CASE REPORT

Extensive acute disseminated encephalomyelitis in a young girl responding to intravenous methylprednisolone

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SUMMARY

Acute disseminated encephalomyelitis (ADEM) is a monophasic clinical syndrome, characterised by immune-mediated demyelination of the central nervous system. Differentiating ADEM from acute viral encephalomyelitis may pose a difficult clinical challenge. We describe a 3-year-old girl who presented with fever, weakness in all four limbs, urinary retention, respiratory distress and altered sensorium. MRI of the brain showed multiple cerebral T2-hyperintense signals with bilateral thalamic and basal ganglia involvement. MRI of the spine showed extensive T2-hyperintensities from cervical to lumbar spinal cord. Cerebrospinal fluid examination was normal. The patient was diagnosed as ADEM and treated with intravenous methylprednisolone. She showed complete clinical and radiological improvement at the end of 1-month follow-up.

CASE PRESENTATION

A 3-year-old girl was brought by her parents with fever for 1 week, weakness in all four limbs for 4 days, urinary retention for 4 days, respiratory distress for 2 days and altered sensorium for 1 day. She had not received any immunisation recently. On clinical examination, the child was drowsy and disoriented. The patient had pulse rate of 124 bpm, blood pressure 80/50 mm Hg and respiratory rate 46 breaths/min. Cranial nerves and fundoscopic examinations were normal. Motor system examination revealed hypotonia in all four limbs; a power of medical research council (MRC) grade 3/5 in upper limbs and 0/5 in both lower limbs; absent deep tendon reflexes in all four limbs and bilateral nonelicitable plantar responses. She was not cooperative for sensory, cerebellar and extrapyramidal system examination. Thus, our patient had acute onset quadriplegia and altered sensorium, suggesting acute transverse myelitis with encephalopathy.

BACKGROUND

Acute disseminated encephalomyelitis (ADEM) is a monophasic clinical syndrome, characterised by immune-mediated demyelination of central nervous system neurons, which results in widespread damage in the brain and spinal cord. It usually affects children and young adults following infections or immunisation. Various viral infections implicated in its causation include measles, influenza, Epstein-Barr virus, cytomegalovirus, human herpes virus, varicella, rubella, hepatitis A, hepatitis B and HIV. Similarly, vaccinations like rabies, diphtheria, tetanus, pertussis, smallpox, measles, Japanese B encephalitis, polio, hepatitis B and influenza can lead to ADEM.¹ Initial symptoms of ADEM may begin within 4–21 days after the inciting event. However, in clinical practice, if the inciting infection is subclinical, then it may become difficult to differentiate the clinical syndrome from acute viral encephalitis, especially in a country like India where diseases like Japanese encephalitis are endemic. This diagnostic dilemma has important consequences as the immunosuppressive therapy used in management of ADEM may lead to worsening of viral encephalitis. We describe a 3-year-old girl who presented with a short history of fever and neurological features. The diagnosis of ADEM was made on the basis of clinical and MRI features. Treatment with high-dose methylprednisolone resulted in complete clinical recovery and resolution of radiological lesions.

INVESTIGATIONS

The patient's routine haematological and biochemical investigations were within normal limits. Cerebrospinal fluid (CSF) analysis showed 5 cells/mm³ which were all lymphocytes, Gram-negative staining for bacteria, proteins 65 mg/dL, sugar 58 mg/dL and chloride 112 mEq/L. CSF ELISA for herpes simplex virus, dengue, Japanese encephalitis virus, measles, mumps and cytomegalovirus were negative. MRI of the spine showed diffuse hyperintensity extending from cervical to lumbar spinal cord and cord swelling in cervical region (figure 1A–C). However, considering the presence of fever and altered sensorium, MRI of the brain was also performed, which revealed multifocal hyperintensities on T2-weighted sequences involving bilateral caudate nuclei, thalami and patchy hyperintense lesions in pons and subcortical white matter (figure 2A–C).

TREATMENT

This presentation of fever, altered sensorium and quadriplegia with extensive demyelination affecting the brain and spinal cord left us with differential diagnoses of ADEM and viral encephalitis. However, considering the absence of CSF pleocytosis and the negative CSF ELISA for common viruses and the fact that the simultaneous extensive involvement of the spinal cord is unusual in viral encephalitis, viral encephalitis was ruled out. We made a diagnosis of ADEM and started treatment

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Figure 1 (A) and (B) T2-weighted sagittal images of the spinal cord showing hyperintense lesions extending from cervical to lumbar cord. (C) T2-weighted axial image of cervical the spinal cord showing hyperintensities involving entire thickness of cord.

with intravenous methylprednisolone 30 mg/kg or 5 days along with supportive care and physiotherapy. The patient was catheterised to relieve urinary retention.

OUTCOME AND FOLLOW-UP

Gradual clinical improvement was observed over the next 2 weeks. The fever subsided in next 3–4 days, power in the limbs steadily improved so that she was able to walk unsupported and use her hands after 2 weeks. The urinary catheter was removed after 2 weeks and she achieved complete urinary sphincter control in 3 weeks. She regained complete activities in 1 month and rejoined her playschool. A repeat MRI of the brain (figure 3A–C) and spine (figure 4A,B) after 1 month revealed complete resolution of the lesions.

DISCUSSION

Salient features in our patient include a clinically and radiologically indistinguishable condition from viral encephalitis and a remarkable response to intravenous methylprednisolone therapy. This case illustrates the importance of early diagnosis and immunosuppressive treatment in ADEM, as delay in treatment can lead to irreversible neurological sequelae.

ADEM is a consequence of immune-mediated damage to the central nervous system following exposure to foreign antigens in the form of infections or vaccinations. It has been termed as 'postinfectious,' 'parainfectious,' 'postexanthematous' or 'post-vaccinal' encephalomyelitis.² An important mechanism of immune activation is molecular mimicry due to sharing of epitopes between self-antigens in the nervous system and non-self molecules presented by the pathogens.³ These molecules are presented by the cells of innate immune system to naïve lymphocytes, causing their activation and a cell-mediated as well as humoral immune response. Direct neuronal damage by neurotropic viruses may release neuronal antigens, which may lead to immune activation against nervous tissue. The clinical picture of ADEM is characterised by altered mental statuses, motor features like hemiparesis, paraparesis or quadriparesis, cranial neuropathies, extrapyramidal features, seizures and optic neuritis.¹ Unusual presentations such as psychosis, autonomic dysfunction, fever of unknown origin and cerebellar mutism have also been described.^{4–7}

Initial symptoms of ADEM may arise 4–21 days after the inciting infection.¹ But a diagnostic dilemma may arise in cases where the preceding infection is subclinical or when the latent period between the infection and clinical symptoms is too short.

Figure 2 (A–C) T2-weighted MRI of the brain showing hyperintense lesions in bilateral basal ganglia, thalami and pons.

Figure 3 (A–C) T2-weighted MRI of the brain after 1 month showing complete resolution of lesions.

In such cases, it is difficult to clinically distinguish between ADEM and viral encephalomyelitis. We faced a similar problem in our case. Furthermore, our patient had bilateral thalamic involvement in MRI, a feature that is very commonly seen in Japanese encephalitis.⁸ Most common MRI features in ADEM include bilateral asymmetrical, frontoparietal white matter changes.⁹ However, bilateral thalamic involvement in ADEM has been described in 12% cases.¹⁰

This clinical distinction is important, as the immunosuppressive treatment administered in a patient of viral encephalitis for presumed ADEM can have disastrous consequences by flaring up the infection. A reactive CSF in the form of lymphocytic pleocytosis may favour viral encephalitis and increased CSF protein in lieu of increased cells may favour ADEM. However this distinction is far from being definitive. Further, CSF ELISA or PCR for viruses such as herpes simplex, Japanese encephalitis

Figure 4 (A) and (B) T2-weighted sagittal image of the spinal cord after 1 month showing complete resolution of lesions.

or other viruses may be positive in both cases. Thus, on the basis of current literature, it is difficult to make this distinction and we need further studies to determine the clinical, radiological and laboratory markers to distinguish these two entities.

MRI is the best modality to demonstrate the demyelinating lesions of ADEM. Usually, the lesions of ADEM appear at the time of clinical presentation. However, Honkaniemi *et al*¹¹ have demonstrated that the MRI lesion may appear after a delay of more than a month. The MRI features of ADEM include multiple patchy lesions, involving cerebral white matter, basal ganglia, thalamus, brainstem, cerebellum, optic nerves and spinal cord. These lesions are hyperintense in T2 and fluid attenuated inversion recovery sequence images and are usually of same age. Lesions involving the brainstem and cerebellum are more commonly observed in children. The corpus callosum is usually spared in ADEM, differentiating it from multiple sclerosis (MS), in which it is commonly affected. On the other hand, the thalamus is affected in 40% patients with ADEM and spared in MS.¹ Tumour-like lesions have also been observed in a few ADEM cases.¹² Involvement of the cerebellum and brainstem is more common in children. The blood–brain barrier disruption in ADEM is patchy and is mainly due to perivenular inflammation. Hence, the contrast enhancement pattern is variable, and may be described as nodular, diffuse, gyral, complete and incomplete ring. In different series, contrast enhancement in ADEM has been demonstrated in 30–100% patients.¹³ Role of diffusion-weighted imaging (DWI) in ADEM has been recently studied and it has been observed that changes in DWI are not only variable but also dependent on the stage of the disease. Within first 7 days from clinical onset (acute stage), DWI may show restricted diffusion at the periphery of the lesions, with normal diffusion in the central region. On the other hand, if DWI is performed after 7 days (subacute stage), an increased diffusion may be demonstrated.¹⁴ Inflammation, myelin sheath swelling and reduced blood supply in the acute stage may contribute to restricted diffusion. The increased diffu-

sion in subacute stage may result from extracellular space expansion due to demyelination and oedema.¹⁴ However, a T2 shine-through effect is more common than true restriction of diffusion.¹³

The principle strategy in management of ADEM includes controlling the immune response against nervous tissue by using immunosuppressant agents, as soon as possible. High dose corticosteroids are presently considered as first-line therapy in ADEM.¹⁵ Other modalities of immunosuppression in steroid unresponsive cases include plasmapheresis,¹⁶ intravenous immunoglobulin,¹⁷ mitoxantrone and cyclophosphamide.¹⁵ Our patient received intravenous methylprednisolone therapy at an early stage, leading to complete clinical and radiological resolution. Thus, our case exemplifies the importance of early immunosuppressive therapy in ADEM.

Contributors RV made the hypothesis, TBP and RL helped in drafting the manuscript and MK read MRI of the patient.

Competing interests None.

Patient consent Obtained.

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Learning points

- Acute disseminated encephalomyelitis (ADEM) is an acute monophasic, immune-mediated neurological disorder with multifocal central nervous system damage following viral infections or immunisations.
- Diagnosis of ADEM needs a high index of suspicion.
- Differentiating ADEM from acute viral encephalomyelitis can be difficult, especially in countries endemic for viral encephalitis.
- Clinical clues and cerebrospinal fluid findings may help make a distinction between ADEM and acute viral encephalomyelitis.
- Early diagnosis and prompt immunosuppressive therapy are crucial in ensuring a favourable outcome in ADEM.

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