5 Wernicke Encephalopathy

Aaron B. Paul

INTRODUCTION

Wernicke encephalopathy (WE) was first described in 1881 by Carl Wernicke as a "superior acute hemorrhagic polioencephalitis."[1] WE is now recognized as a complication of thiamine (vitamin B1) deficiency and results in the following clinical triad: mental confusion, gait ataxia, and ocular dysfunction. Diagnosing WE is straightforward when a known alcoholic demonstrates all of these symptoms. Unfortunately, this occurs in a minority of patients. One study investigating 245 patients over a 10-year period discovered that only 33% of patients demonstrated the complete triad. Consequently, WE is believed to be underdiagnosed.[2]

The most common symptoms of WE are mental status abnormalities (82%), ocular dysfunction (29%), ataxia (23%), and polyneuropathy (11%).[3] Mental status abnormalities include disorientation, indifference, and inattentiveness, with impaired learning and memory.[3] Ocular abnormalities include nystagmus, bilateral cranial nerve VI palsies, and conjugate gaze palsies.[4] Ataxia affects both stance and gait and is secondary to a combination of polyneuropathy, cerebellar involvement, and vestibular dysfunction.[5] Korsakoff syndrome is a memory disturbance with amnesia and confabulation that may develop if the thiamine deficiency is left untreated.[6]

WE can be identified at autopsy in 0.4% to 2.8% of the population.[7] Aside from alcoholism, WE has been reported in a variety of conditions that disrupt thiamine absorption. Examples include following gastrointestinal surgery, prolonged vomiting, chemotherapy, systemic infections, noninfectious disease, and dietary imabalances.[4]

Thiamine is needed for a variety of cellular processes including the maintenance of membrane osmotic gradients and glucose metabolism.[4] With insufficient dietary intake, the human body's stores become depleted in approximately 1 month.[8] At histopathology, both vasogenic and cytotoxic edema can be identified, along with swelling of astrocytes and oligodendrocytes, proliferation of microglia, necrosis, demyelination, vascular proliferation, petechial hemorrhage, and disruption of the blood-brain barrier.[9] The intravenous administration of thiamine is the treatment for WE. Importantly, glucose should never be administered without thiamine because doing so can precipitate or worsen WE.

WERNICKE ENCEPHALOPATHY IMAGING EVOLUTION: OVERVIEW

Optimal management of WE depends on a timely and accurate diagnosis. However, the diagnosis can be missed due to the disease's occasionally subtle imaging findings, its temporal evolution, and the challenge of perceiving symmetric involvement of brain anatomy. Fortunately, characteristic imaging features within the appropriate clinical context can be used to confidently diagnose WE.

WE can be conceptually organized into early and late stages (Fig. 5.1). Early WE begins with symmetric T2/FLAIR hyperintensity involving the thalami, mammillary bodies, hypothalamus, walls of the third ventricle, tectal plate, and periaqueductal gray matter. Contrast enhancement of the mammillary bodies can also be seen, is more common in alcoholic patients,[10] and may be the only imaging finding.[11] Contrast should therefore be administered when clinical suspicion is high (Fig. 5.2). In late WE, mammillary body atrophy and enlargement of the third ventricle are seen (Fig. 5.3). Cases demonstrating subtle T2/FLAIR hyperintensity isolated to the mammillary bodies and periaqueductal gray matter without involvement of the walls of the third ventricle or thalami, and without enhancement are less conclusive. Table 5.1 contrasts the differences in the imaging findings of early versus late WE.

WERNICKE ENCEPHALOPATHY IMAGING VARIANTS

There are important imaging variants of WE that are essential for an expert understanding. Symmetric T2 hyperintensity can also involve the cerebral cortex, fornix, splenium, caudate nuclei, red nuclei, cranial nerve nuclei, cerebellum, vermis, and dentate nuclei.[12–17] These imaging variants may occur in conjunction with the more typical WE imaging findings, and therefore their presence should not necessarily suggest a superimposed process (Fig. 5.4).

DIFFERENTIAL DIAGNOSIS

The most important differential diagnoses for WE can be divided into the following four categories: ischemic, infectious-inflammatory, toxic, and metabolic.

Ischemic considerations include artery of Percheron infarction, top of the basilar infarction, and deep cerebral vein thrombosis.

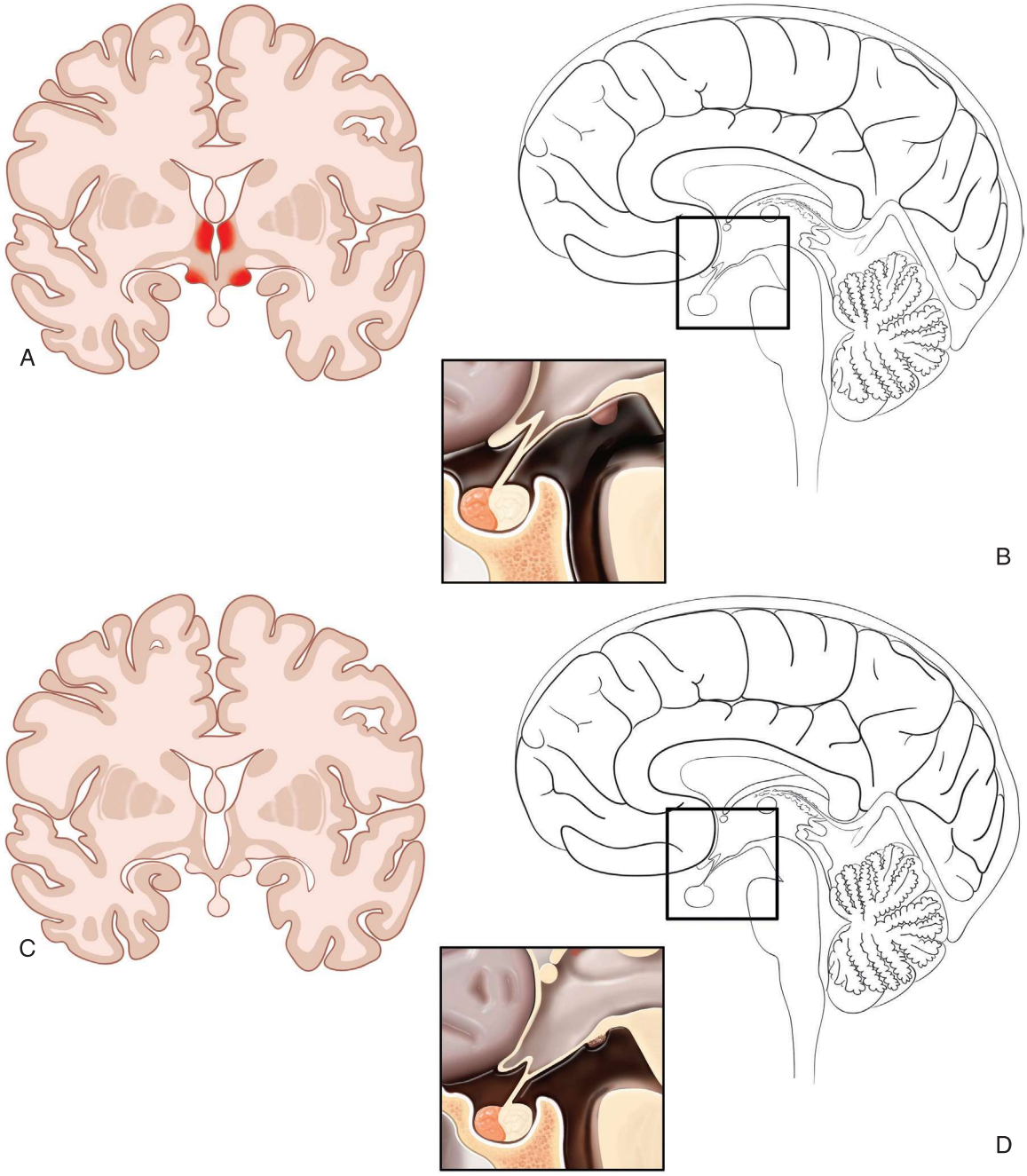

Figure 5.1. Wernicke encephalopathy (WE) temporal evolution. Early WE (A and B) demonstrates signal abnormality involving the thalami, mammillary bodies, walls of the third ventricle, tectal plate, and periaqueductal gray. Late WE (C and D) demonstrates mammillary body atrophy and enlargement of the third ventricle.

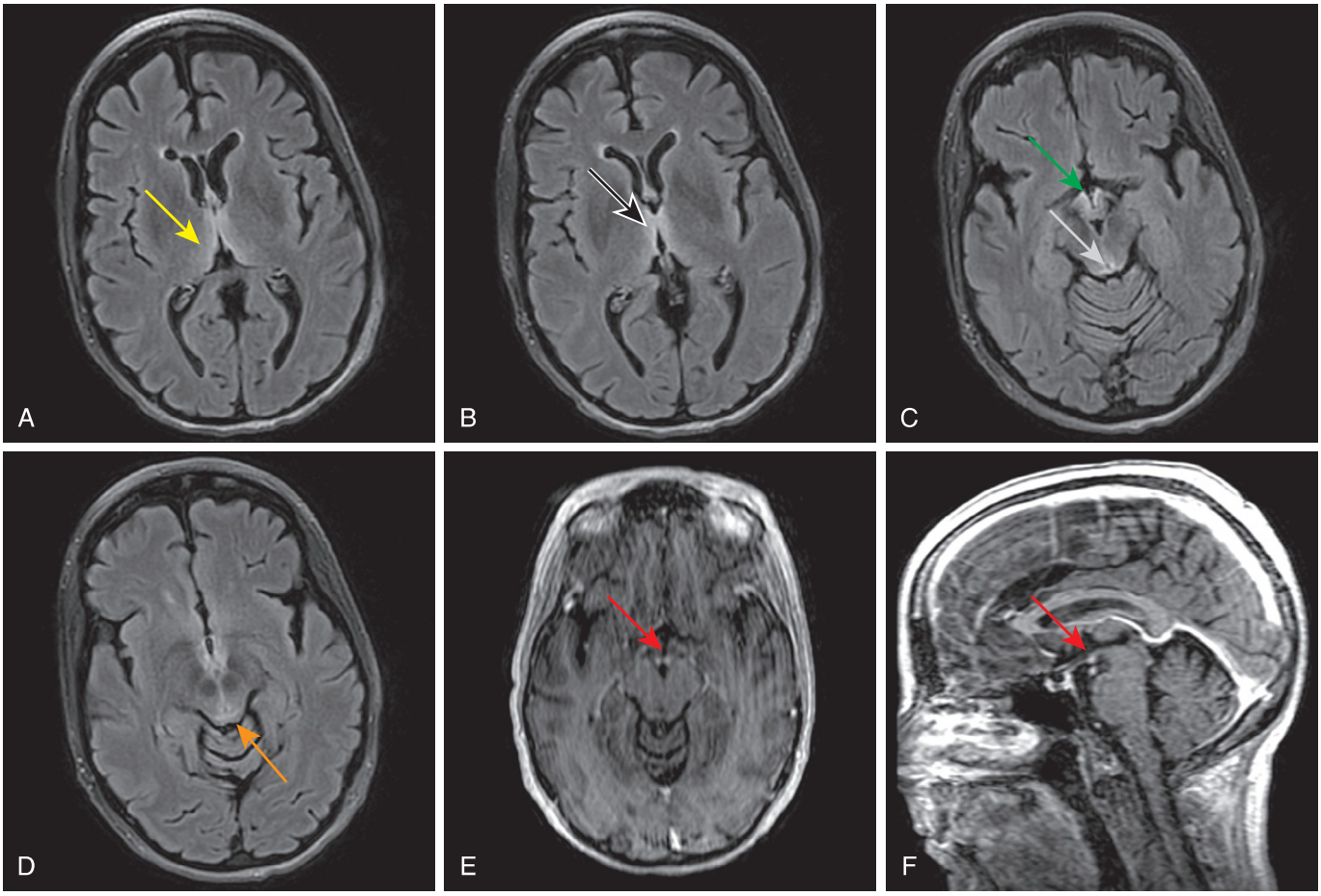

Figure 5.2. Early Wernicke encephalopathy. Middle-aged female with history of depression and alcoholism presents with catatonia after overdosing on Seroquel. Her mental status was noted to dramatically improve with IV thiamine. Axial FLAIR (A to D) images demonstrate hyperintensity involving the thalami *(yellow arrow)*, walls of the third ventricle *(black arrow)*, periaqueductal gray matter *(gray arrow)*, tectal plate *(orange arrow)*, and hypothalamus *(green arrow)*. Axial (E) and sagittal (F) contrast-enhanced T1-weighted images show enhancement of the mammillary bodies *(red arrows)*.

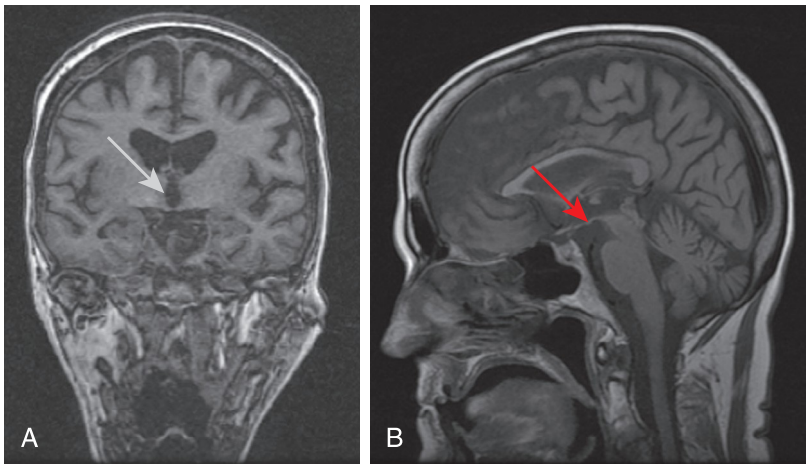

Figure 5.3. Late Wernicke encephalopathy. Middle-aged male with a two-decade history of alcoholism requiring multiple hospitalizations. Coronal T1 (A) and sagittal T1 (B) images demonstrate enlargement of the third ventricle *(gray arrow)* and atrophy of the mammillary bodies *(red arrow)*.

Artery of Percheron infarction typically produces T2 hyperintensity and restricted diffusion in the bilateral thalami and may also extend into the midbrain[18] (Fig. 5.5). Top of the basilar infarction involves these areas, as well as the bilateral posterior cerebral artery (PCA) distributions. Deep cerebral vein thrombosis results in T2 hyperintensity with increased and/or decreased diffusion in the bilateral thalami and basal ganglia, often with associated hemorrhage. The involvement of a distinctive vascular territory, as well as the clinical history and presentation, help to differentiate these diagnoses from WE.

Infectious-inflammatory considerations include acute disseminated encephalomyelitis (ADEM), Creutzfeldt-Jakob disease, and West Nile virus. ADEM typically involves the deep gray nuclei and white matter with multifocal T2 hyperintense lesions and enhancement along the leading edge of inflammation.[19] Creutzfeldt-Jakob disease produces T2 and diffusion-weighted imaging (DWI) hyperintensity (with variable signal on apparent diffusion coefficient [ADC] maps) in the basal ganglia, thalami, and cerebral cortex. West Nile virus involves the basal ganglia and thalami with T2 hyperintensity.[20] The clinical history, presentation, and distribution of findings help to differentiate these diagnoses from WE.

Toxic considerations include carbon monoxide, heroin, and metronidazole-induced encephalopathy. Mild carbon monoxide poisoning results in T2 hyperintensity in the globi pallidi. More severe poisoning results in T2 hyperintensity in the remainder of the deep gray nuclei and cortex. Heroin results in a toxic leukoencephalopathy with T2 hyperintensity predominantly involving the posterior limbs of the internal capsules extending superiorly into the perirolandic white matter and inferiorly into the pontine corticospinal tracts with relative sparing of the subcortical U-fibers.[21] Metronidazole-induced encephalopathy involves the dentate nuclei, vestibular nuclei, and tegmentum with T2 hyperintensity and less frequently involves the corpus callosum, midbrain, pons, and medulla (Fig. 5.6).[22] The clinical history, presentation, and distribution of findings again help to differentiate these diagnoses from WE.

TABLE 5.1 Summary of Wernicke Encephalopathy (WE) Evolution Pattern

	Early WE	Late WE
FLAIR hyperintensity	Yes	No
Enhancement	Yes	No
Atrophy	No	Yes

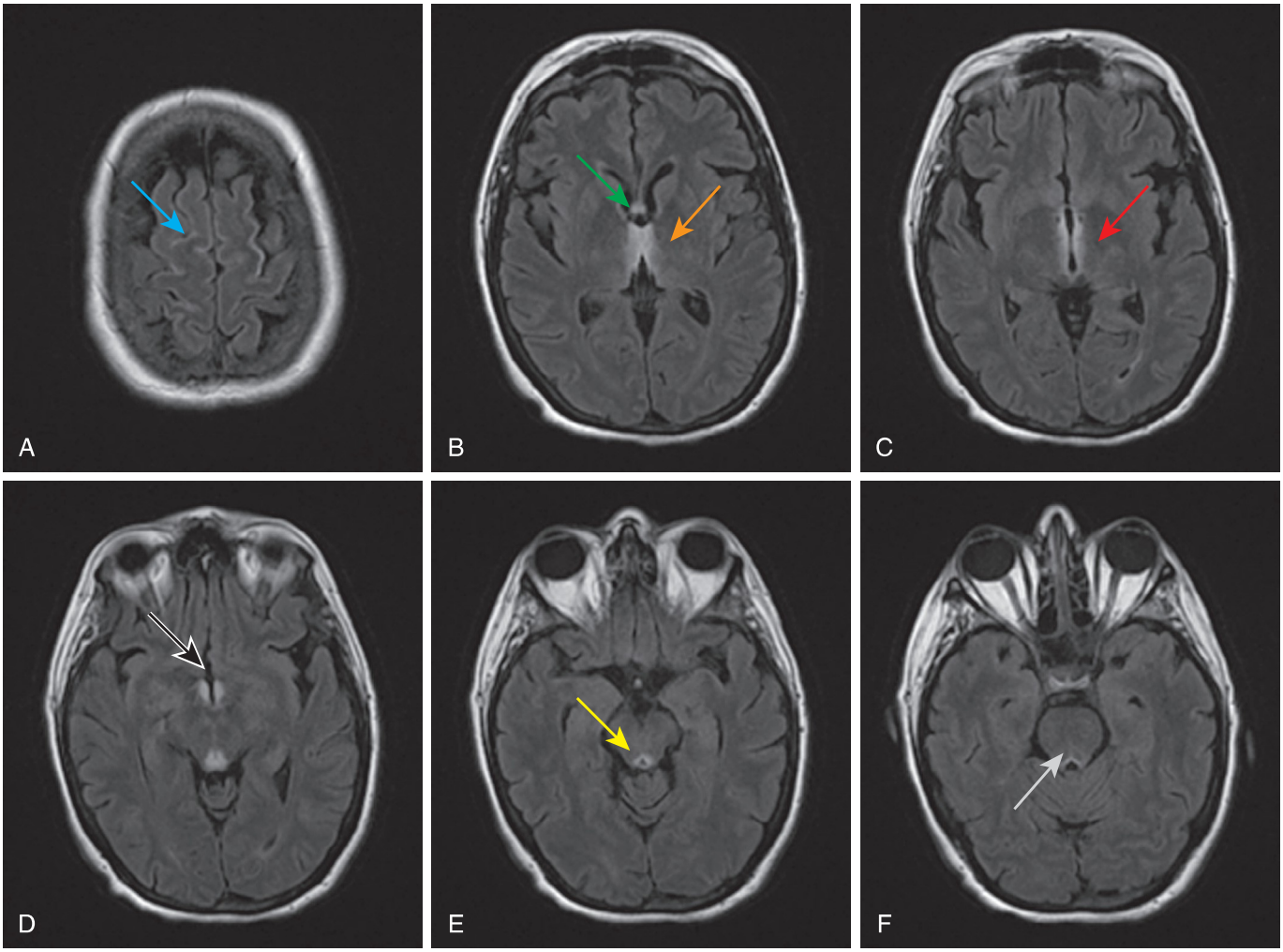

Figure 5.4. Atypical Wernicke encephalopathy. Middle-aged female found down. Axial FLAIR images (A to F) demonstrate atypical FLAIR hyperintensity involving the bilateral frontal cerebral cortex *(blue arrow)* and fornices *(green arrow)*, in addition to the more typical involvement of the thalami *(orange arrow)*, walls of the third ventricle *(red arrow)*, periaqueductal gray matter *(yellow arrow)*, tectal plate *(gray arrow)*, and hypothalamus *(black arrow)*.

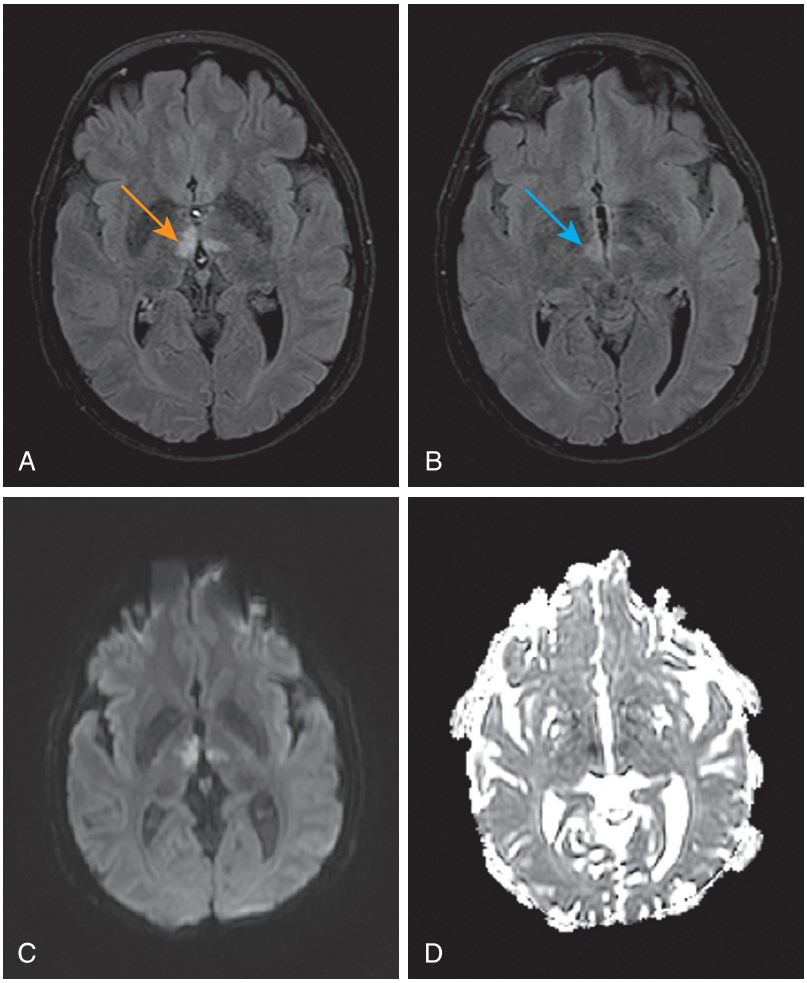

Figure 5.5. Artery of Percheron infarction. Middle-aged male presents with sudden onset of unresponsiveness. Axial FLAIR (A and B) images demonstrate bilateral hyperintense thalamic lesions *(yellow arrow)* extending into the rostral midbrain *(blue arrow)*. The lesions have restricted diffusion (hyperintense on DWI [C] and hypointense on apparent diffusion coefficient map [D], typical of acute to subacute infarctions).

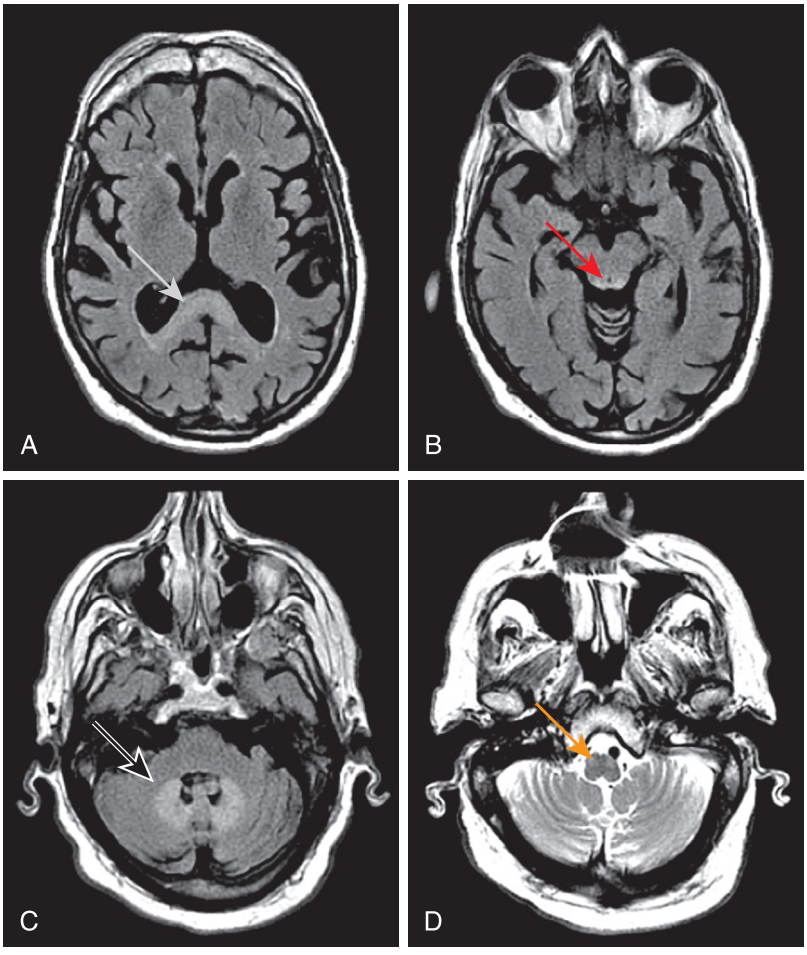

Figure 5.6. Metronidazole-induced encephalopathy. Elderly male with a history of recurrent *Clostridium difficile* infection on a 6-month course of metronidazole presents with dysmetria and dysarthria. Axial FLAIR (A to C) and Axial T2 (D) images demonstrate abnormal signal involving the splenium of the corpus callosum *(gray arrow)*, superior colliculi *(red arrow)*, dentate nuclei *(black arrow)*, and inferior olivary nuclei *(orange arrow)*.

Central pontine myelinosis is the most important metabolic consideration. Central pontine myelinosis results in T2 hyperintensity and restricted diffusion in the central pons and less frequently involves the corpus callosum, midbrain, and medulla.[23] The classic pontine involvement and imaging configuration help to differentiate this entity.

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