Fulminant Acute Disseminated Encephalomyelitis

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Abstract

Acute disseminated encephalomyelitis, or post infectious encephalomyelitis is an immunologically mediated demyelinating disorder affecting the central nervous system after infection or vaccination. Young and adolescents are mostly affected with characteristic diffuse neurological signs. Prognosis is generally favorable, however, fulminant acute disseminated encephalomyelitis can be fatal if not diagnosed and treated early. With an increase in intracranial pressure, the treatment of choice is methylprednisolone, followed by immunoglobulin, plasmapheresis or cytotoxic drugs. We present a case of acute disseminated encephalomyelitis in a 17 year male who presented with a sudden onset recurrent generalized tonic-clonic seizures and rapidly become comatose. Magnetic resonance imaging along with other investigations helped in establishing the diagnosis. Treatment resulted in full recovery with uneventful follow up of four years.

Key words: ADEM, Acute disseminated encephalomyelitis, post infectious encephalomyelitis.

Introduction

Acute disseminated encephalomyelitis (ADEM) is a disorder with pathophysiology not fully understood, however, the most accepted etiology is an autoimmune response to myelin basic protein activated by infectious or vaccination agent1-3. Acute severe inflammatory processes affect the white matter of the central nervous system. It is difficult to distinguish ADEM from first presentation of multiple sclerosis (MS). On magnetic resonance imaging (MRI)/ acute disseminated encephalomyelitis is characterized by diffuse periventricular confluent symmetrical lesions as in our patient (Figure-1). Acute disseminated encephalomyelitis is rare in adults and is mostly described in pediatric population. Diagnosis is based on clinical features supported by characteristic demyelinating neuro-radiological lesions4. Cerebrospinal fluid examination helps in excluding other differential diagnosis. The prognosis of ADEM is generally favorable, however, if not diagnosed and treated promptly, fulminant ADEM can be fatal.

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Case Report

A 17 years right handed, previously healthy male presented to our emergency department at King Abdulaziz Medical City, Riyadh, with sudden onset of recurrent generalized tonic clonic seizures without gaining consciousness in between seizures. Trachea was intubated and mechanically ventilated. Physical examination showed normal vital signs and was afebrile. Cardiovascular, respiratory and abdominal examinations were unremarkable. Neurological examination showed comatose young man with pupils equal, normal size, and reactive to light. There was no neck stiffness, cranial nerves examination was normal, motor examination showed bilateral hyperactive corticospinal tracts with bilateral extensor toes responses. Brain Computer tomography (CT) scan revealed multiple hypo-densities, involving both subcortical white matters (not shown). His blood tests showed normal values for complete blood count (CBC), serum electrolytes, renal and liver function tests. The serological testing for common viruses was unremarkable. Cerebrospinal fluid (CSF) examination revealed mild elevation of total proteins (0.47 g/liter) (normal less than 0.45g/liter) with normal white blood count (WBC) and glucose. A diagnosis of ADEM was clinically suspected and patient started on methylprednisolone one gram intravenously daily for five days. Phenytoin loading dose followed by intravenous (IV) maintenance dose and midazolam infusion were administered. MRI brain showed extensive bilateral confluent, diffuse hyper-intensities (Figure-1) which supported the clinical diagnosis of ADEM.

Figure 1: MRI at the time of presentation.
Legend:
A: MRI of the brain done at time of presentation;
B: Axial T2 Weighted image (T2WI)
C: Axial Fluid Attenuated inversion recovery (FLAIR)
D: Diffusion weighted image (DWI)
E: Apparent Diffusion Coefficient (ADC map)
F: Axial T1 weighed image after gadolinium (T1WI C+)

Seizures were controlled but as there was no clinical response to steroids, intravenous immunoglobulin (IVIG) were started in 0.4g/kg body weight daily for five days. There was still no improvement after two weeks in the intensive care unit (ICU) still being intubated and mechanically ventilated. Plasma exchange was started for five sessions on alternative days. The patient started showing improvement thereafter; he was extubated and transferred to the ward. He showed gradual improvement and was put on regular physiotherapy and discharged home after three months of hospitalization.

He went back to school, however, he reported attention deficit disorder and lack of concentration. This was successfully treated by benzhydrylsulphinylacetamide 200 mg orally twice a day. Now, patient is a university student with normal cognitive and physical activities and he performed Hajj last year. He is still on piracetam 500mg orally twice a day. MRI brain repeated one year later showed significant improvement with residual white matter changes (Figure-2).

Figure 2: Follow up MRI after treatment.
Legend:
Figure (2): Follow up MRI of the brain done After treatment:
A: Sagittal T2 Weighted image (T2WI)
B: Axial Fluid Attenuated inversion recovery (FLAIR)
C: Diffusion weighted image (DWI)
D: Apparent Diffusion Coefficient (ADC map)
E: Axial T1 weighted image after gadolinium (T1WI C+)
(A,B,C) show multiple large confluent patchy high T2/FLAIR signal abnormality in cortical and subcortical regions of both cerebral hemispheres involving deep white matter and corpus callosum to a lesser extent. Patchy restriction on diffusion images seen (D,E) with no enhancement after gadolinium (F).

Discussion

We present a young man who developed fulminant ADEM, diagnosed by clinical history,
neurological examination and treatment started in the emergency department few hours after presentation. Brain CT scan and MRI supported the clinical diagnosis. CSF examination and other blood work up, helped in excluding other differential diagnosis, particularly, infectious causes. Acute disseminated encephalomyelitis is a childhood disease. In most cases, presentation is gradual over days or weeks, and in many cases proceeded by prodromal symptoms. The case we are discussing is atypical. He presented with sudden onset, status epilepticus, necessitate tracheal intubation and mechanical ventilation in the ICU. The second, atypical feature is resistant to first line immunomodulation therapy of steroids where most of patients with ADEM respond to. The third atypical character our case is his complete recovery of cognitive and physical function and returning back to school, and proceed to university, his attention deficit and lack of concentration treated successfully with Provigil, which in fact, a narcolepsy-cataplexy syndrome treatment. This may encourage double bind placebo control studies of Provigil in patients with attention deficit hyperactive (ADHD) disorder.

These patients with fulminant ADEM, are at risk for future, overt multiple sclerosis. De Seze J and at el. retrospectively evaluated 60 cases of fulminant ADEM for the risk of future multiple sclerosis, and found some differences concerning the risk of evolution to clinically definite multiple sclerosis following the first severe demyelinating attack. Those findings that are atypical for multiple sclerosis include recurrent seizures, confusion, absence of oligoclonal bands in CSF, and gray matter involvement. Neuro radiological examination particularly MRI is crucial in the diagnosis. Thirty percent ADEM patients will have a relapsing-remitting disease similar to multiple sclerosis (MS). The diagnosis of ADEM at first neurological presentation is in fact the first attack of MS. Brainstem involvement has a poor prognostic value. Repeated MRI at least 6 months from onset of neurological presentation should reveal no new lesions in case of ADEM. Two out of three features (1. Absence of diffuse bilateral lesions, 2. Presence of black holes. 3. Presence of two or more periventricular lesions) on MRI may help to differentiate MS from ADEM in children.

Common precipitating, infectious diseases mostly of upper respiratory type (viral, bacterial or rickettsial) take 1-2 weeks before having a neurological presentation, however this is not a precondition for diagnosis as was seen in the case presented, who had no infectious disease. PCR (polymerase chain reaction) is commonly used to support infectious process, though it is difficult to prove a causative relationship of ADEM and positive PCR for specific pathogen. Acute hemorrhagic encephalomyelitis is considered as severe variant of ADEM by some experts. About 25-30% ADEM cases develop into multiple sclerosis. Treatment of fulminant ADEM depends on the clinical presentation, in sub-acute cases methylprednisone one gram IV for 3-5 days with close monitoring of neurological condition is recommended. If the condition deteriorates, there is no literature/guideline to choose between IVIG and plasma exchange. However, other immunosuppressive agents such as cyclophosphamide, methotrexate are reportedly used in non-responding cases.

Prognosis of ADEM in the past used to be poor. However, due to the decreased incidence of post infectious measles the prognosis has improved by the early diagnosis and use of high dose steroids. Full recovery is expected in 70-90% cases with or without minor neurological deficits like narcolepsy, attention deficit and Klüver-Bucy syndrome. Mortality may reach 5% especially in those having rapid severe onset of disease, and extensive brain lesions particularly severe involvement of brain stem. The clinical outcome may be poor if the lesions are extended into white matter or infratentorial structures. Occurrence of seizure is often associated with a poor outcome.

**Conflict of Interest**

All authors declare to have no conflict of interest.

**References**


