

# Acute disseminated encephalomyelitis associated with enteroviral infection

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## ABSTRACT

يعتبر التهاب الدماغ والنخاع الشوكي المنتشر (ADEM) عبارة عن التهاب زوال النخاعين الحاد في الجهاز العصبي المركزي الذي تم وصفه بواسطة المادة البيضاء متعددة البؤر التي غالباً ما تتبع لالتهاب أو تطعيم. تلقى طفل يبلغ من العمر 16 عام عقار ريسبريدون لمدة 7 عام لمعالجة اضطراب فرط النشاط / ونقص الانتباه والذي تمت معالجته مع مضاعفات ازدواج الرؤية خلال الشهر الماضي وضعف في الجانب الأيمن، وعدم الانتظام والتقيد خلال الثلاثة أيام الماضية. تم تشخيص المريض بالتهاب الدماغ والنخاع الشوكي المنتشر (ADEM) بعد إجراء الفحوصات السريرية وأشعة الرنين المغناطيسي MRI للحجم. بعد الثلاثة أيام الأولى من العلاج بعقار ميثيلبريدونزولون ظهر على المريض تحسن ملحوظ. تم اكتشاف حمة معدية معوية CSF كنتيجة للفحص. تبين أن هذا الطفل يعاني من حالة مثيرة وتم تشخيصه بالإصابة بالتهاب الدماغ والنخاع الشوكي المنتشر (ADEM) المصاحب لالتهاب حموي معوي، نتيجة لحالات قليلة تم الإبلاغ عنها في الأدبيات.

Acute disseminated encephalomyelitis (ADEM) is an acute demyelinating infection of the CNS that is characterized by multifocal white matter involvement often following an infection and vaccination. A 16-year-old child receiving risperidone for 7 years for the treatment of attention-deficit/hyperactivity disorder was hospitalized with complaints of double-vision during the past month and weakness on his right side, ataxia, and vomiting over the past 3 days. The child was diagnosed with ADEM after clinical, laboratory, and cranial MRI was conducted. Following an initial 3-day therapy with pulsed methylprednisolone, the child showed obvious clinical improvement. The treatment was continued with prednisolone and significant improvement was achieved. Enterovirus was detected in the results of the viral examination of the CSF. This child was found to be an interesting case having been diagnosed with ADEM associated with enteroviral infection, because of the rarity of few case reports in the literature.

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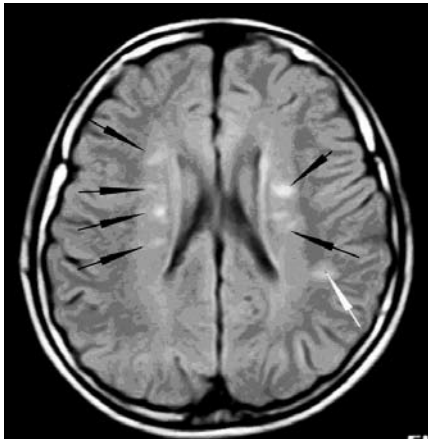
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Acute disseminated encephalomyelitis (ADEM) is an inflammatory, demyelinating, and treatable disease that predominantly involves the white matter. It generally occurs through immune-mediated mechanisms following an infection and vaccination. In most cases, an infectious agent is not identified. It is frequently observed in children and young adolescents. Involvement is equal in boys and girls. Amongst infectious agents, viruses, in particular, have been held responsible as the cause for the past century.<sup>1,2</sup> In this paper, a child with an enterovirus associated ADEM who received treatment for attention deficit/hyperactivity disorder is presented because of the limited case reports in the literature.<sup>3</sup>

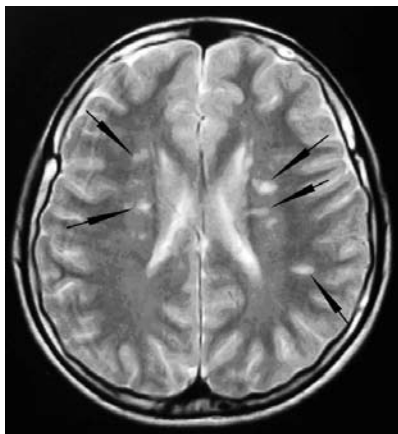
**Case Report.** A 16-year-old child receiving risperidone for 7 years for the treatment of attention-deficit/hyperactivity disorder was admitted to our hospital's emergency service with complaints of double vision during the past month. He had complained of weakness on his right side, ataxia, and vomiting over the past 3 days. On physical and neurological examination, he was conscious and fully cooperative, bilateral abduction deficit in the cranial nerves during horizontal gaze, horizontal and vertical nystagmus, diplopia, anisocoria, reduced light reflex in the left pupil with ptosis and mydriasis were observed. The ocular fundus was normal. In the muscular power examination, right hemiparesis was present, predominantly in the lower extremity. There were increased deep tendon reflexes on the right side. The following laboratory and biochemical examinations were found; hemoglobin: 14.5 gr/dl, leucocytes: 9600/mm<sup>3</sup>, thrombocytes: 255000/mm<sup>3</sup>, erythrocyte



**Figure 1** - Axial FLAIR weighted image shows multiple foci of T2 prolongation (black arrows) located bilaterally at the periventricular white matter. Subcortical foci of demyelination is seen at the gray matter-white matter junction of the left hemisphere (white arrow).



**Figure 2** - Axial FLAIR image shows abnormal hyperintensity in the caudate nuclei, lentiform nuclei, and internal capsules (arrows).



**Figure 3** - T2 weighted image confirmed lesions, which were of high signal intensity in the bilateral periventricular white matter (arrows).

sedimentation rate: 2 mm/hour, and C-reactive protein: 0.35 mg/dl. The CSF examination yielded the following results; protein: 30 mg/dl, glucose: 63 mg/dl (simultaneous blood glucose: 81 mg/dl). Pleocytosis was identified on the microscopic CSF examination. Enterovirus was detected by cell culture. No oligoclonal bands were detected in the CSF. The result of the CSF bacterial culture was obtained as negative. Cranial MRI demonstrated hyperintensity in the brain stem, basal ganglia, and periventricular region (Figures 1-3). Based on the cranial MRI, the clinical, and laboratory findings, a diagnosis of ADEM was made. After administration of methylprednisolone, 30 mg/kg/day for 3 days, the child showed obvious clinical improvement. Treatment was continued with prednisolone 2 mg/kg/day. The child's neurological findings regressed on the fifth day of hospitalization, and his walking performance improved in the second week of treatment. The oral prednisolone therapy was terminated after 6 weeks. The child demonstrated regressed diplopia and no neurological sequelae throughout the 6-month clinical follow-up.

**Discussion.** A T-cell mediated autoimmune response against myelin protein triggered by an infection or vaccination is held responsible for the pathogenesis of ADEM.<sup>4</sup> Vaccines against Semple-type rabies, polio, varicella, measles-mumps-rubella, and BCG as well as infections such as measles, enteroviruses, human herpes-6, influenza, Epstein-Barr virus, cytomegalovirus, HTLV-1, hepatitis C, hepatitis A, legionella, mycoplasma, Group A beta hemolytic streptococcus, salmonella, chlamydia, pasteurilla multocida, and cryptococcus neoformans are reported to be factors that create susceptibility to ADEM. In addition, viral upper respiratory tract infections are also held responsible. However, the specific factors cannot be identified in most cases.<sup>1-4</sup> Enterovirus was detected in the viral examination of our child's CSF cell culture and the enteroviral infection of the CNS was thought to have created susceptibility to ADEM. In children, ADEM is seen in winter and spring, especially within 7-14 days after a viral upper respiratory tract infection. The clinical onset is rapid and begins with fever, fatigue, headache, nausea, vomiting and, rarely, encephalitis-like symptoms such as convulsions and coma. Clinically, the most frequently observed neurological findings are motor disorders such as ataxia and paresis, changes in consciousness, sensory disorders, urinary disorders, cranial nerve neuropathy, convulsions, nystagmus, aphasia, and coma.<sup>5,6</sup> Our patient was suffering from double vision that had begun one month ago and sudden weakness in her right side, ataxia, and vomiting. On the physical examination, abduction deficit with sixth cranial nerve, anisocoria with third cranial nerve, and horizontal and vertical nystagmus as a

result of brainstem invasion were identified. In addition, right hemiparesis was present in the muscular power examination. Cranial MRI is an indispensable imaging method for diagnosis. The detection of multiple, broad, symmetrical, peripheral, and subcortical white matter lesions are quite specific to ADEM. The lesions may be asymmetrical in rare cases.<sup>1,5</sup> Demyelination may be identified in the cerebrum, cerebellum, and brain stem. Frontal and parietal lobe involvement is observed in nearly all patients. On the cranial MRI, hyperintense areas were detected in the brain stem, basal ganglia, and periventricular region, and were found to be compatible with ADEM. Differentiating ADEM from the initial attack of multiple sclerosis (MS) is crucial in terms of determining the treatment and prognosis.<sup>2</sup> In contrast to MS, the lesions are frequently located in the subcortical white matter and/or centrum semiovale. Furthermore, lesions of the thalamus are more frequently observed in ADEM.<sup>4</sup> In cases where CSF findings are mistaken for MS, CSF oligoclonal band negative findings should be interpreted in favor of ADEM.<sup>5</sup> A rapid and multifocal clinical onset as well as preceding viral infections or vaccinations should also be considered in favor of ADEM.

The patient's acute clinical findings, radiological appearance, CSF oligoclonal negative findings, and enterococcus yielded in the culture of the CSF culture were considered to be findings compatible with ADEM.

Corticosteroids, intravenous gamma globulins, and plasmapheresis are used for therapy. While most patients recover, relapses have been reported in 25% of the patients.<sup>1,6</sup> Our patient was administered 3-day therapy with methylprednisolone 30 mg/kg/day followed by oral prednisolone 2 mg/kg/day. She showed clinical improvement with no neurological sequels during the 6 months of follow-up.

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## CASE REPORTS

Case reports will only be considered for unusual topics that add something new to the literature. All Case Reports should include at least one figure. Written informed consent for publication must accompany any photograph in which the subject can be identified. Figures should be submitted with a 300 dpi resolution when submitting electronically or printed on high-contrast glossy paper when submitting print copies. The abstract should be unstructured, and the introductory section should always include the objective and reason why the author is presenting this particular case. References should be up to date, preferably not exceeding 15.