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Anti–*N*-methyl-D-aspartate Receptor Encephalitis:

Characteristic Behavioral And Movement Disorder

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Anti–*N*-methyl-D-aspartate (anti-NMDA) receptor encephalitis is a treatable paraneo-plastic disorder predominantly affecting young women. It is characterized by a combination of psychotic encephalopathy, seizures, and abnormal movements of the trunk and face, particularly in the form of jaw dystonia. Enhanced awareness of the typical presentation can increase the index of suspicion and facilitate initiation of appropriate treatment.

A previously healthy 26-year-old African American woman presented to the emergency department after an acute episode of psychotic behavior in which she was described as becoming abruptly agitated and restless. Over the next few days, she developed seizures and sustained impairment of consciousness for which she required intubation and intensive care monitoring. She showed intermittent agitation with screaming and crying spells. Electroencephalography revealed bilateral independent temporal epileptiform discharges, which prompted treatment with phenytoin. On neurological examination, she was awake but unresponsive to verbal or noxious stimulation. Several episodes of jaw-opening dystonia, paroxysmal opisthotonus, and catatonic postures were observed (Figure 1A and B, video [http://www.archneurol.com]).

Analysis of cerebrospinal fluid showed lymphocytic pleocytosis (white blood cell count, 200/μL), with normal glucose and protein levels. Results from cytology, Gram stain, cultures, and polymerase chain reaction for herpes simplex virus, varicella zoster virus, Epstein-Barr virus, and West Nile virus in cerebrospinal fluid were negative. Brain magnetic resonance imaging disclosed hyperintensities in both cerebellar hemispheres (Figure 1C). Results for human immunodeficiency virus, rapid plasma reagin, serum cultures, autoimmune panel, and thyroid-stimulating hormone, free thyroxine, folic acid, and B12 levels were within normal limits. Results from the following paraneoplastic antibody tests were negative: antineuronal nuclear, cytoplasmatic Purkinje cell, amphiphysin, collapsing-response mediator protein type 5, calcium channel, acetylcholine receptor ganglionic neuronal, antiglial nuclear, and voltage-gated potassium channel. Using human embryonic kidney 293 cells transfected with NR1/NR2

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heteromers,[1] antibodies against NMDA receptors were found in cerebrospinal fluid (serial dilutions; titer, 1:160) and serum (titer, 1:40). Although initial pelvic computed tomographic and ultrasonographic results were unrevealing, a pelvic magnetic resonance image demonstrated a right 9-mm ovarian mass (Figure 2A), which proved to be a teratoma on histopathological analysis (Figure 2B). Surgical teratoma excision and intravenous methylprednisolone sodium succinate led to noticeable improvement in function over the next few days. Five weeks after this treatment, the patient had returned to work.

COMMENT

Reversible anti-NMDA receptor encephalitis is associated with antibodies against NR1/NR2 heteromers of the NMDA receptor.[1] In young women (aged 15–45 years), more than one-fourth of all unexplained new-onset epileptic encephalopathies, especially when psychiatric symptoms and pleocytosis are documented, are due to NMDA receptor antibodies.[2] Although not associated with an underlying malignant neoplasm, prompt identification of the characteristic presentation should lead to a search for and, when present, removal of ovarian teratoma and initiation of immunomodulation.3 A recent series4 of 81 patients showed that the chance to identify a tumor is sex and age dependent. While 56% of female patients older than 18 years had a teratoma, only 9% of patients aged 14 years or younger had a teratoma. None of the 12 male patients of the study had a tumor.

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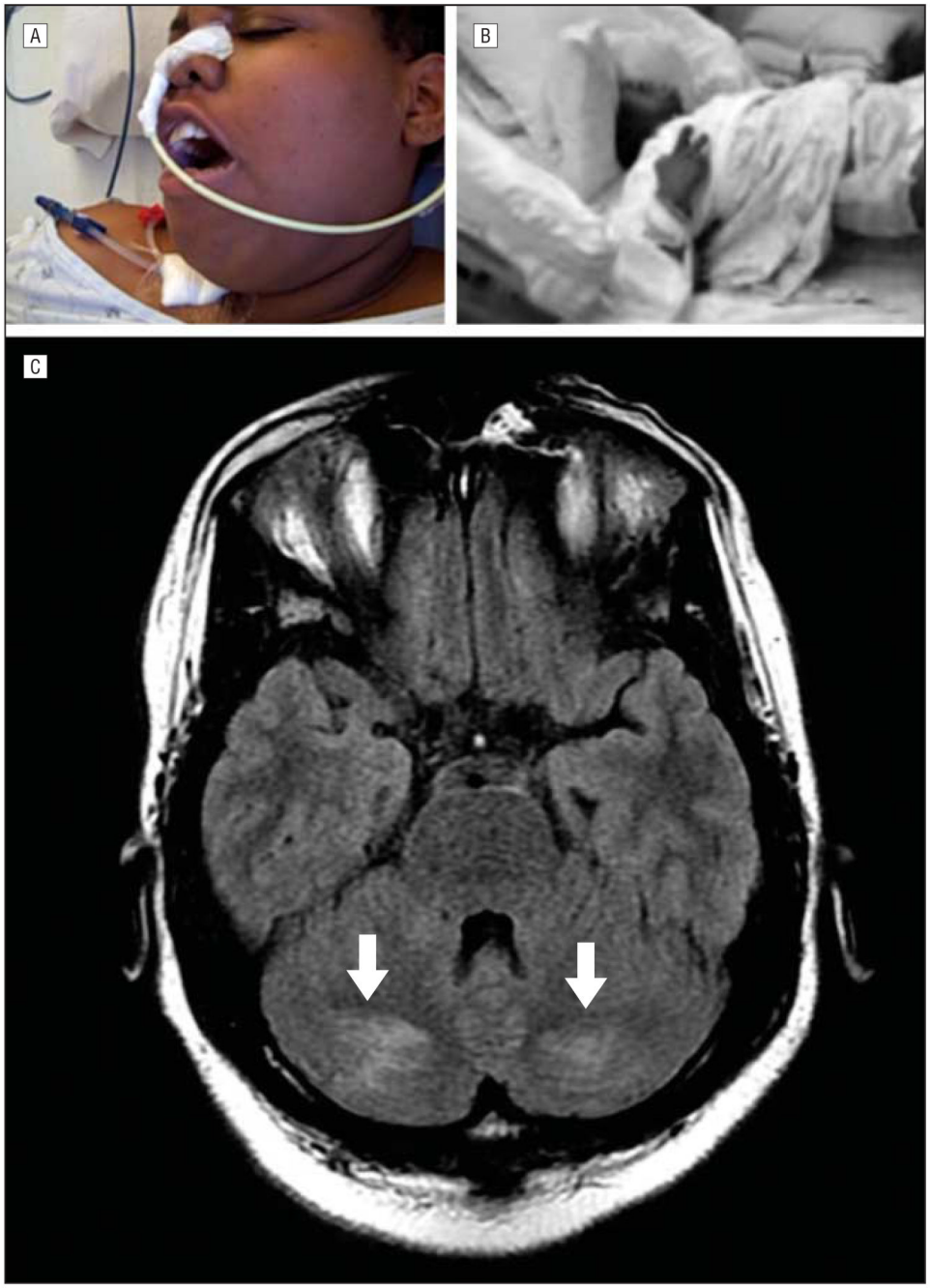

Figure 1.
Jaw-opening dystonia (A) and opisthotonic posture (B) are observed. C, A fluid-attenuated inversion recovery sequence of an axial brain magnetic resonance image shows symmetric hyperintensities in the cerebellar hemispheres (arrows).

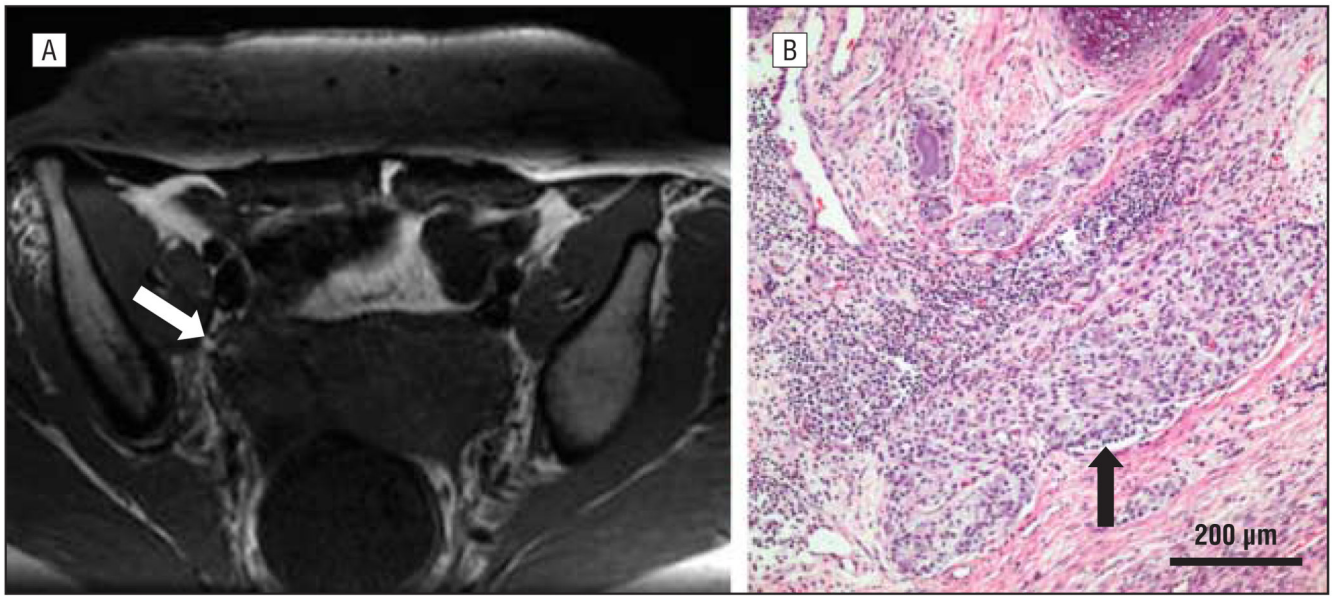

Figure 2.
Imaging and histopathological findings. A, A T1-weighted magnetic resonance image of the pelvis shows a 9-mm high-signal mass in the right ovary, suggestive of a small teratoma (arrow). B, Hematoxylin-eosin staining of the ovarian mass demonstrates typical mature components including benign cartilage, smooth muscle, and a cluster of ganglion cells with prominent nucleoli (arrow), confirming the diagnosis of teratoma.