

Acute Diseminated Encephalomyelitis: A Case Report and Review of Literature

Akut Disemine Ensefalomiyelit; Olgu Sunumu Ve Literatür İncelemesi

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Abstract

Acute disseminated encephalomyelitis (ADEM) is an autoimmune and monophasic central nervous system disease that principally affects brain and spinal cord by causing non-vasculitic inflammatory diffuse demyelination. ADEM is one of the rare causes of impaired consciousness in childhood. Incidence of the disease under the age of 20 is 1.5-3 / 100000 per year and it mostly occurs in children between the ages of 5-8 years. Underlying causes aren't defined clearly yet, however, infections and vaccinations are known as predisposing factors for the disease. Multifocal white matter lesions on magnetic resonance imaging (MRI) are characteristic signs of ADEM. In our case, hyperintense lesions in cerebrum were detected on cranial MRI subsequent to impaired consciousness and convulsion. No specific feature was found in cerebrospinal fluid analysis of the patient. In this paper, we present a three-year-old boy who developed ADEM subsequent to viral upper respiratory tract infection and had full recovery after high dose steroid therapy.

Keywords: Acute Disseminated Encephalomyelitis; Cranial MRI; Multiple Lesions; High Dose Steroid Treatment.

Öz

Amaç: Akut disemine ensefalomiyelit (ADEM) otoimmün, monofazik, vaskülitik ve inflamatuvar olmayan yaygın demiyelinizasyon ile seyreden, özellikle de beyin ve spinal kordu etkileyen bir santral sinir sistemi hastalığıdır. ADEM çocukluk çağıının nadir görülen bilinç bozukluğu nedenlerinden biridir. 20 yaştan önce hastalığın görülme sıklığı 1.5-3/100000'dir ve sıklıkla 5-8 yaş arasında görülür. Altta yatan neden tam olarak bilinmese de enfeksiyonlar ve aşılamalar hastalığın ortaya çıkmasında önemli faktörlerdir. Multifokal beyaz cevher lezyonları manyetik rezonans görüntülemeye (MR) hastalığın karakteristik özelliğidir. Bizim hastamız da bilinç bulanıklığı ve nöbet sonrası yapılan beyin MR'da serebrumda beyaz cevherde hiperintens lezyonlar saptandı. Hastanın beyin omurilik sıvı incelemesinde hastalığa ait bir özellik saptanmadı. Bu yazıda yüksek doz steroid tedavisi sonrası tam düzelme gösteren, viral üst solunum yolu enfeksiyonu sonrası ADEM gelişen 3 yaşındaki erkek hasta sunulmuştur.

Anahtar Kelimeler: Akut Disemine Ensefalomiyelit; Beyin MR; Multiple Lezyonlar; Yüksek Doz Steroid Tedavisi.

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INTRODUCTION

Acute disseminated encephalomyelitis (ADEM) is an acute autoimmune, monophasic, nonvasculitic inflammatory demyelinating disease. Symptoms that are related to central nervous system (CNS) like convulsion, ataxia, paraparesis can bring about this disease while it also affects the white matter of the brain (1). The first case was defined in the 18th century as an uncommon presentation of measles and smallpox (2). The etiology is still unclear but the reasons behind the condition are thought to be immune-mediated since the cases generally have a history of viral infection or immunization (1). The incidence of this syndrome throughout the world is unknown but it may be approximately 1.5-3/100,000 in the USA. ADEM is more common in winter and spring and 80% of the cases occur in the first decade of life (2). Male-female ratio of ADEM is unknown but a study conducted in Japan showed a ratio of 2.3:1 (3). Geographical differences are still unknown and no study confirms the differences according to the geographical areas (4). There are no available definitive tests for this disease, thus the diagnosis is mostly made by depending on the clinical course, magnetic resonance imaging (MRI) characteristics and by excluding other disorders. Although ADEM is a rare disease, it should be distinguished from any other acute neurological diseases. MRI is the most sensitive method to show the number of lesions and extent of involvement; electroencephalography (EEG), cerebrospinal fluid (CSF) analysis and viral etiologic factors surveillance can also be useful for diagnosis (2). The outcome and prognosis are mostly good especially after using gamma globulin, steroids, plasmapheresis and immune suppressive treatments. Most of the cases present without any neurological deficits. Sometimes convulsion, ataxia, paraparesis and headache can persist and rarely it can progress to acute hemorrhagic leukoencephalitis, acute hemorrhagic encephalitis or acute necrotising hemorrhagic leukoencephalitis, all of which are considered as hyperacute forms of ADEM (1). Fulminant forms of ADEM have very poor prognosis and high mortality rate although there are reported cases that

have revealed complete recovery using mild hypothermia therapy and high doses of steroids (5).

CASE REPORT

A 3 year-old boy was admitted to our emergency room (ER) in January with generalized convulsion, reduced response to stimulations, drowsiness, fever with history of cough and vomiting. Physical examination showed that he had the signs and symptoms of upper respiratory tract infection; other systems were normal with worsened general condition. On presentation, he was febrile to 38, 8 °C with normal blood pressure; he was also irritable and the abdomen was a little tender but also soft with no organomegaly. There was no guarding or any sign of peritoneal irritation. A number of tests were performed including blood tests, MRI, chest radiography in ER. The evaluation revealed significantly elevated count of white blood cells (WBC count up to 47.400/mm³), a C-reactive protein (CRP) level of 50.5g/dL and an ammonia concentration of 48.5µmol/L with normal lactate (1.87 mmol/L) level. He had normal metabolic panel with negative blood and urine cultures and urine analysis was completely normal as was the chest radiograph. Lumbar puncture and CSF analysis demonstrated normal erythrocytes, glucose (59 mg/dL; serum glucose: 83mg/dL), protein (263 mg/L; N: 150-430), culture, immunoglobulin G, and negative oligoclonal bands. The patient was treated with ceftriaxone and vancomycine for concerns of partially treated meningitis. The presumed diagnosis was ADEM which could be viral in origin so acyclovir was started. Cranial MRI showed hyperintense lesions in right cerebellar hemisphere, right middle cerebellar peduncle, bilateral globus pallidus predominantly on right, left internal capsule, frontotemporoparietal regions, in subcortical white matter, corpus callosum right hemisphere and in bilateral thalami. In addition, hyperintense lesions similar to those in thalami were observed in both nucleus caudatus and nucleus lentiformis inferior parts, too (Figure 1).

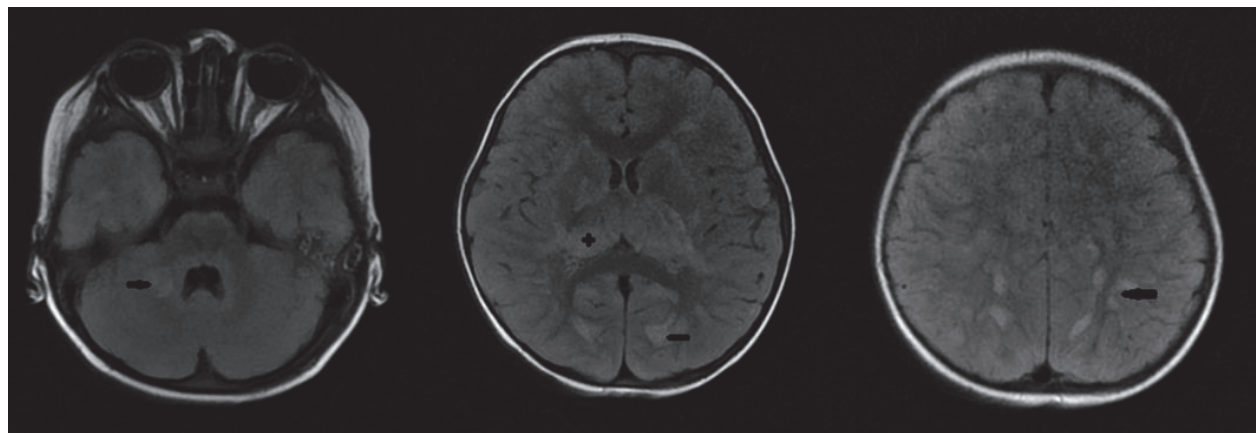


Figure 1. (a) Axial T2 section, right nucleus dentatus; (b) basal ganglia; and (c) on convex plan, subcortical white matter hyperintense lesions.

Imaging was compatible for eudema and inflammation in both temporal lobes, at right parahippocampal gyrus localization and in both parietal lobes. Patient was diagnosed with ADEM with these findings. Three days after the admission, the patient had no fever and his WBC count was 10.900/mm³, CRP was 3.45 g/dL, but intentional tremor was observed. High dose corticosteroid (methyl prednisolone) was started at the dose of 30 mg/kg/day for three days followed by oral prednisolone treatment at a dose of 2 mg/kg/day for

tapering over 6 weeks. The patient was kept under motorization for 10 days. On discharge, the patient was completely normal. The first follow-up visit was 6 weeks after the discharge; the steroid treatment was completely stopped after 6 weeks and the patient was completely normal. After 6 months, MRI scans were performed to see the degree of improvement, new lesions and enhancement and there were no pathological findings on MRI (Figure2).

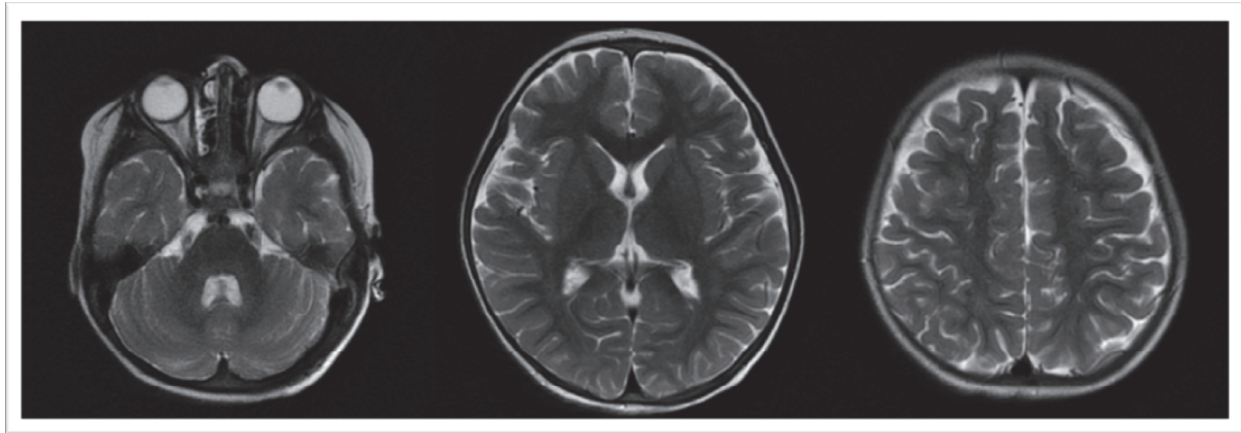


Figure 2. Post-treatment control cranial MRI, axial T2A image (2a) on nucleus dentatus location; (2b) on basal ganglions location; and (2c) on convex plan subcortical white matter lesions disappeared.

DISCUSSION

ADEM principally involves the white matter tracts of the cerebral hemispheres, brainstem, optic nerves, and spinal cord. It is a disease of the young, with an estimated incidence of 1.5-3/100 000/year among people less than 20 years old. The mean age at presentation in children ranges from 5 to 8 years (6). Our patient was under the mean age of the onset of the disease. ADEM is post or peri-infectious reaction and it is usually preceded by an infection such as mycoplasma, Epstein-Barr virus (EBV), measles, rubella, varicella or mumps. It may even occur consequent to vaccination. There are reported cases of non-vaccinated patients who had underwent splenectomy that developed ADEM after bacterial meningitis. ADEM may arise secondary to molecular mimicry in which similarity between pathogenesis and myelin protein starts an autoimmune reaction against central nervous system. The cause of the disease is unknown in 1/3 of the cases (5, 7, 8). It is considered that the responsible factor for the case that was presented in this paper was a viral agent that may have caused upper respiratory tract infection symptoms. It affects especially cerebrum and spinal cord, so any patient with ADEM can express widespread of motor and sensory deficits, symptoms like ataxia, paraparesis, hemiparesis, monoparesis, loss of tonus, or generalized or focal convulsion. Eye aches, visual disturbances, oculomotor nerve palsy and urinary symptoms like transient retention of urine, dysarthria and nystagmus may be seen in the spectrum of clinical manifestations as well. These symptoms are mostly seen within 7-14 days

following a viral infection or immunization (1, 2, 5). Ocular examination was normal in our patient and encephalopathy and convulsion came out without any paralytic condition. On the third day of admission, tremor manifested.

In the cerebrospinal fluid, lymphocytic pleocytosis and mild elevation of protein, oligoclonal bands, Ig G or myelin basic protein can be detected. In our case, CSF did not show any abnormality, which might indicate ADEM. EEG may show focal discharge and slowing visual evoked potential may be seen. Cerebral MRI is considered to be the most helpful technique, by showing focal or multifocal hyperintense lesions that mainly affect CNS (8). The most commonly acquired demyelinating diseases of CNS are ADEM and multiple sclerosis (MS). MS is an acquired, chronic inflammatory demyelinating disease of the brain (9). ADEM can be distinguished from MS by its monophasic character, prepubertal onset and presence of encephalopathy. The disease affects specific anatomical fields and some cases of recurrent or multiphasic courses have been reported. Demyelinating lesions may be seen after three months from the onset of ADEM or four weeks after completing steroid therapy (7, 10, 11). Recurrence of clinical or radiological findings is more frequent in MS and may exist after many years from the first manifestation. Therefore, patients who are suspected for MS should be followed-up for a long time (1, 2). International MS Study Group monophasic ADEM criteria:

- No history of prior demyelinating events

- First clinical event with presumed inflammatory or demyelinating cause
- Acute or subacute onset
- Affects multifocal areas of central nervous system
- Must be polysymptomatic
- Must include encephalopathy (i.e., behavioral change or altered level of consciousness)
- Neuroimaging shows focal/multifocal lesion(s) predominantly affecting white matter
- No neuroimaging evidence of previous destructive white matter changes
- The event should be followed by clinical/radiologic improvements (although may be residual deficits)
- No other etiology can explain the event
- New or fluctuating symptoms, signs or magnetic resonance imaging findings occurring within 3 months are considered to be a part of the acute event (12).

Clinical international pediatric MS work team criteria of Miller et al. for ADEM are

- 1- Subacute encephalopathy
- 2- Clinical course from 1 week to 3 months
- 3- Improvement (but neurological deficit can remain)
- 4- MRI, white matter lesions
 - Acute
 - Multiple
 - At least one lesion (1-2 cm)
 - Supra and infra-tentorial lesions
 - Gadolin enhanced lesions (not necessary)
 - Lesion of basal ganglion (not necessary) (13).

The most important MRI finding of ADEM is multifocal hyperintense lesions. In our case, multifocal lesions were seen as settled in the supratentorial area, cerebrum, thalamus, capsula interna, nucleus caudatus and nucleus lentiformis. The lesions that had settled in infratentorial area were 4-12 mm in diameter and those in the supratentorial area were 5-24 mm. Gadolin enhanced lesions were not seen. Some lesions were placed in basal ganglions.

The prognosis of ADEM is generally favorable. Farag et al. suggested that 76,2% of children were neurologically normal on the discharge and 23.8% were completely neurologically normal after the first year of follow-up and relapses had occurred in 9.5% of the children and no relation were present between relapse and tapering steroid treatment (2). In another study, 57-89% of children showed full recovery while the rest developed widespread neurological deficits like epileptic seizures that required antiepileptic drug treatment, headache, abnormal behaviors and hemiparesis (1). In our patient, we observed tremor at first but there were no clinical findings on discharge. Six months later, there were still no clinical or MRI findings. Prognosis of this patient was well and we did not observe any recurrences.

Cranial MRI is the most important method for the diagnosis of ADEM. Patients may recover without any sequellae with corticosteroid treatment. ADEM is one of the rare causes of impaired consciousness and it should be considered in children with sudden neurological deficit and encephalopathy.

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