnancy. It is underdiagnosed in patients with HIV.

Acute lesions can be detected by MRI. Lesions affect the gray matter around the third and fourth ventricle and aqueduct, the colliculi, and mammillary bodies. Histopathology consists of capillary proliferation, congestion, and pericapillary hemorrhages acutely, with neuron loss and gliosis chronically.

Senocak E, Oguz KK, Ozgen B, et al. Imaging features of CNS involvement in AIDS. *Diagn Interv Radiol.* 2010 Sep;16(3):193–200.



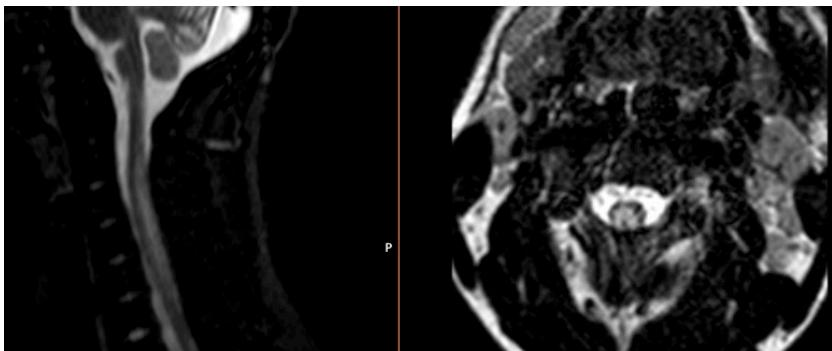
Question #

373 ADULT NEUROLOGY**CORE KNOWLEDGE****Clinical Aspects of Disease**

Nitrous oxide irreversibly binds and inactivates vitamin B12, resulting in subacute combined degeneration. Dorsal column dysfunction is seen, supported by the posterior cord signal on MRI and corticospinal tract dysfunction with weakness and hyperreflexia on exam.

Heroin use could result in corticospinal tract dysfunction due to a consequent cerebral leukoencephalopathy, but altered mental status is a more likely finding and with tetrahydrocannabinol and phencyclidine use. Cocaine use would not likely result in longitudinal cord pathology (especially dorsally); stroke is a more likely neurologic consequence.

Thayabaran D, Burrage D. Nitrous oxide-induced neurotoxicity: a case report and literature review. Br J Clin Pharmacol. 2021 Sep;87(9):3622–3626.



Question #

1 ADULT NEUROLOGY

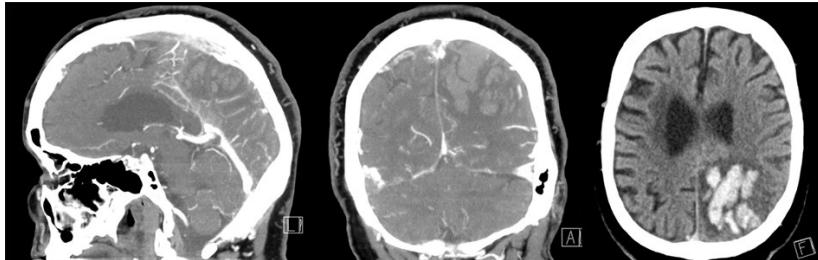
Treatment/Management

This patient's imaging studies show a left parasagittal hemorrhage and filling defects in the superior sagittal sinus, findings consistent with superior sagittal sinus thrombosis.

Pregnancy increases the risk of cerebral vein thrombosis (CVT), particularly the third trimester through the first 6 weeks postpartum. Once a diagnosis of CVT is confirmed, anticoagulant therapy should be considered.

Intracranial hemorrhage as a consequence of CVT is not a contraindication for anticoagulation. In case of mass effect with midline shift or herniation, decompressive hemicraniectomy should be considered.

Saposnik G, Bushnell C, Coutinho JM, et al; American Heart Association Stroke Council; Council on Cardiopulmonary, Critical Care, Perioperative and Resuscitation; Council on Cardiovascular and Stroke Nursing; and Council on Hypertension. Diagnosis and Management of Cerebral Venous Thrombosis: a scientific statement from the American Heart Association. *Stroke*. 2024 Mar;55(3):e77–e90.



Question #

14 ADULT NEUROLOGY **SUBSPECIALTY KNOWLEDGE****Diagnostic Procedures**

Atrial fibrillation associated with moderate to severe mitral stenosis requires treatment with a vitamin K antagonist, while atrial fibrillation without the presence of significant mitral stenosis can be treated with a non-vitamin K antagonist anticoagulant unless the patient has a mechanical heart valve. Most mitral stenosis is rheumatic in origin, although there are other more rare etiologies. Most aortic stenosis and bioprosthetic valves in place for more than 3 months do not require anticoagulation.

Otto CM, Nishimura RA, et al. 2020 ACC/AHA guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation*. 2021 Feb;143(5) e72-e227.

Kleindorfer DO, Towfighi A, et al. 2021 Guideline for the prevention of stroke in patients with stroke and transient ischemic attack: a guideline from the American Heart Association/American Stroke Association. *Stroke*. 2021 Jul;52(7):e364-e467.

34 ADULT NEUROLOGY **CORE KNOWLEDGE****Clinical Aspects of Disease**

Multivariate analysis of factors in patients with primary intracerebral hemorrhage (ICH) document patient age >65 years, Glasgow Coma Scale score ≤8, infratentorial location, ICH volume >30 mL, and intraventricular extension as independent predictors for in-hospital and 30-day mortality. Blood pressure at admission is not reported to be an independent predictor of in-hospital and 30-day mortality.

Ruiz-Sandoval JL, Chiquete E, Romero-Vargas S, et al. Grading scale for prediction of outcome in primary intracerebral hemorrhages. *Stroke*. 2007;38:1641-1644.

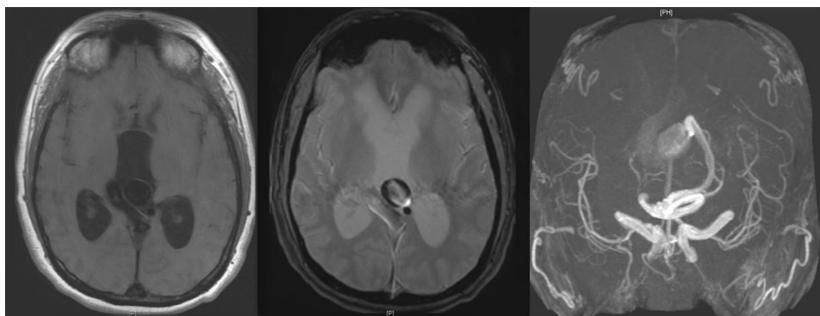
Hemphill JC 3rd, Bonovich DC, Besmeritis I, et al. The ICH score: a simple, reliable grading scale for intracerebral hemorrhage. *Stroke*. 2001;32:891-897.

Question #

47 NO SPECIFIED PATIENT AGE**CORE KNOWLEDGE****Neuroimaging**

This patient's imaging studies demonstrate a large flow void with the appearance of an arterial vessel feeding into an enlarged great vein of Galen. These views show flow voids, not thrombosis. No pineal tumor mass is seen. A persistent trigeminal artery is a persistent fetal communication between the basilar artery and the internal carotid artery.

Atlas SW (ed). Magnetic Resonance Imaging of the Brain and Spine. 5th ed. Philadelphia, PA: Wolters Kluwer; 2017.

**61 ADULT NEUROLOGY****CORE KNOWLEDGE****Neuroanatomy**

The middle cerebellar peduncle consists of crossed afferent fibers from the pontine nucleus, the pontocerebellar tract.

Blumenfeld H. Neuroanatomy Through Clinical Cases. 3rd ed. Sunderland: Sinauer Associates; 2021.

Question #

72 NO SPECIFIED PATIENT AGE**SUBSPECIALTY KNOWLEDGE****Treatment/Management**

Andexanet alfa was approved by the FDA in May 2019 as a specific reversal agent designed to neutralize the anticoagulant effects of both direct and indirect factor Xa inhibitors. Andexanet is a recombinant modified human factor Xa decoy protein that is catalytically inactive but that retains the ability to bind factor Xa inhibitors in the active site with high affinity. It binds and sequesters factor Xa inhibitors within the vascular space, thereby restoring the activity of endogenous factor Xa and reducing levels of anticoagulant activity, as assessed by measurement of thrombin generation and anti-factor Xa activity.

Among the apixaban-treated group, anti-factor Xa activity was reduced by 94% among those who received an andexanet bolus (24 subjects), compared with 21% among those who received placebo (9 subjects) ($P<0.001$), and thrombin generation was fully restored in 100% versus 11% of the subjects ($P<0.001$) within 2 to 5 minutes.

Among the rivaroxaban-treated group, anti-factor Xa activity was reduced by 92% among those who received an andexanet bolus (27 subjects), compared with 18% among those who received placebo (14 subjects) ($P<0.001$), and thrombin generation was fully restored in 96% versus 7% of the subjects ($P<0.001$).

Idarucizumab is a humanized monoclonal antibody fragment developed as a specific reversal agent for dabigatran.

Siegal DM, Curnutt JT, Connolly SJ, et al. Andexanet alfa for the reversal of factor Xa inhibitor activity. *N Engl J Med*. 2015 Dec 17; 373(25):2413–2424.

Question #

86 PEDIATRIC NEUROLOGY**Clinical Aspects of Disease**

This patient's angiogram shows stenosis of the right internal carotid artery with formation of the capillary network, consistent with moyamoya changes.

Moyamoya disease has been found to be associated with several susceptibility genes, particularly *RNF213* (mysterin) among individuals with eastern Asian ancestry. In contrast to this population, moyamoya disease among Caucasians peaks much later (40 to 49 years) and is usually linked to a different susceptibility gene.

Moyamoya syndrome is a term used for similar angiographic changes secondary to an identifiable cause such as neurofibromatosis, trisomy 21, radiation therapy, and sickle cell disease. Neurofibromatosis would be suggested clinically by axillary freckles or a history of optic nerve glioma or sphenoid wing dysplasia.

Majersik J. Inherited and uncommon causes of stroke. *Continuum Lifelong Learning Neurol.* 2017 Feb;23(1):211-137.

Berry JA, Cortez V, Toor H, et al. Moyamoya: an update and review. *Cureus.* 2020;12(1):e10994.

Ihara M, Yamamoto Y, Hattori Y, et al. Moyamoya disease: diagnosis and interventions. *Lancet Neurol.* 2022;21:747-758.

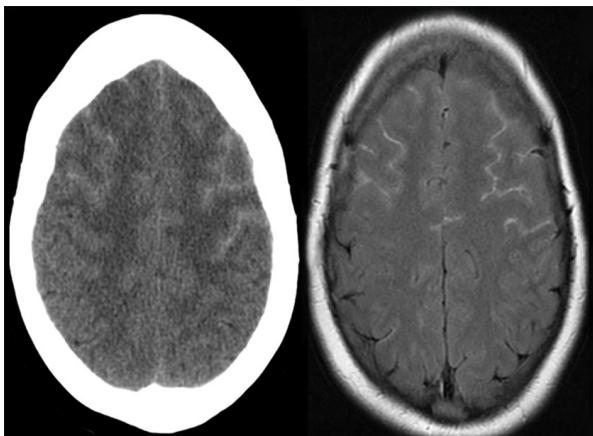


Question #

103 ADULT NEUROLOGY**CORE KNOWLEDGE****Neuroimaging**

The increased density and FLAIR signal in the subarachnoid spaces of both frontal lobes are typical of subarachnoid hemorrhage. There is no trauma in the history, and the pattern is likely due to reversible cerebral vasoconstriction syndrome. There is no evidence of infarction and no abnormal calcification.

Atlas SW (ed). Magnetic Resonance Imaging of the Brain and Spine. 5th ed. Philadelphia, PA: Wolters Kluwer; 2017.



Question #

115 ADULT NEUROLOGY**CORE KNOWLEDGE****Treatment/Management**

Clopidogrel is a potent oral antiplatelet agent often used in the treatment of coronary artery disease, peripheral vascular disease, and cerebrovascular disease. Its mechanism of action is an irreversible blockade of the adenosine diphosphate (ADP) receptor on platelet cell membranes. This receptor, named P2Y12, is important in platelet aggregation, which is the cross-linking of platelets by fibrin. The blockade of this receptor inhibits platelet aggregation by blocking activation of the glycoprotein IIb/IIIa pathway.

Dipyridamole inhibits the uptake of adenosine into platelets, endothelial cells, and erythrocytes *in vitro* and *in vivo*. This inhibition occurs in a dose-dependent manner at therapeutic concentrations (0.5 to 1.9 µg/mL), resulting in an increase in local concentrations of adenosine that in turn act on the platelet A2-receptor. The result is stimulation of platelet adenylate cyclase and an increase in platelet cyclic-3',5'-adenosine monophosphate (cAMP) levels. Via this mechanism, platelet aggregation is inhibited in response to various stimuli such as platelet-activating factor (PAF), collagen, and ADP.

Aspirin's ability to suppress the production of prostaglandins and thromboxanes is due to its irreversible inactivation of the cyclooxygenase (COX) enzyme. Cyclooxygenase is required for prostaglandin and thromboxane synthesis. Long-term use of low-dose aspirin irreversibly blocks the formation of thromboxane A2 in platelets, producing an inhibitory effect on platelet aggregation. Tissue-type plasminogen activator (tPA) is one of the two mammalian serine proteases that activates plasminogen into plasmin, the primary plasmatic function being fibrinolysis.

Savi P, Herbert JM. Clopidogrel and ticlopidine: P2Y12 adenosine diphosphate-receptor antagonists for the prevention of atherothrombosis. *Semin Thromb Hemost*. 2005;31(2):174–183.

125 PEDIATRIC NEUROLOGY**CORE KNOWLEDGE****Clinical Aspects of Disease**

Blunt trauma to the neck or forced torsion can cause carotid dissection. The headache is constant, severe, and often unilateral. Thrombi can form at the dissection site and cause an infarction either by embolization or closing off the lumen.

Swaiman AF, Ashwal S, Ferriero DM, et al (eds). Swaiman's Pediatric Neurology. Principles and Practice. 6th ed. Philadelphia: Elsevier, 2017.

Ropper AH, Samuels MA, Klein JP, et al (eds). Adams and Victor's Principles of Neurology. 11th ed. New York: McGraw-Hill Education; 2019.

Question #

133 ADULT NEUROLOGY**CORE KNOWLEDGE****Contemporary Issues**

This patient appears to be unaware of the seriousness of his illness. This state, known as anosognosia, is frequently caused by a lesion in the nondominant hemisphere, particularly frontoparietal or frontoparietotemporal. A lesion with diameter >5 cm is more likely to cause anosognosia. Fortunately, anosognosia for hemiplegia is typically an acute phenomenon and tends to resolve within a few hours or days after stroke onset. Given his lack of clear understanding regarding the seriousness of his illness, the next-of-kin should be his surrogate medical decision maker.

Vocat R, Staub F, Stroppini T, et al. Anosognosia for hemiplegia: a clinical-anatomical prospective study. *Brain*. 2010 Dec;133(Pt 12):3578–3597.

Kortte KB, McWhorter JW, Pawlak MA, et al. Anosognosia for hemiplegia: the contributory role of right inferior frontal gyrus. *Neuropsychology*. 2015 May;29(3):421–432.

Orfei MD, Robinson RG, Prigatano GP, et al. Anosognosia for hemiplegia after stroke is a multifaceted phenomenon: a systematic review of the literature. *Brain*. 2007 Dec;130(Pt 12):3075–3090.

141 NO SPECIFIED PATIENT AGE**CORE KNOWLEDGE****Neuroanatomy**

The posterior cerebral artery (PCA) is identified by the green pin. The PCA is formed by the terminal bifurcation of the basilar artery.

Blumenfeld H. *Neuroanatomy Through Clinical Cases*. 3rd ed. Sunderland: Sinauer Associates; 2021.



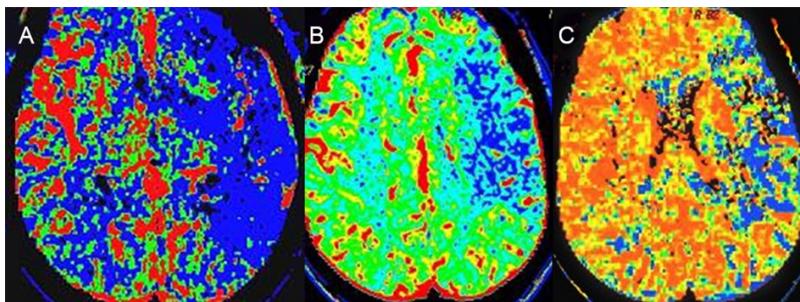
Question #

162 ADULT NEUROLOGY**CORE KNOWLEDGE****Neuroimaging**

The images show decreased cerebral blood flow and decreased cerebral blood volume, along with increased mean transit time in the left middle cerebral artery territory. By convention, color maps are coded red for higher values and blue for lower values. A CT angiogram demonstrated a thrombus within the M1 segment of the left middle cerebral artery. Left internal carotid artery is incorrect as there is normal perfusion in the left anterior cerebral artery territory.

Greenberg JO (ed). Neuroimaging: A Companion to Adams and Victor's Principles of Neurology. 2nd ed. New York: McGraw-Hill, 1999.

Marco de Lucas E, Sánchez E, Gutiérrez A, et al. CT protocol for acute stroke: tips and tricks for general radiologists. RadioGraphics 2008; 28:1673–1687

**169 PEDIATRIC NEUROLOGY****CORE KNOWLEDGE****Clinical Aspects of Disease**

This patient shows signs of early handedness; at 7 months age, one would not anticipate a significant asymmetry in which hand is used for reaching or activities. Parachute reflex is a postural reflex elicited by moving a child quickly forward such that the arms extend outward. Asymmetry in this instance suggests prior injury.

The history is not suggestive of a brachial plexus injury or MELAS. Alternating hemiplegia of childhood would not present with unilateral weakness.

Amie-Lefond, C. Evaluation and acute management of ischemic stroke in infants and children. Continuum Lifelong Learning Neurol. 2018 Feb;24(1):150–170.

Dunbar M, Kirton A. Perinatal stroke. Semin Pediatr Neurol. 2019 Dec;32:100767.

Question #

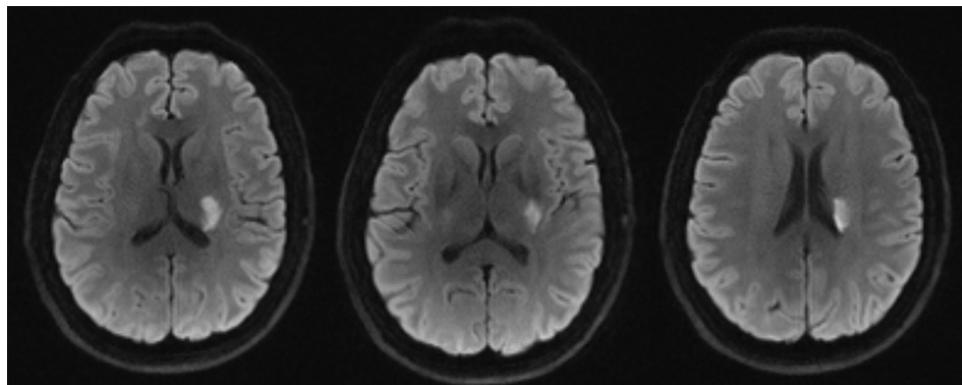
176 ADULT NEUROLOGY**Clinical Aspects of Disease**

The first report of the anterior choroidal artery infarction was in 1925 by Foix, Chavany, and associates in which they described the classic triad of hemiparesis, hemianesthesia, and hemianopia. The visual field defect is typified by loss of the upper and lower visual fields, sparing the horizontal meridian, a disorder also referred to as sectoranopia. The most common stroke mechanism is small vessel disease.

Cheng Z, Duan H, Meng F, et al. Acute anterior choroidal artery territory infarction: a retrospective study. *Clin Neurol Neurosurg*. 2020;195:105826.

Helgason C, Caplan LR, Goodwin J, et al. Anterior choroidal artery-territory Infarction: report of cases and review. *Arch Neurol*. 1986;43(7):681-686.

Foix Chavany H, Hillemand P, et al. Obliteratio de l'artere choroidienne anterieure: ramollissement de son territoire cerebral: hemiplegie, hemianesthesia, hemianopsie (seance du 25 mai). *Bull Soc Ophthalmol* 1925;37:221-223.



Question #

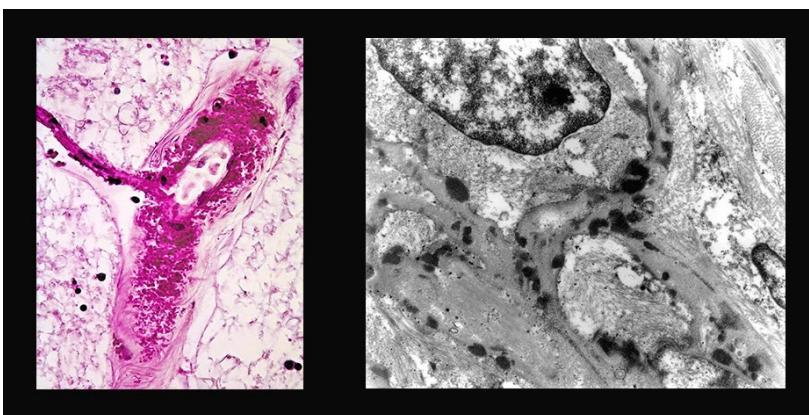
189 ADULT NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Neuropathology**

The images show classic features of cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL). CADASIL is a nonatherosclerotic, nonamyloid vascular disorder that primarily affects small to medium-sized arteries of the white matter. Abnormal vessels are PAS-positive.

The characteristic electron microscopic finding is the deposition of granular osmophilic material (GOM) between degenerating vascular smooth muscle cells. The defective gene in CADASIL is *NOTCH3*, which encodes a multifunctional protein that specifies cell fate. Mitochondrial gene defects would characterize the mitochondrial encephalopathies.

Ellison DW, Love S (eds). *Neuropathology: A Reference Text of CNS Pathology*. 3rd ed. San Francisco: Elsevier; 2013.

Pastores GM. Leukoencephalopathies and leukodystrophies. *Continuum Lifelong Learning Neurol*. 2010 Apr;16(2):102–119.



Question #

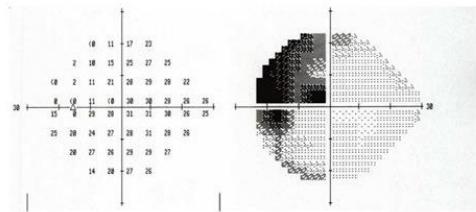
190 ADULT NEUROLOGY**Neuroscience and Mechanism of Disease**

This patient's visual field test shows an incongruous left superior and inferior sectoranopia and a right sectoranopia. The diffusion-weighted MRI scan shows an acute stroke in the right basal ganglia and temporal lobe in the territory of the posterior choroidal artery. The posterior choroidal artery is a branch off the posterior cerebral artery.

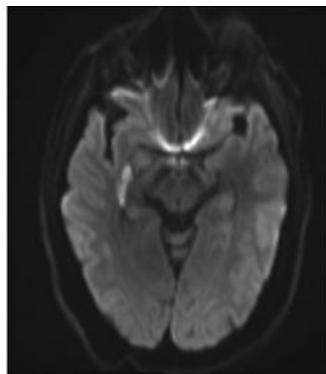
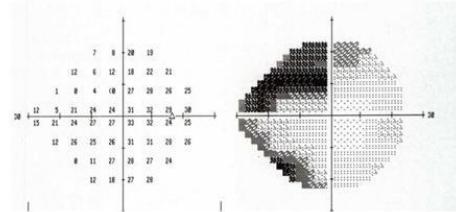
The anterior choroidal artery is a branch off the internal carotid artery and produces a horizontal sectoranopia; the stroke involves the posterior limb of the internal capsule, basal ganglia, and corona radiata. A stroke in the superior cerebellar artery would not produce visual field deficits. The anterior cerebral artery does not supply the right basal ganglia and right temporal lobe.

Osborne BJ, Liu GT, Galetta SL. Geniculate quadruple sectoranopia. *Neurology*. 2006 Jun 13;66(11):E41-E42.

Left eye



Right eye



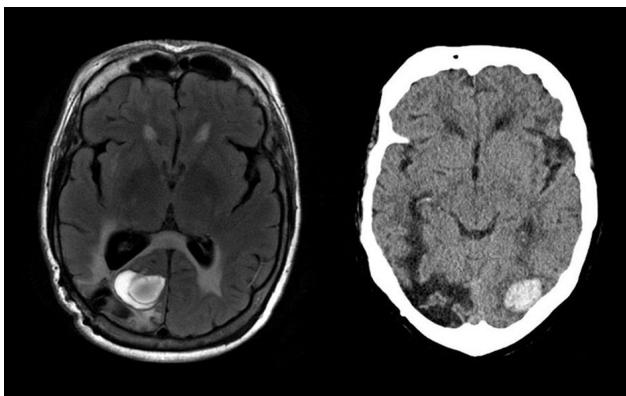
Question #

205 ADULT NEUROLOGY**CORE KNOWLEDGE****Clinical Aspects of Disease**

This patient has consecutive occipital lobar hemorrhages. Multiple hemorrhages restricted to lobar, cortical, or cortico-subcortical regions are characteristic of probable cerebral amyloid angiopathy according to the Modified Boston Criteria. The diagnosis can also be suggested by a single lobar hemorrhage accompanied by focal or disseminated superficial siderosis in a patient age >55 years in the absence of other likely causes of hemorrhage or superficial siderosis.

The 5-year time interval between the hemorrhages in this patient argues against hemorrhagic venous infarction from cerebral sinus venous thrombosis or hemorrhagic metastases. The lobar location of the lesions is atypical for hypertensive intracranial hemorrhage. Hemorrhagic conversion of cerebral infarcts is possible but less likely than cerebral amyloid angiopathy.

Hakimi R, Gard A. Imaging of hemorrhagic stroke. *Continuum Lifelong Learning Neurol.* 2016 Oct;22(5):1424-1450.

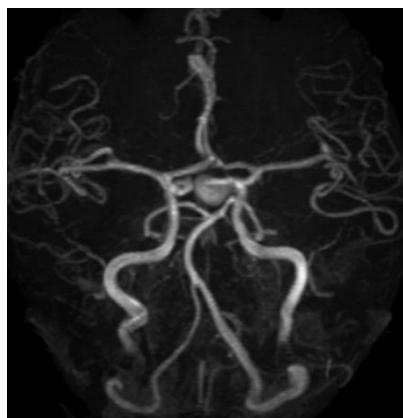


Question #

222 ADULT NEUROLOGY**CORE KNOWLEDGE****Neuroimaging**

The 1.6– x 0.9-cm mass seen represents a saccular aneurysm of the left internal carotid artery that projects medially. After diagnosis, this aneurysm was successfully treated with endovascular coil.

Brazis PW, Masdeu JC, Biller J (eds). *Localization in Clinical Neurology*. 8th ed. Philadelphia: Wolters Kluwer; 2022.

**238 ADULT NEUROLOGY****CORE KNOWLEDGE****Neuroanatomy**

An aneurysm in the posterior communicating artery may compress cranial nerve III, leading to ipsilateral pupillary dilation and ophthalmoparesis.

Blumenfeld H. *Neuroanatomy Through Clinical Cases*. 3rd ed. Sunderland: Sinauer Associates; 2021.

251 ADULT NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Clinical Aspects of Disease**

Gerstmann syndrome includes agraphia, finger agnosia, right-left disorientation, and acalculia. When all four features are present, the lesion is most often in the dominant (usually left) inferior parietal lobule, which includes the supramarginal and angular gyri.

Blumenfeld H. *Neuroanatomy Through Clinical Cases*. 3rd ed. Sunderland: Sinauer Associates; 2021.

Tang-Wai D, Freedman M. Bedside approach to the mental status assessment. *Continuum Lifelong Learning Neurol*. 2018 Jun;24(3):672-703.

Question #

264 ADULT NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Diagnostic Procedures**

This patient's echocardiogram findings are consistent with an intrapulmonary shunt, suggested by passage of bubbles in the later stage of the test, on or after five cardiac cycles. This finding can be seen in pulmonary arteriovenous malformations (AVMs), which is a source of ischemic stroke. The next step in workup is to confirm or rule out an pulmonary AVM via CT angiography of the chest.

Cardiology consult is not necessary as the test does not show a patent foramen ovale, which would involve early passage of bubbles to the left atrium. Pulmonary function tests, chest radiography, and cardiac MRI do not help characterize or rule out pulmonary AVM.

Bhatia N, Abushora MY, Donneyong MM, et al. Determination of the optimum number of cardiac cycles to differentiate intra-pulmonary shunt and patent foramen ovale by saline contrast two- and three-dimensional echocardiography. *Echocardiography*. 2014 Mar;31(3):293–301.

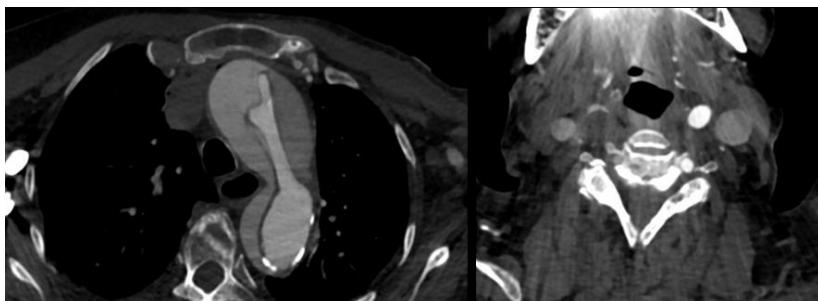
Question #

276 ADULT NEUROLOGY**Neuroscience and Mechanism of Disease**

The axial CT angiogram shows separation of the aorta with a true and false lumen due to an aortic dissection (left) with extension into the right common carotid artery, resulting in the lumen forming a crescent shape (right). Carotid artery dissection leads to reduced blood flow in the right internal carotid artery, which produces left-sided weakness.

Congestive heart failure is not seen in the angiogram and would not cause focal left-sided weakness, nor is aortic inflammation seen to support either Takayasu or giant cell arteritis. There is no evidence of mycotic aneurysm; these aneurysms are typically seen in the distal cerebral vasculature near the circle of Willis.

Salehi Omran S. Cervical artery dissection. *Continuum Lifelong Learning Neurol*. 2023 Apr;29(2):540–565.



Question #

283 ADULT NEUROLOGY**CORE KNOWLEDGE****Treatment/Management**

The window for administering IV thrombolysis is within 4.5 hours of the patient's last known well time. Thrombectomy should be a consideration in those who present beyond the 4.5-hour window. Patients who present within a 6-hour window and whose head CT scans are consistent with an ASPECTS score >6 need no additional imaging beyond a CT angiogram demonstrating a large vessel occlusion. Given this patient's last known well time was 5 hours ago, he should be taken for thrombectomy as soon as possible.

Silva GS, Nogueira RG. Endovascular treatment of acute ischemic stroke. *Continuum Lifelong Learning Neurol*. 2020 Apr;26(2):310–331.

Rabinstein AA. Update on treatment of acute ischemic stroke. *Continuum Lifelong Learning Neurol*. 2020 Apr;26(2):268–286.

300 ADULT NEUROLOGY**CORE KNOWLEDGE****Neuroanatomy**

The thalamus is supplied mainly by the branches of the posterior cerebral, posterior communicating, and posterior choroidal arteries.

Campbell WW, Barohn RJ (eds). *DeJong's The Neurologic Examination*. 8th ed. Philadelphia: Wolters Kluwer; 2020.

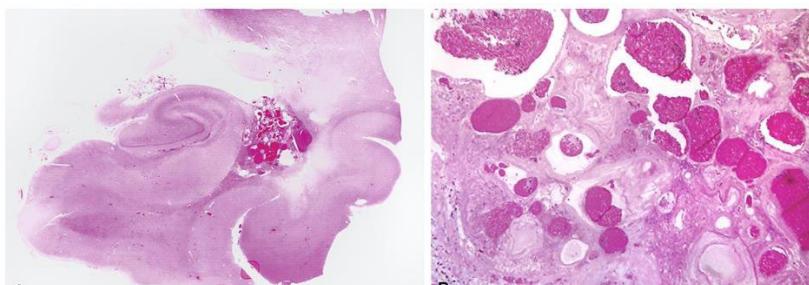
Brazis PW, Masdeu JC, Biller J (eds). *Localization in Clinical Neurology*. 8th ed. Philadelphia: Wolters Kluwer; 2022.

Question #

307 ADULT NEUROLOGY**Neuropathology**

The images show a cavernous malformation, not the hemangioblastoma of von Hippel-Lindau disease or the superficial angiomyomatosis of Sturge-Weber disease. CREST syndrome (calcinosis, Raynaud, esophageal motility disorders, sclerodactyly, telangiectasia) does not have CNS manifestations. Familial amyloidosis usually affects peripheral nerves; most cerebral amyloid angiopathy is sporadic and not familial with the exception of Dutch, Icelandic, and British variants. Patients with autosomal dominant cerebral cavernous malformation syndrome may have mutations of the *KRIT1* gene on chromosome 7q. Other familial cases have been linked to genes on chromosomes 7p and 3q.

Ellison DW, Love S. Neuropathology: A Reference Text of CNS Pathology. 3rd ed. San Francisco: Elsevier, 2013.



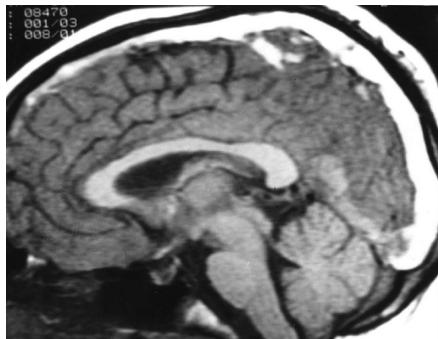
Question #

324 PEDIATRIC NEUROLOGY**CORE KNOWLEDGE****Neuroimaging**

This patient's sagittal T1-weighted image shows that the normal flow void (low signal) is replaced by intraluminal high signal related to thrombosed superior sagittal sinus. The signal intensity of the thrombus over time has the same evolution pattern as intracerebral hematomas.

Greenberg JO (ed). *Neuroimaging: A Companion to Adams and Victor's Principles of Neurology*. 2nd ed. New York: McGraw-Hill, 1999.

Al-Hashel JY1, John JK, Vembu P. Venous thrombosis of the brain. Retrospective review of 110 patients in Kuwait. *Neurosciences (Riyadh)*. 2014 Apr;19(2):111-117.

**331 ADULT NEUROLOGY****Neuroscience and Mechanism of Disease**

The vitamin K antagonists (VKAs) produce their anticoagulant effect by interfering with the cyclic interconversion of vitamin K and its 2,3 epoxide (vitamin K epoxide), thereby modulating the carboxylation of glutamate residues (Gla) on the N-terminal regions of vitamin K-dependent proteins.

The vitamin K coagulation factors II, VII, IX, and X require carboxylation for their procoagulant activity, and treatment with warfarin results in the hepatic production of partially carboxylated and decarboxylated proteins with reduced coagulant activity. Carboxylation is required for a calcium-dependent conformational change in coagulation proteins 9, 10, 11 that promote binding to cofactors on phospholipid surfaces. In addition, vitamin K antagonists inhibit carboxylation of the regulatory anticoagulant proteins C and S and thereby have the potential to be procoagulant.

Ansell J, Hirsh J, Poller L, et al. The pharmacology and management of the vitamin K antagonists: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. *Chest* 2004;126(3 Suppl):204S-233S.

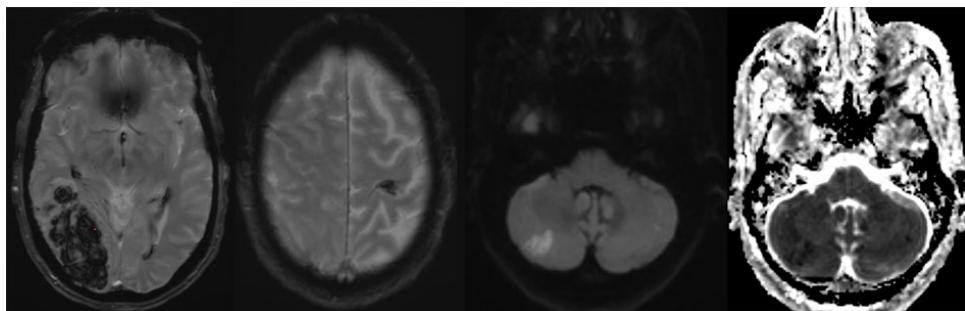
Question #

343 ADULT NEUROLOGY**CORE KNOWLEDGE****Neuroimaging**

This patient's presentation is consistent with ischemic stroke, a large region of likely ischemic stroke with hemorrhagic transformation, and subarachnoid hemorrhage. Stroke and hemorrhage in an immunocompromised patient (transplant) with recent concern for infection should raise concern for infective endocarditis. Infectious vasculopathy would be an additional consideration. Systemic inflammatory markers are nonspecific and could be elevated in both clinical scenarios.

Meschia JF. Diagnostic evaluation of stroke etiology. *Continuum Lifelong Learning Neurol*. 2023 Apr;29(2):412-424.

Sotero FD, Rosário M, Fonseca AC, et al. Neurological complications of infective endocarditis. *Curr Neurol Neurosci Rep*. 2019 Mar 30;19(5):23.

**350 PEDIATRIC NEUROLOGY****CORE KNOWLEDGE****Treatment/Management**

Cerebrovascular disease occurs in 25% of patients with sickle cell disease. Eighty percent of events occur at or before age 15 years, with most caused by a progressive cerebral vasculopathy that can be partially arrested by chronic transfusion therapy to maintain the hemoglobin S level <30%. Most events are thrombotic.

Swaiman AF, Ashwal S, Ferriero DM, et al (eds). *Swaiman's Pediatric Neurology. Principles and Practice*. 6th ed. Philadelphia: Elsevier, 2017.

Question #

356 NO SPECIFIED PATIENT AGE**CORE KNOWLEDGE****Treatment/Management**

Dabigatran, an FDA-approved oral anticoagulant, is a direct thrombin inhibitor that has been demonstrated to reduce the incidence of stroke and systemic emboli compared with dose-adjusted warfarin in patients with nonvalvular atrial fibrillation. The pivotal Randomized Evaluation of Long-term Anticoagulant Therapy (RE-LY) study reported that dabigatran also concomitantly decreases the risk of bleeding.

Two other new oral anticoagulants, apixaban and rivaroxaban, inhibit factor Xa and have also demonstrated noninferiority with warfarin in patients with atrial fibrillation in prevention of stroke and with a lower bleeding risk.

Alberts, MJ. Antithrombotic therapy for secondary stroke prevention. *Continuum Lifelong Learning Neurol.* 2011 Dec;17(6):1255–1266.

Connolly SJ, Ezekowitz MD, Yusuf S, et al. RE-LY Steering Committee and Investigators. Dabigatran versus warfarin in patients with atrial fibrillation. *N Engl J Med.* 2009;361:1139–1151.

Question #

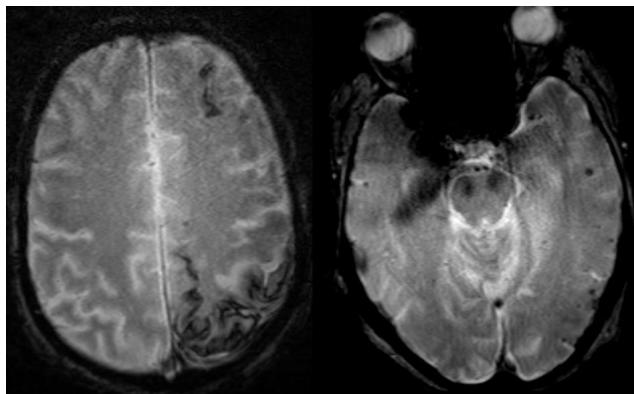
368 ADULT NEUROLOGY**Neuroimaging**

This patient's imaging studies are consistent with cerebral amyloid angiopathy. Gradient echo images are sensitive to blood products, which appear hypointense. On the left image, left frontal and left parietal superficial siderosis is seen. The right image shows multiple cortical and subcortical microhemorrhages.

Superficial siderosis results from degraded blood products (hemosiderin) within the cortical gyral subpial space. Blood in this distribution can result from amyloid-related microhemorrhages.

Lobar microhemorrhages with superficial siderosis are not characteristic of CADASIL, carcinomatosis, or prion disease. Hypertensive hemorrhages tend to occur in deeper brain regions such as the basal ganglia and brainstem.

Ropper AH, Samuels MA, Klein JP, et al (eds). Adams and Victor's Principles of Neurology. 11th ed. New York: McGraw-Hill Education; 2019.

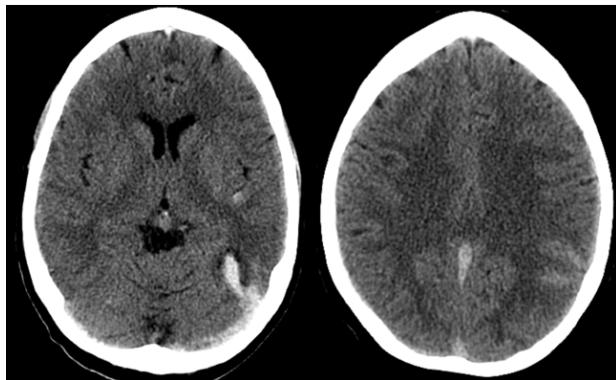


Question #

374 ADULT NEUROLOGY**CORE KNOWLEDGE****Neuroimaging**

This patient's CT scans show a region of hemorrhage, as well as hyperdensity of the left transverse and straight sinus. These findings point to extensive venous sinus thrombosis as the etiology of the intracerebral hemorrhage. Clinically, the patient's history of preceding headache and an episode concerning for seizure also fit well with venous sinus thrombosis. Venous imaging would confirm the diagnosis after which anticoagulation would be initiated.

Lberman AL. Diagnosis and treatment of cerebral venous thrombosis. *Continuum Lifelong Learning Neurol*. 2023 Apr;29(2):519–539.



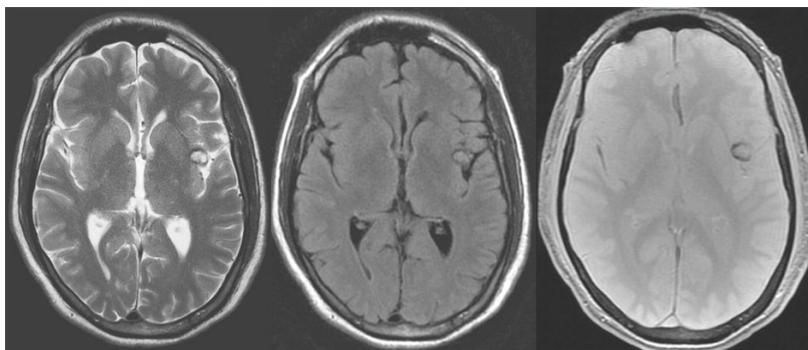
Question #

380 ADULT NEUROLOGY**CORE KNOWLEDGE****Neuroimaging**

Cavernous malformations are histologically clusters of uniform-sized tiny vessels that can form anywhere in brain. They may bleed, but usually not catastrophically. If they have hemorrhaged in the past, it is common to see a ring of hemosiderin deposition on gradient echo sequences.

Subependymal nodules are located at the ventricular surface but can sometimes be calcified. This would be an atypical appearance for chronic infarct or dystrophic calcification.

Brazis PW, Masdeu JC, Biller J (eds). Localization in Clinical Neurology. 8th ed. Philadelphia: Wolters Kluwer; 2022.

**388 NO SPECIFIED PATIENT AGE****Neuroanatomy**

The great vein of Galen enters the dura of the tentorium and is joined by the inferior sagittal sinus to form the straight sinus (sinus rectus).

Blumenfeld H. Neuroanatomy Through Clinical Cases. 3rd ed. Sunderland: Sinauer Associates; 2021.