Case report

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A Case of Acute Disseminated Encephalomyelitis Mimicking Leukodystrophy

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Summary: Acute disseminated encephalomyelitis (ADEM) is a monophasic, immune-mediated demyelinating disorder that can follow immunizations or more often infections including rubeola, rubella, varicella, herpes zoster, mumps, *Mycoplasma pneumoniae*, or, more commonly, other nonspecific upper respiratory tract infections. Documentation of a preceding illness is not required to make this diagnosis. This report examines the case of a 9-month-old male patient presenting with the features of an acute leukodystrophy following innoculation with the mixed vaccine Pentaxim (Sanofi Pasteur, Lyon- France) while suffering from a lower respiratory tract infection, and who was eventually diagnosed as ADEM. The case is presented as a reminder that ADEM can sometimes be linked to lower respiratory tract infection and vaccination, and that the features in such cases can be confused with leukodystrophy.

Key words vaccination, demyelinating, leukodystrophy

INTRODUCTION

Acute disseminated encephalomyelitis (ADEM) is a monophasic, immune-mediated demyelinating disorder that can follow immunizations or more often infections including rubeola, rubella, varicella, herpes zoster, mumps, *Mycoplasma pneumoniae*, or, more commonly, other nonspecific upper respiratory tract infections. Documentation of a preceding illness is not required to make this diagnosis [1]. The present case was pathologically characterized by perivascular inflammation, edema and demyelination. Clinically, this disease can be restricted to systemic features and observations that are not specific to it, or fast evolving focal or multifocal neurological function deficiencies can be observed [2]. In this report, the case of a 9-month-old male patient presenting with the features of an acute leukodystrophy following treatment with the mixed vaccine Pentaxim (Sanofi Pasteur, Lyon-France) while suffering from a lower respiratory tract infection, and eventually diagnosed as ADEM is examined.

CASE PRESENTATION

A 9-month-old male patient was hospitalized after suffering a seizure during a fever. Patient history revealed repeating episodes of fever and dry cough in the two weeks prior to admission. Cefixime and ibuprofen treatment had been started after a diagnosis of bronchitis at a local health center. During a period of fever experienced two hours before admission, the patient suffered three five-minute long generalized tonic-clonic type convulsions. This patient, who did not have any insect sting antecedents, had been vaccinated with mixed Pentaxim vaccine five days earlier. A cyst in the

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Abbreviations: ADEM, acute disseminated encephalomyelitis; CSF, cerebrospinal fluid; RPLS, reversible posterior leukoencephalopathy syndrome.

cerebral choroid plexus had been identified by intrauterine ultrasonography. The patient's father had a history of posttraumatic epilepsy from which he had recovered.

At physical examination, the general condition of the patient was mean and he exhibited postictal awareness. The body temperature was 39°C. The maximal heart rate was 142/minute and his arterial tension was 100/70 mmHg. The pupillary isochoric, direct and indirect light reflexes were obtained. His deep tendon reflexes were regular. The patient weighed 10.4 kg (75-90 percentile), and his height was 73 cm (75-90 percentile). The frontal fontanella was 2×2 cm and at a normal cambering level. Crepitant rales were present on the right side at some locations in the respiratory system.

Laboratory examinations revealed a leukocyte count of 13,840/mm^3, a hemoglobin value of 10.4 g/dL, and a thrombocyte count of 451,000/mm^3. Prothrombin time and activated partial thromboplastin time were normal. The blood gas values were within normal limits. The C-reactive protein was 3 mg/L and the sedi-

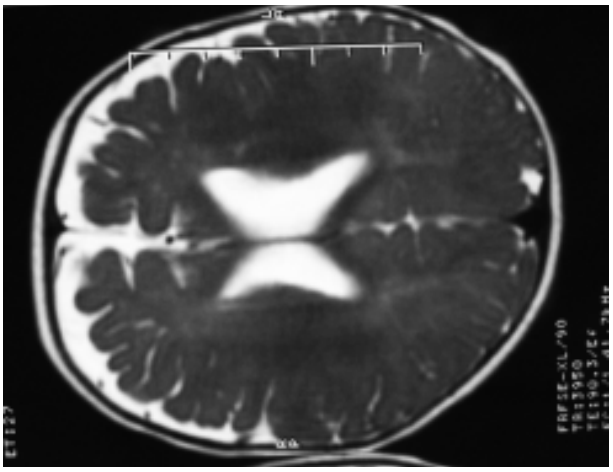


Fig. 1. Brain magnetic resonance imaging made during the eighth month (Axial T2-weighted image).

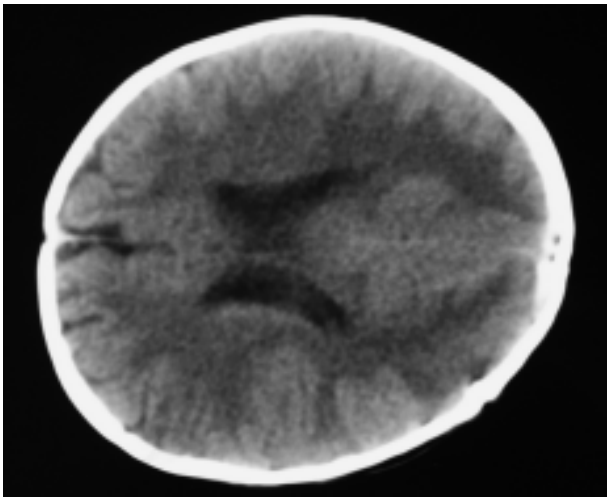
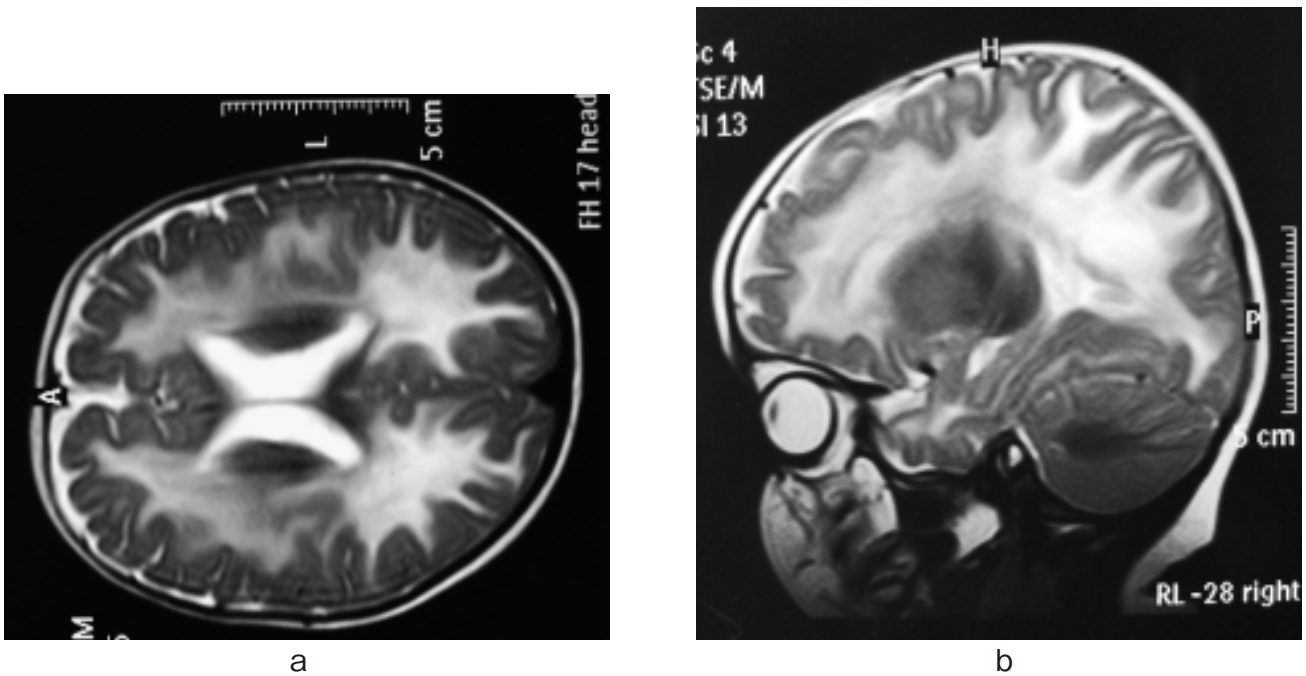


Fig. 2. Diffuse decrease of the white matter density in the emergency brain computed tomography.



a b

Fig. 3. A large signal increase in the white matter, especially on axial (a) and saggital (b) T2 series was obtained.

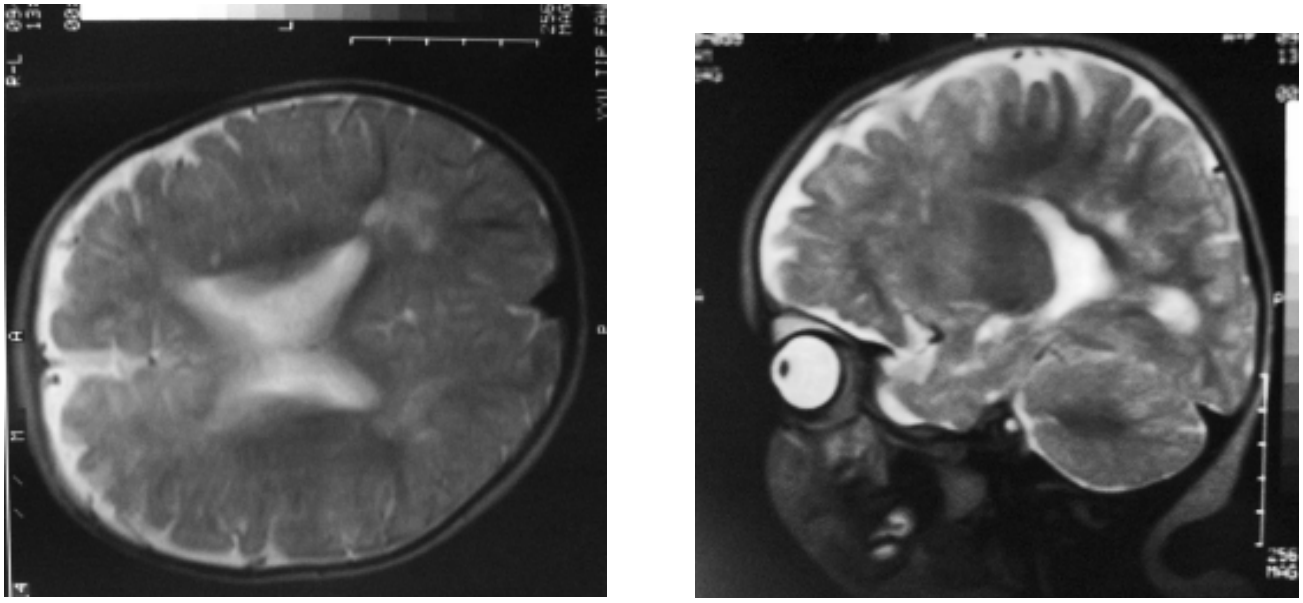


Fig. 4. Axial (a) and saggital (b) brain magnetic resonance imaging results obtained following 45 days.

mentation was 30 mm/h. Liver and renal function, vitamin B_{12}, folate hormone and thyroid hormone levels were also normal. The cerebrospinal fluid (CSF) obtained by lumbar puncture did not contain any cells by direct observation. The glucose and protein levels of the CSF were normal. The results of electroencephalogram were within normal range. Metabolic screening tests performed by tandem MASS spectrometer were negative.

The patient was admitted because of pneumonia and febrile convulsions. Intravenous penicillin and chloramphenicol treatment was started. A cyst in the cerebral choroid plexus had been identified in the intrauterine ultrasonography. A brain magnetic resonance imaging (MRI) obtained during the eighth month was used to manage this cyst (Fig. 1). The three seizures of the patient and the observation of a diffuse decrease of the white matter density in the emergency computed tomography of the brain (Fig. 2) led to the observation of a large signal increase in the white matter of the two cerebral hemispheres, especially on T2 series by MRI (Fig. 3).

The disappearance of symptoms on the tenth day of monitoring allowed the discharge of the patient with a single antiepileptic (phenobarbital). The large extent of the involvement on brain MRI led to the diagnosis of Cree leukodystrophy. That is why no steroid treatment was given. On follow-up, the brain MRI results obtained at 45 days after admission were normal, so the diagnosis of Cree leukodystrophy was rejected and a diagnosis of ADEM was proposed. The patient was then considered as having experienced a lower respiratory tract infection followed by ADEM (Fig. 4).

DISCUSSION

The onset of Cree leukoencephalopathy is between 3 and 9 months of age with 100% mortality by 21 months of age. Hypotonia is often noted in early infancy followed by a relatively sudden onset of seizures, spasticity, hyperventilation, vomiting, and diarrhea, often in the setting of a febrile illness. Onset is followed by developmental regression, lethargy, blindness, and cessation of head growth seen as flattening of the head circumference curve [3]. Computerized tomography of the head shows symmetrically hypodense white matter. Similar images were obtained on T1-weighted head MRI that showed symmetrical diffuse attenuation of hemispherical and often cerebellar white matter [4]. T2-weighted MRI showed hyperintense white matter that included the subcortical fibers, basal ganglia, and thalamus. Microscopic examination showed diffuse white matter vacuolation in some cases and astrogliosis with presence of oligodendrocytes and cells described as lipid-laden macrophages [3,4].

In countries where vaccination coverage is inadequate, the most recurrent causes of ADEM are measles, mumps, rubella, and varicella, while in other countries nonspecific upper respiratory infection and coronavirus can constitute a factor. Almost half of the

patients are older than five years [5]. Around 0 to 12% of the cases with ADEM report a vaccination episode before the attack [6].

Pentaxim contains diphteria toxoid, Tetanos toxoid, the antigens of *Bordetella pertussis*, the inactivated polyomyelitis virus and the type b polysaccharide of *Hemophilus influenza*. Routine vaccination with Pentaxim started in Turkey at the beginning of 2008.

The levels of CSF constituents are normal in 25 to 75% of the patients with ADEM. An increased CSF pressure, a lymphocytic pleiocytose (up to 1000/mm^3; sometimes polymorph leukocytes are preponderant in the beginning period) and an increase of protein level can be determined [5]. In our patient, there were no CSF cells and his biochemistry was normal. The diagnosis of ADEM can be established using clinical and cerebral MRI. The lesions observed by MRI are usually large and asymmetrical, and tend to be numerous and always present with bilateral localization. The distribution of the lesions can be quite variable. The most commonly observed localizations are the corticomedullar section, the corpus callosum, the medial cerebellar stem, the cerebellum, the brain stem and basal ganglions, but ar especially noted in the semiovale central and corona radiata white matter [7].

Three MRI examinations were performed in the present case. The first took place after the identification of a cerebral choroid plexus cyst by intrauterine ultrasonography. This MRI showed a bifrontal enlargement combined with benign subarachnoidal distance increase and mega cisterna magna. The emergency brain computed tomography performed after the patient's three seizures led to the observation of a diffuse decrease in white matter density, which was the reason for the second MRI examination. It has been suggested that MRI could be useful in the diagnosis of ADEM. The third MRI examination was performed 45 days after the hospitalization as a control, and the results were normal. So the final diagnosis was made of lower respiratory tract infection and ADEM linked to Pentaxim vaccine. ADEM cases linked to vaccines have been reported in Turkey [8] and abroad [9,10], however, this is the first case in which an ADEM appeared after lower respiratory tract infection and innoculation with Pentaxim vaccine.

In more than 70% of ADEM cases, healing occurs in the first 6 months [5]. Some neurological traces remain at different levels in 11 to 30% of the patients. The sequelae proportion is higher in patients presenting large or bilateral thalamus lesions [5]. Although the mortality rate can reach 10 to 20%, most patients experience a complete recovery [11].

Most ADEM lesions are asymmetrical, but rapidly developing and symmetrical ones have also been reported. According to Nishimura et al, [12] "MRI showed extensive symmetric high signal lesions in the bilateral cerebellar and cerebral white matters." Imamura and Sakai [13] reported a case of early-onset acute disseminated encephalomyelitis in which "MRI showed extensive symmetric high signal lesions in bilateral cerebral white matters which were demonstrable in the sagittal image." Kawashima et al. [14] reported in two cases "fluid attenuated inversion recovery (FLAIR) sequenced MRI showed multiple symmetric hyperintense lesions in the internal capsule and the brainstem at the subacute stage."

Although the presence of lesions suggested reversible posterior leukoencephalopathy syndrome (RPLS), fever and associated convulsion was observed in our patient. In RPLS, convulsions can be observed without fever. Our patient was mildly hypertensive, but this condition was transient, and there was no need to use antihypertensive medication. On the other hand, serious hypertension is expected in RPLS [15]. The lesions are located posteriorly in RPLS [15], whereas there was widespread involvement in our case.

Patients diagnosed with ADEM are treated for 3 to 5 days with a high dose of intravenous methylprednisolone (20-30 mg/kg/day). Depending on the pace of regression of the clinical features, treatment with oral prednisolone at a dose of 2 mg/kg/day can be started and a decreasing dose can be administrated for 4 to 6 weeks [16]. If the treatment is not adequate, plasmapheresis or intravenous immunoglobulines constitute an alternative treatment [17]. However, Cree leukoencephalopathy was the initial diagnosis in our patient and he was followed-up accordingly. After the disappearance of the lesions present in the brain, a diagnosis of ADEM was accepted. That is why no treatment was given. Our patient healed spontaneously without treatment.

CONCLUSION

The present case may serve as a useful reminder that it is possible to observe ADEM linked to lower respiratory tract infection and vaccination, and that the features of such cases can be confused with leukodystrophy.

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