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Clinical Observations

Acute Disseminated Encephalomyelitis: A Gray Distinction

Amal Abu Libdeh MBBS, Howard P. Goodkin MD, PhD, Denia Ramirez-Montealegre MD, PhD, J. Nicholas Brenton MD *

Division of Pediatric Neurology, Department of Neurology, University of Virginia, Charlottesville, Virginia

ABSTRACT

BACKGROUND: Acute disseminated encephalomyelitis (ADEM) is an immune-mediated, inflammatory acquired demyelinating syndrome predominantly affecting the white matter of the central nervous system. **METHODS:** We describe a three-year-old boy whose clinical presentation was suspicious for ADEM but whose initial imaging abnormalities were confined to the deep gray matter (without evidence of white matter involvement). His clinical course was fluctuating and repeat imaging one week after presentation demonstrated interval development of characteristic white matter lesions. **RESULTS:** Treatment with adjunctive intravenous immunoglobulin and high-dose corticosteroids resulted in significant clinical improvement. **CONCLUSIONS:** Isolated deep gray matter involvement can precede the appearance of white matter abnormalities of ADEM, suggesting that repeat imaging is indicated in individuals whose findings are clinically suspicious for ADEM but who lack characteristic imaging findings.

Keywords: acute disseminated encephalomyelitis, encephalitis, ADEM, autoimmune, gray matter

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Introduction

Acute disseminated encephalomyelitis (ADEM) is an inflammatory demyelinating disease of the central nervous system (CNS) that manifests with encephalopathy (unexplained by fever) and polyfocal neurological signs and symptoms (e.g., ataxia, limb weakness, sensory changes, visual loss, cranial nerve impairment, or speech dysfunction). Seizures may occur during the course of ADEM but are typically noted in those patients aged five years or younger.[1-3] Infection or immunization may precede ADEM by days to weeks. Although most children are febrile during the prodromal illness, fever at ADEM onset is variable. Occasionally, ADEM may follow a prolonged course of fever of unknown origin.[4] Unlike pediatric-onset multiple sclerosis (MS), ADEM typically exhibits a monophasic course with characteristic imaging findings and preferentially affects prepubertal children.

Magnetic resonance imaging (MRI) is the radiologic modality of choice and will characteristically show diffuse, large (greater than one to two cm) fluid attenuation inversion recovery (FLAIR) and T2-hyperintensities with indistinct borders that predominately involve the cerebral white matter of the brain and spinal cord. Although often considered to be an acquired "white matter disease," ADEM commonly manifests with lesions of the cortical gray-white matter junction and deep gray matter (e.g., basal ganglia, thalamus).[5,6] Gadolinium enhancement occurs in up to 30% of individuals with ADEM.[1] Periventricular lesions and T1-hypointense lesions (i.e., "black holes") are uncommon in ADEM and are more suggestive of MS. The lesions of ADEM are typically present at the onset of clinical manifestations and often resolve as neurological symptoms improve.[1,7,8] However, the MRI may be normal early in the disease course.[9,10] The symptoms and imaging findings fluctuate throughout the clinical course of ADEM, particularly within the first three months of the disease.[7]

In an attempt to establish consistency among providers, the International Pediatric Multiple Sclerosis Study Group (IPMSSG) developed consensus criteria to assist in the

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* Communications should be addressed to: Dr. Brenton; Division of Pediatric Neurology; Department of Neurology; University of Virginia; PO Box 800394; Charlottesville, VA 22908.

E-mail address: jnb8h@virginia.edu

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diagnosis of ADEM. As part of these diagnostic criteria, white matter abnormalities are an essential requirement of ADEM diagnosis.[7,11] We describe a child with ADEM manifesting initially with brain lesions only in the deep gray matter and a distinct lack of characteristic white matter involvement.

Patient Description

This three-year-old previously healthy boy presented to his pediatrician with new-onset fever and a two-week history of upper respiratory symptoms. He began oral antibiotics for presumed sinusitis with subsequent resolution of the respiratory symptoms; however, his fever persisted. He presented to the hospital after remaining intermittently febrile for more than a week with a myriad of symptoms including headache, diffuse abdominal pain, decreased appetite, fatigue, malaise, and refusal to walk. Initial evaluation with serologic and urine studies was unrevealing. He was managed conservatively and gradually improved, although he remained intermittently febrile. Approximately three weeks after his fever began, he developed worsening somnolence, headache, decreased appetite, body aches, slurred speech, ataxic gait, bilateral hand tremors, and urinary retention. Neurological consultation documented encephalopathy (manifesting as lethargy and irritability), dysarthric speech, bilateral arm dysmetria and intention tremor, wide-based gait, whole body dysesthesias, and exaggerated deep tendon reflexes.

Differential diagnosis at the time included acute or subacute CNS infection, postinfectious cerebellar ataxia, and ADEM. Further evaluation with lumbar puncture showed a monocytic and lymphocytic pleocytosis (64 cells/μL) with no red blood cells and normal protein and glucose. Cerebrospinal fluid (CSF) studies including bacterial culture, herpes simplex virus polymerase chain reaction, enterovirus polymerase chain reaction, and cytology were all unremarkable.

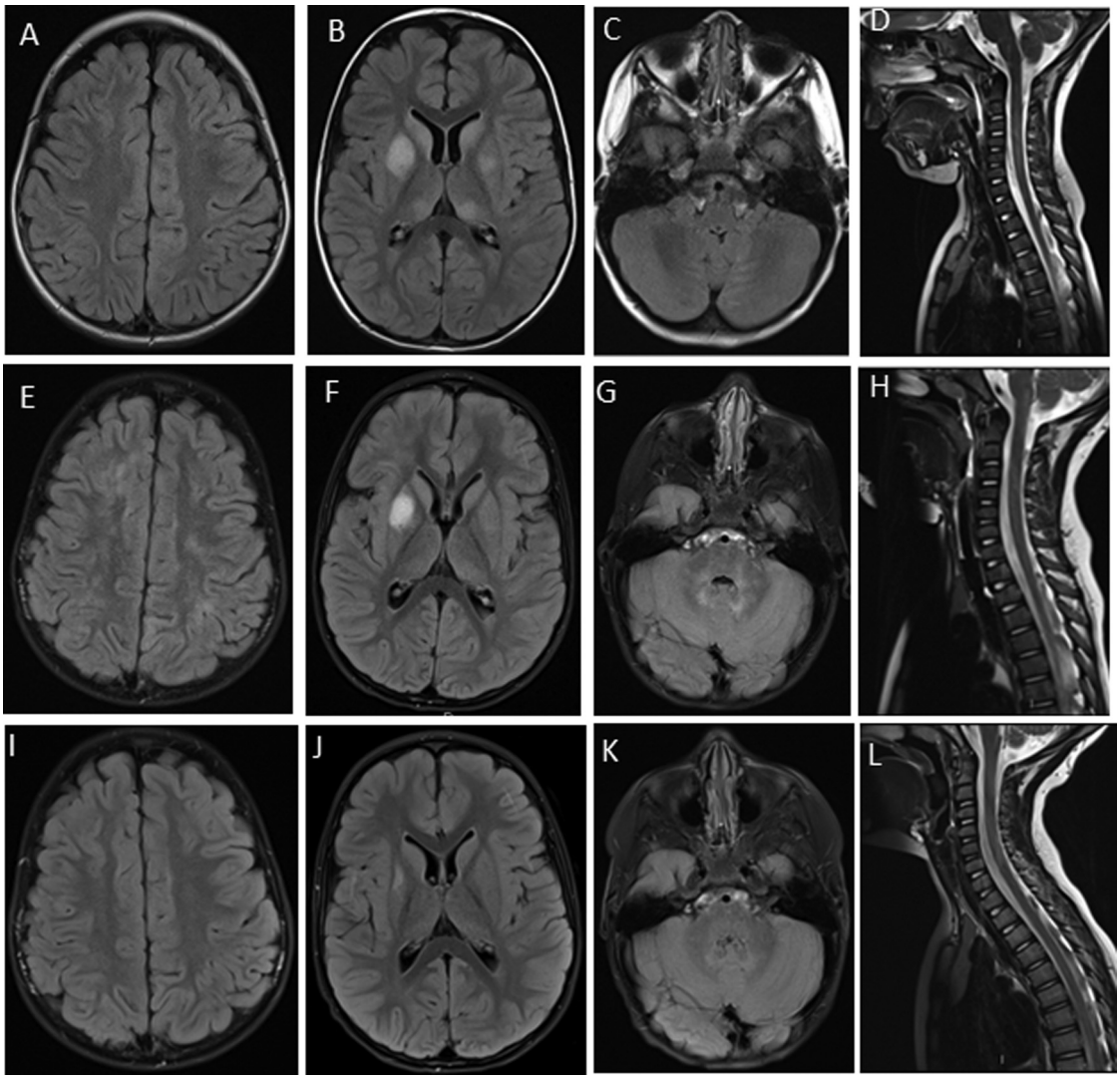

FIGURE.
Brain and cervical spine magnetic resonance imaging (MRI) completed at the onset of neurological symptoms: (A-D) Axial fluid attenuation inversion recovery (FLAIR) images of the brain showing hyperintense signal and mild swelling, within the basal ganglia and dorsal thalami bilaterally. Sagittal T2 image of the cervical spine showing mild cord swelling and diffuse hyperintense signal from C2 to C7. MRI completed one week after obtaining first imaging: (E-H) Axial FLAIR images demonstrating multiple patchy foci with indistinct margins of subcortical and deep white matter hyperintense signal within the bilateral cerebral hemispheres. Improved but persistent signal abnormality within the basal ganglia and thalami. Sagittal T2 image of the cervical spine showing largely unchanged mild cord swelling and diffuse hyperintense signal from C2 to C7. MRI completed 5 months after initial neurological presentation: (I-L) Axial FLAIR images demonstrating near complete resolution of the hyperintense patchy foci within the white matter with residual gliosis in the right putamen. Sagittal T2 image of the cervical spine showing improvement in the hyperintense signal of the long segment from C2 to C7.