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Published online 2016 January 26. **Case Report and Review of Literature**

Acute Disseminated Encephalomyelitis: A Review of Eleven Cases in Childhood in North of Iran

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Abstract

Background: Acute disseminated encephalomyelitis (ADEM) is an inflammatory demyelinating disorder. The pathogenesis is unclear, but it is thought to be immune-mediated. The prognosis is favorable, with most children making a full recovery.

Objectives: The present report analyzed different clinical presentations, response to treatment and outcome in a series of 11 patients with ADEM who referred to our tertiary center in north of Iran from 2010 to 2014.

Materials and Methods: In this retrospective simple descriptive review, eleven cases with ADEM admitted in the neurology ward from 2010 to 2014 were enrolled. The clinical findings and laboratory and imaging results of patients were reviewed. All of these cases were evaluated with neurological examination, serologic tests for bacterial meningitis and viral encephalitis (especially, herpes simplex virus) and brain MRI without contrast. After discharge, patients were followed for at least six months (6 to 12 months) clinically and radiologically.

Results: Of 11 children, 8 were male and 3 female. Their ages ranged between 4 and 10 years. The mean interval between the preceding infection and symptoms of encephalomyelitis was nine days. The most common presenting symptoms were ataxia in 45.4%, fever and headache in 36.4% and altered consciousness in 18.2% of patients. Neurological examination revealed pyramidal motor signs such as brisk deep tendon reflexes (hyperreflexia) (81.8%), cranial nerve involvement (18.2%), dysarthria (9.1%) and abnormal movements (9.1%). We followed up these patients in long-term for 6 to 12 months. Only in 1 child who received IVIG, mild ataxia had reminded.

Conclusions: The prognosis of acute disseminated encephalomyelitis (ADEM) is favorable. Early diagnosis and prompt treatment of ADEM would probably reduce morbidity.

Keywords: Acute Disseminated Encephalomyelitis, ADEM, Children, Outcome, Iran, Case Series

1. Introduction

Acute disseminated encephalomyelitis (ADEM) is an inflammatory demyelinating, autoimmune, monophasic disorder of the CNS white matter (1). ADEM almost involves children with the incidence rate of 0.4/100,000 yearly in patients less than 20 years old (2). ADEM is more common in winter months and in 80% of childhood cases occurs in the first decade of life (2). The pathogenesis is unclear, but it is thought to be immune-mediated, because in up to three-fourths of cases, it follows an antecedent infection or immunization (3). In general, clinical presentation of ADEM may be very heterogeneous. However, a combination of altered consciousness or behavior and multifocal neurological deficits, especially in close relation to an infection, should raise clinician's suspicion to consider ADEM in the differential diagnosis (3, 4). Some children never have focal neurological signs, whereas in others the initial feature suggests a focal mass lesion (5). High-dose intravenous methyl prednisolone (MP), intravenous immunoglobulin (IVIG) and plasmapheresis have all been used in the treatment of ADEM (4). The prognosis is favorable, with most children making a full recovery, but a favorable outcome is not a rule (5, 6).

2. Objectives

The present report analyzed different clinical presentations, response to treatment and outcome in a series of 11 patients with ADEM who referred to our tertiary center from 2010 to 2014.

3. Materials and Methods

Eleven cases with ADEM who admitted in the neurology ward from 2010 to 2014 were enrolled and followed. In this retrospective record review, clinical findings and laboratory and imaging results of patients were reviewed. Diagnosis of ADEM was based on the International pediatric MS group classification (5): polysymptomatic encephalopathy with acute or subacute onset, showing focal or multifocal hyperintense lesions predominantly affecting CNS with white matter changes should be present, and there should be no history of a previous clinical episode with features of a demyelinating event. The diagnosis was made in each case by a pediatric neurologist with radiologist consultation. On admission, all these cases were evaluated with neurological examination, serologic tests for bacterial meningitis and viral encephalitis (especially

herpes simplex virus) and brain MRI without contrast. After discharge, patients were followed for at least six months (6 to 12 months) clinically and radiologically.

4. Results

Of 11 children, 8 were male and 3 females. The mean age at presentation was 76.3 ± 28.8 months (ranged 4 - 10 years). Preceding infections were determined in 8 (72.7%) of our cases (6 upper respiratory tract infection and 2 varicella). There was no history of vaccination 2 - 4 weeks before involvement. The mean interval between the preceding infection and symptoms of encephalomyelitis was 9 days (5 - 16 days). The most common presenting symptoms were ataxia in 45.4%, fever and headache in 36.4% and altered consciousness in 18.2% of patients. Neurological examination revealed pyramidal motor signs such as brisk deep tendon reflexes (hyperreflexia) (81.8%), cranial nerve involvement (18.2%), dysarthria (9.1%) and abnormal movements (9.1%) (Table 1). CSF examination was performed in 6 cases referred with loss of consciousness or fever and headache. Four patients had normal CSF examination and two patients had mild CSF lymphocytosis with normal protein. Cranial MRI was performed in all cases; on cerebral MRI T2-weighted images and FLAIR sequences, multiple symmetrical high signal areas were detected in the basal ganglia, thalamus, white-gray matter junction, cerebellum and brainstem (Figures 1 - 3). Steroid treatment or IVIG was given to all patients. In nine patients, high-dose intravenous methylprednisolone (IV MP) 30 mg/kg per day (max; 1 g/day) for 3 - 5 days followed by oral prednisolone at a dose of 1 - 2 mg/kg/day with tapering over 2 weeks was given; two of them also received IVIG therapy at the dose of 400 mg/kg/day for 5 days consecutively (because of unstable condition of these patients steroid was not appropriate). After discharge, we followed up these patients for 6 to 12 months. Only in one child who received IVIG, mild ataxia had reminded and his second brain MRI showed hyperintensities in periventricular white matter (Figure 4). The demographic details, presenting features, imaging findings, treatments and outcomes are shown in Table 2.

Table 1. Clinical Symptoms and Signs of Patients

Clinical Symptoms and Signs	Values, %
Ataxia	45.4
Fever and headache	36.4
Altered consciousness	18.2
Weakness	NA
Hemiparesis	NA
Cranial neuropathy	18.2
Pyramidal signs	81.8
Abnormal movements	9.1
Dysarthria	9.1
Nystagmus	NA
Spinal cord involvement	NA

Abbreviation: NA, not available.

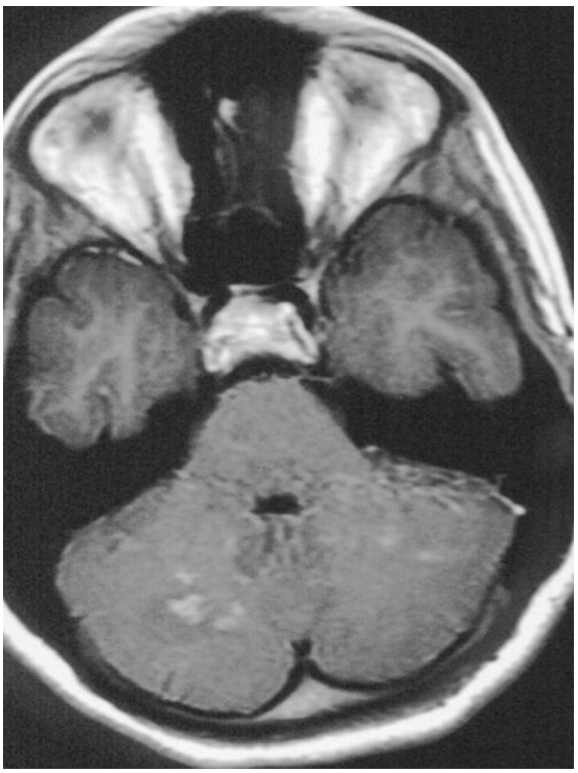
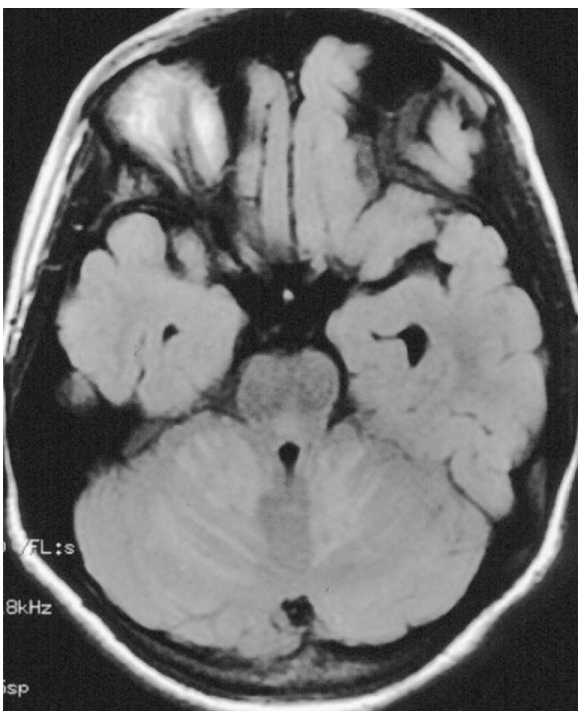


Figure 1. Axial T1WI MR in a 4-Year-Old Boy Showing Hyperintensities Foci in Both Cerebellar Hemispheres

Figure 2. Axial FLAIR MR in a 4-Year-Old Boy (Case Figure 1) six Months After Treatment With Mild Gliosis in Cerebellum



This boy was Asymptomatic.

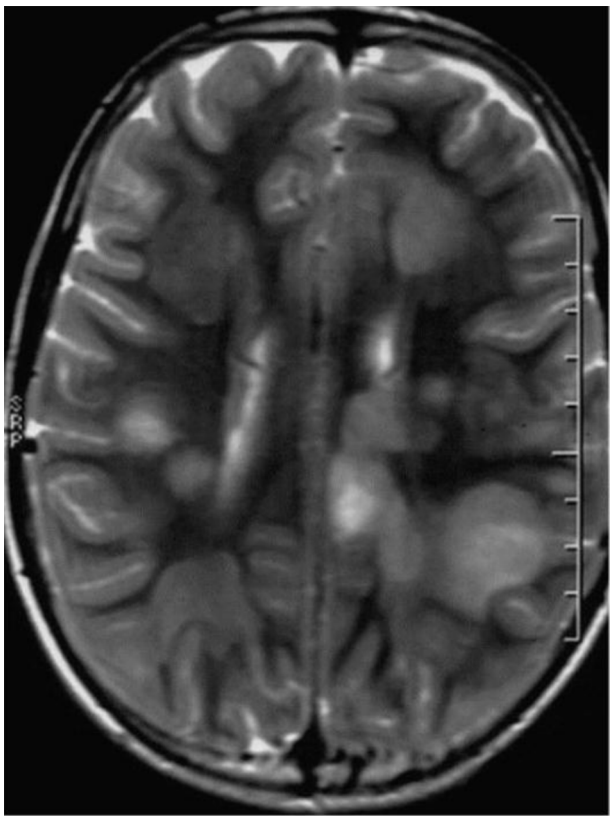
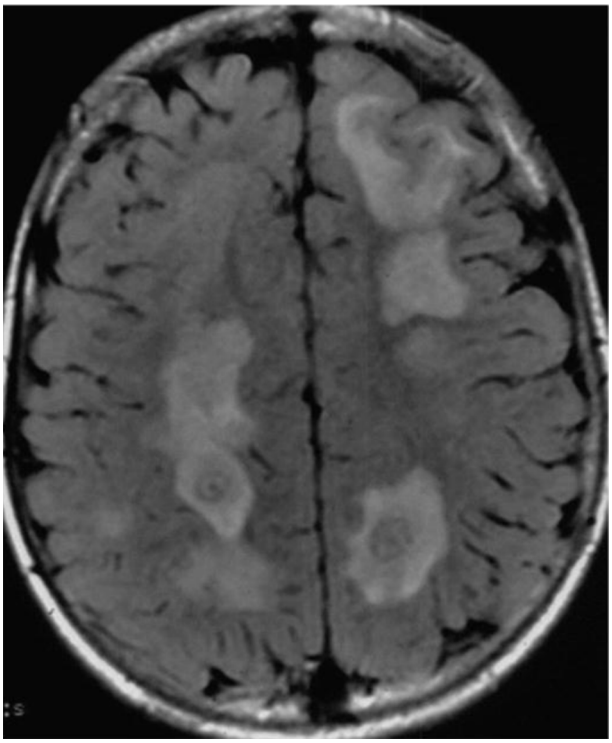


Figure 3. Axial T2WI MR in a 4-Year-Old Boy Showing Multifocal High Signal Periventricular Lesions in Both Hemispheres

Figure 4. Axial FLAIR MR in a 4-Year-Old Boy (Case Figure 3) 12 Months After Treatment With Multifocal High Signal Periventricular and Subcortical White Matter Lesions in Both Hemispheres



He had Ataxia and Hyperreflexia.

Table 2. Demographic Details, Clinical Features, Treatments and Outcomes

No	Sex	Age, y	Presenting Features	Neurological Examination	MRI Findings	Treatment	Follow-Up, mo	Out Come
1	F	8	Acute encephalopathy	Hyperreflexia	Basal ganglia involvement	MP 5 Days, OP 2 Weeks	6	Normal
2	M	10	Ataxia	Hyperreflexia	Brain stem involvement	MP 3 Days, OP 2 Weeks	10	Normal
3	F	8	Ataxia	Hyperreflexia	Periventricular white matter involvement	MP 3 Days, OP 2 Weeks	9	Normal
4	M	6	Headache, Fever	Hyperreflexia	Periventricular white matter involvement	MP 3 Days, OP 2 Weeks	6	Normal
5	M	4	Fever, Headache	Cranial nerve paresis	Brainstem involvement	IVIG5 Days	12	Ataxia
6	M	5	Fever, Headache	Hyperreflexia abnormal movements	Basal ganglia involvement	IVIG 5 Days	7	Normal
7	M	4	Ataxia	Hyperreflexia	Cerebellum involvement	MP 5 Days, OP 2 Weeks	6	Normal
8	F	5	Ataxia	Hyperreflexia	Brainstem involvement	MP 5 Days, OP 2 Weeks	8	Normal
9	M	4	Fever, Headache	Cranial nerve paresis	Periventricular white matter involvement	MP 5 Days, OP 2 Weeks	9	Normal
10	M	6	Acute encephalopathy altered consciousness	Hyperreflexiadysarthria	Brainstem+ cerebellum involvement	MP 5 Days, OP 2 Weeks	11	Normal
11	M	7	Ataxia	Hyperreflexia	Periventricular white matter involvement	MP 3 Days, OP 2 Weeks	6	Normal

Abbreviations: F, female; IVIG, intra venous immunoglobulin; M, male; MP, methyl prednisolone; OP, oral prednisolone.

5. Discussion and Review of Literature

Acute disseminated encephalomyelitis (ADEM) is usually a monophasic inflammatory demyelinating disease of the CNS defined by a polysymptomatic presentation and encephalopathy. It is often seen 7 - 14 days following a viral infection or immunization (7). There may be prodromal findings such as fever, malaise, headache and vomiting. Clinical features are determined by distribution of lesions in the CNS. Multifocal neurological signs such as hemiparesis, bilateral upper motor neuron signs, cerebellar ataxia, cranial nerve palsies, dysarthria, seizures and disturbances in micturition may be seen (8). There are no pathognomonic clinical or laboratory findings for ADEM. CSF is usually normal, but may show lymphocytic pleocytosis and mild elevation of protein. Other markers such as oligoclonal bands, IgG or myelin basic protein (MBP) are sometimes detectable, but not diagnostic (9). Electroencephalogram (EEG) often shows non-specific features of an encephalopathic process. In the absence of specific biologic markers, the diagnosis of ADEM is based on clinical and radiologic features. Cerebral MRI shows high signal lesions of the same age on T2-weighted images in the subcortical white matter, with or without involvement of the cerebellum, gray matter and spinal cord (10, 11). Presentation and clinical course can be quite variable because of the distribution of lesions in CNS. Tosun et al. (10) reported 12 patients who presented fever (50%), loss of consciousness and seizures (33.3%). In our study, 36.4% had fever and headache and 18.2% of patients had loss of consciousness at admission. In another series Gupte et al. (11) reported the most common presenting symptoms as ataxia, loss of vision and headache. Anlar et al. (12) reported 46 patients with common symptoms and signs pertaining to the motor system and consciousness. In our patients, the most common clinical features were ataxia, fever and headache. In previous literature, spinal cord involvement was reported in 3% - 25% of cases (7). In our study, cord lesion was not found. We could not identify herpes virus with serologic test (CSF PCR) in our cases. In the treatment of ADEM, dexamethasone and high-dose IV methylprednisolone (MP) have also been used (8, 12). In addition, IVIG and plasmapheresis have been reported to be effective, particularly in patients who do not respond to steroids (13). It has been practical to use high-dose IV MP 20 mg/kg per day for 3 - 5 days followed by oral prednisolone commencing at 1 - 2 mg/kg per day, with tapering over two weeks. We administered high-dose IV MP followed by oral prednisolone in nine patients and IVIg in two patients. The outcome of ADEM is generally good, with 57% - 89% of children making a full recovery (7, 14). Rezai and Abbaskhanian (15) reported 7 cases of ADEM who received appropriate treatment and finally 4 patients reached complete recovery. In our group, two children had loss of consciousness, four children headache and fever and two children cranial neuropathy on admission. After 3 to 9 months follow-up, only in one child who received IVIG, mild ataxia had reminded and his second brain MRI showed hyperintensities in cerebellum. The other patients recovered completely (91%).

5.1. Conclusion

The prognosis of acute disseminated encephalomyelitis (ADEM) is favorable. The widespread availability of MRI means that more cases are now recognized. Early diagnosis and prompt treatment of ADEM would probably reduce morbidity. In this study, only one patient reminded ataxic who received IVIG. We think that maybe he could be asymptomatic if he had received IV MP.

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