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A Case of Acute Disseminated Encephalomyelitis in a Middle-Aged Adult

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BACKGROUND

Acute disseminated encephalomyelitis (ADEM) is a monophasic inflammatory demyelinating disorder of the white matter that is often preceded by viral infection or recent vaccination. Encephalopathy and focal neurological deficits usually manifest one to three weeks after a prodromal illness with neurologic decline progressing rapidly over days to weeks. Approximately 25% of patients will develop multiple sclerosis (MS) within five years of initial presentation of ADEM but the majority of individuals do not progress beyond three months.¹ ADEM is most commonly seen in children and young adults, where prognosis is favorable, but very few cases have been reported of middle-aged or elderly patients. The clinical course of these patients as compared to younger patients with ADEM is unclear. Here we present a case of ADEM in a middle-aged adult that recovered well after treatment with high-dose corticosteroids.

CASE SUMMARY

A 62-year-old man with a history of hypertension initially presented with progressive development of gait dysfunction, urinary incontinence, and encephalopathy. He underwent an MRI of the brain on the first hospital day (HD) that revealed extensive supratentorial white matter hyperintensities extending from the periventricular region through subcortical fibers without contrast enhancement (see figure 1). Thus he was started on 250 milligrams (mg) of intravenous (IV) methylprednisolone every 6 hours for presumed ADEM. He also underwent a lumbar puncture on HD #1 prior to administration of IV steroids that revealed an opening pressure of 20, with cerebrospinal fluid (CSF) containing 0 red blood cells. 47 white blood cells of which 85% were lymphocytes, glucose of 79 and protein of 100. CSF bacterial cultures were negative, as well as no evidence of active HSV or EBV infection. CSF cytology revealed the presence of white blood cells but was negative for malignancy. RPR was also negative. Two subsequent MRIs of the brain were performed on HD #13 and HD #21 showing no significant change in the appearance of the prior white matter lesions and no new contrast enhancing lesions. In addition, an MRI of the cervical and thoracic spine with contrast performed on HD #22 did not show any prior or new enhancing white matter lesions. With continued treatment with high dose IV steroids at 250 mg of IV methylprednisolone every 6 hours for another 7 days, his mental status improved and thus he was safely extubated on HD #10 and continued on a taper of oral prednisone. He underwent a brain biopsy on HD #13 that revealed multiple small foci of macrophage accumulation and widespread white matter inflammation secondary to demyelination (figure 2). He was subsequently discharged on HD #63 to acute rehab on a prolonged oral steroid taper. His physical exam on discharge was notable for a GCS of 15, fully oriented, full strength on the left, and a residual right hemiparesis. Upon outpatient follow up four months later, he made further improvements, now ambulating without assistance, cognitively back to his baseline, and independent in his activities of daily living, with a modified Rankin score (mRS) of 0. He underwent a follow up MRI brain five months later that showed overall improvement in the diffuse white matter changes previously seen on initial presentation (see figure 1).
ADEM is theorized to be an immunologically mediated demyelinating disease triggered by a febrile illness or recent vaccination, eliciting an inflammatory response affecting the central nervous system (CNS). Possible mechanisms may include either molecular mimicry or direct inflammatory damage to myelinated neurons. The prevalence of ADEM is higher in children and young adults and thought to be related to the increased frequency of viral infections and vaccination in this patient population. The demonstration of multifocal hyperintensities most often affecting the subcortical white matter on fluid attenuated inversion recovery (T2/FLAIR) MRI of the brain make the identification of ADEM difficult given various other inflammatory, infectious, and rheumatologic disorders that have similar clinical and radiological presentations. Given such ambiguity, the International Pediatric Multiple Sclerosis Study Group proposed a consensus definition for the pediatric population with the mandatory inclusion of encephalopathy in the criteria for diagnosis. Despite this useful aid in identifying young patients, there still remains no clear diagnostic criterion for ADEM in adults, and therefore older individuals are more difficult to prognosticate given the paucity of reported cases and outcomes following standard ADEM therapies such as high dose corticosteroids, intravenous immunoglobulin (IVIG), and plasmapheresis (PLEX). Our patient presented with a suggestive clinical history of symptoms, physical exam and radiological signs, along with a CSF profile and histopathology suggestive of ADEM. Given both the therapeutic and prognostic implications of considering this a case as the first demyelinating event of MS, it important to make clear that this most likely does not represent MS given the initial subacute presentation of encephalopathy, the presence of multifocal lesions with ill-defined margins, and pathology showing widespread inflammation. In contrast, MS often presents with distinct episodes of focal neurological deficits with concomitant confluent demyelinating lesions of varying ages appearing ovoid in shape, often affecting the white matter more than gray matter, the latter of which is seen more commonly in ADEM. CSF studies reveal the persistent presence of oligoclonal bands more frequently in MS in comparison to ADEM. Furthermore in this patient, subsequent MRIs confirmed no evidence of new contrast enhancing lesions, with follow up MRI five months later showing resolution of a monophasic demyelinating event with concomitant clinical resolution of neurological deficits. Additionally, due to the negative aforementioned serologies and inflammatory markers, as well as the lack of systemic symptoms, this case likely does not represent a manifestation of an underlying infectious, neoplastic, or rheumatologic condition that may mimic a demyelinating CNS insult.

A small case series of middle-aged adults presenting with ADEM has been described by Wang et al., in which all three patients had a single episode of focal neurological deficits and encephalopathy with typical MRI findings, and clinically improved with steroid treatment. Although typically reserved for more fulminant forms of ADEM, there have also been individual reports of the concomitant use of steroids along with IVIG and PLEX in the treatment of ADEM in older patients with favorable outcomes, suggesting that this presentation in older adults may in fact be of the similar pathophysiology that is well-described in children and young adults.

ADEM rarely presents in the middle-aged to elderly adult and due to the paucity of cases reported in the literature, the prognosis in this age group is unknown. We present a case of ADEM in a middle-aged adult in which the patient had an excellent response to treatment with high dose steroids, resulting in a remarkable neurological recovery. Thus it behooves us to treat suspected cases of ADEM in an adult patient aggressively, as outcome may be favorable.
Figure 2

A. Axial T2/FLAIR showing supratentorial WM hyperintensities extending from the periventricular region through the subcortical fibers. 
B. Sagittal T2/FLAIR MRI showing diffuse periventricular WM intensities. 
C. Axial T2/FLAIR MRI showing interval improvement & resolution of the periventricular WM lesions. 
D. Sagittal T2/FLAIR also demonstrating the improvement of the periventricular WM lesions. 
E. H&E Stain (200x) showing areas devoid of pink-stained myelin consistent with demyelinating plaques. 
F. Immunohistochemistry stain for CD68 (200x) which is a marker for macrophages. This image shows the detection of dark pigment structures that represent macrophages infiltrating the areas of demyelination. 
G. Stain of neurofilaments (brown strands, 400x) confirming the relative conservation of axons even within the areas of demyelination. 
H. Luxol Bluestain (100x) showing staining of lipophilic myelinated axons (blue) with patchy areas of demyelination (purple) with dark structures representing infiltrating macrophages.

REFERENCES