CASE REPORT

Subacute sclerosing panencephalitis presenting as acute disseminated encephalomyelitis and pseudotumour cerebri

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SUMMARY

Subacute sclerosing panencephalitis (SSPE) is a chronic progressive encephalitis of childhood and young adults due to persistent measles virus infection. The usual age of onset is between 5 and 15 years. There are wide varieties of presentations of SSPE described in the literatures. Variable clinical presentations may lead to diagnostic dilemma and unnecessary investigations especially in developing countries, where the measles is quite endemic and vaccination status is not up to the mark because of poor literacy and socioeconomic status. Good clinical correlations, neuroimaging findings, EEG and cerebrospinal fluid (CSF) marker for SSPE yield the clue to diagnosis. This case illustrates a 13-year-old boy presented with short history of intellectual decline, headache, papilloedema, cranial nerve palsy, myoclonus with suggestive neuroimaging mimicking acute disseminated encephalomyelitis (ADEM) and pseudotumour cerebri. Subsequently he was diagnosed to be a case of SSPE on the basis of CSF and serum measles antibody titer.

BACKGROUND

SSPE is a chronic progressive and fatal neurological disorder due to persistent measles virus infection of central nervous system (CNS) characterised by myoclonic jerks, cognitive decline and typical EEG findings. Children with SSPE had natural infection with the measles virus at an early age, half before age of 2 years.¹ It was first clinically described in 1993 as 'subacute inclusion encephalitis' since inclusion bodies were seen in the brain biopsies.² It has a progressive and fulminant course that results in death within 5 years of onset.³ Usually it is not difficult in a child presenting with intellectual decline or behavioural issue followed by myoclonic jerks, which become generalised involving axial body parts. Diagnosis becomes a challenge when there is atypicality in presentations along with non-specific laboratory or electrophysiological values. We describe a young boy with short history of intellectual decline, headache, cranial nerve palsy and myoclonic jerks with clinical and neuroradiological findings mimicking acute disseminated encephalomyelitis (ADEM) and pseudotumour cerebri, the two unusual associations of SSPE.

CASE PRESENTATION

A 13-year-old boy from a low socioeconomic family, born of non-consanguinity with normal birth and development, student of first standard

presented with fever, moderate to high grade without chills and rigour for initial 4 days, 3 weeks prior to medical attention. He had a continuous holocranial headache of moderate-to-severe intensity with intermittent vomiting about three to four times per day that persisted till admission. He had a history of repeated falls due to abnormal jerky movements of his whole body (myoclonus). A week later, he developed acute onset non-fluctuating bilateral horizontal diplopia unaccompanied by ptosis or other cranial nerve involvement. On the third day of diplopia, he developed rapidly progressive bilateral painless vision loss leading to only hand at one meter distance over a span of 24 h. Apart from this he had decreased scholastic performance. He left schooling due to inattentiveness, inability to remember his studies and persistent headaches. There was no history of generalised seizures, limb weakness, gait abnormalities, behavioural problems or altered sensorium. Family history was unremarkable. There was no previous history of measles infection. Vaccination status of measles was doubtful.

General physical examination revealed that the patient was conscious, oriented with normal conversation. His vital parameters were normal. Examinations of cardiovascular, respiratory and gastrointestinal system were unremarkable. Neurological examination showed moderate mental retardation with an IQ of 66. Cranial nerve examinations revealed bilateral decreased visual acuity of finger counting at 1 meter distance. Examination of fundi showed bilateral papilledema. Pupils were bilaterally equal and reacting to light. There was bilateral lateral rectus palsy. Rest of the cranial nerves examination were normal. Motor system examination showed normal tone, power and deep tendon reflexes with left extensor plantar response. Sensory, autonomic and cerebellar examinations were normal. There were no signs of meningeal irritations.

INVESTIGATIONS

The routine blood examinations revealed no abnormality. An MRI of the brain with T2 and fluid-attenuated inversion recovery sequences (figure 1A) revealed bilateral symmetrical confluent white matter hyper intensities involving both cerebral hemispheres with a frontal lobe predilection with negative diffusion restriction (figure 1B). EEG showed generalised periodic sharp wave complexes of 100–600µV with an interval of 0.5–2 s

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Figure 1 (A) MRI of the brain with fluid-attenuated inversion recovery sequence showing bilateral symmetrical, confluent white matter hyperintensity (pseudoleukodystrophic pattern) involving both cerebral hemispheres with frontal predilection. (B) Diffusion-weighted imaging sequence showing no diffusion restriction of the white matter lesion.

suggestive of periodic long-interval diffuse discharges (figure 2). CSF studies showed that the opening pressure was 22 cm H₂O (normal 4–12 cm H₂O). CSF sugar was 85 mg/dL; protein was 55 mg/dL with acellular background. CSF Gram stain, Ziehl-Neelsen stain, India ink and culture for pyogenic, tubercular and fungal organisms were negative. CSF PCR for *Mycobacterium tuberculosis* was negative. Serum and CSF measles immunoglobulin G antibody was positive in high titre. Screening for HIV, neurosyphilis, hepatitis B and C were negative.

TREATMENT

A week prior to admission, he was admitted to an outside tertiary care centre and diagnosed to be ADEM. He was treated with intravenous methylprednisolone 1000 mg daily for 5 days, mannitol (20%, 100 mL thrice daily) and acetazolamide (250 mg thrice daily). As per previous record, his headache and vomiting were decreased and visual acuity improved from hand movement to finger counting at 1 m distance. Based on clinical correlations and detail investigations, SSPE was considered. He was treated with intrathecal interferon α 2b (3 million unit), isoprinosine 100 mg/kg body weight, sodium valproate 20 mg/kg body weight and acetazolamide 750 mg/day in three divided doses.

OUTCOME AND FOLLOW-UP

On follow-up after 4 weeks, his symptoms pertaining to raised intracranial pressure (ICP) such as headache, cranial nerve palsy were subsided. His visual acuity was further improved to 6/36 bilaterally with persistence of papilloedema. Myoclonic jerks and frequency of fall substantially decreased. He was on regular treatment with monthly intrathecal injections of interferon α 2b (3 million units), daily oral isoprinosine 100 mg/kg in three divided doses, sodium valproate 20 mg/kg/day, calcium and vitamin D3 supplementations and acetazolamide (250 mg thrice daily).

DISCUSSION

The neurological complications of measles virus infection include (1) acute measles encephalomyelitis, an immune-mediated disorder resulting in measles-related ADEM. It occurs 5–14 days

after a rash and is found especially in children. (2) Measles inclusion body encephalitis, occurs in immunocompromised state after acquiring measles infection with a latency of 3–6 months. (3) SSPE is a chronic progressive neurodegenerative disease caused by persistent defective measles virus in neurons and oligodendrocytes. It occurs 2–10 years after primary infection.⁴

Among the different clinical manifestations of SSPE, myoclonus (generalised and focal), seizure (generalised and focal), cognitive impairment, pyramidal signs, visual symptoms, extra pyramidal and behavioural problems are common.⁵ However atypical presentations with regard to clinical spectrums, laboratory and electroencephalographic findings likely pose the diagnostic challenge. Familial occurrence, perinatal and neonatal presentations, manifestation at less than 2 years or adult onset are quite uncommon. Onset with seizures other than myoclonus, hemiparesis, transcortical sensory aphasia, dystonia, unilateral myoclonus, pseudotumour cerebri, acute vision loss, chorioretinitis, optic neuritis, cortical blindness or Balint's syndrome are the early rare manifestations of SSPE. Fulminant course with death within 3 months and long-term survival or remission may create diagnostic dilemma.⁶

Pseudotumour cerebri is a condition with increased ICP without any space occupying lesion or hydrocephalus. It may or may not be associated with any identifiable cause.

Pseudotumour cerebri results from alterations in CSF production and absorption, cerebral oedema, abnormalities in vasomotor control and cerebral blood flow as well as a venous obstruction. The direct relationship between pseudotumour cerebri and infection is still undefined. Cerebral venous sinus thrombosis secondary to infections may be attributed to raised ICP. In certain circumstances, autoimmune-mediated postvaricella vasculitis and Lyme disease have been postulated as the cause of pseudotumour cerebri.^{7,8}

Few anecdotal case reports are described as an association of pseudotumour cerebri and SSPE.⁹ The exact mechanism of increased ICP in SSPE is unknown but underlying acute inflammatory reaction might play a role.¹⁰ Olmez *et al*¹⁰ found that most of the patients with SSPE who had raised ICP were asymptomatic.

ADEM is an inflammatory demyelinating disease of the CNS that often follows a viral illness or vaccination. It is clinically

Figure 2 EEG showing generalised periodic sharp wave complex of 100–600 μ V persisting for 0.5–2 s with an interval of 2–3 s suggestive of periodic long interval diffuse discharges in subacute sclerosing panencephalitis (settings: amplitude 15 μ V/min, paper speed=20 mm/s, high and low filter 70 and 1 μ V).

characterised by the acute or subacute onset of multifocal neurological disturbances that typically follow a monophasic course with MRI evidence of widespread demyelination predominantly involving the white matter of the brain and sometimes the spinal cord. The clinical presentations of ADEM in paediatric patients include: altered sensorium, unilateral or bilateral long tract signs (60–95%); hemiplegia (76%); ataxia (18–59%); meningism (26–31%); seizures (13–35%); spinal cord involvement (24%); visual involvement (7–23%); and speech impairment or aphasia.¹¹ The MRI findings vary from person to person. Five patterns of MRI findings are described in the literature that include (1) small lesions (<5 mm); (2) large confluent tumefactive lesion; (3) additional symmetric bithalamic involvement; (4) haemorrhagic encephalitis pattern and (5) diffuse, bilateral, symmetrical, usually non-enhanced white matter involvement (pseudoleukodystrophic pattern).^{11 12}

Our patient presented with short history of fever, headache, vomiting followed by cranial nerve palsy (bilateral lateral rectus palsy), simultaneous bilateral painless vision loss, myoclonus and intellectual decline. With the above clinical findings and evidence of long tract sign and pseudoleukodystrophic pattern of white matter tract involvement in MRI of the brain with partial steroid responsiveness which mimic ADEM. Furthermore features of raised ICP, objective evidence of raised CSF pressure and papilloedema without any evidence of intracranial mass lesion or hydrocephalous raise the possibility of pseudotumour cerebri. Few case reports were described in literatures as an association of ADEM and SSPE.¹³ The association of ADEM and pseudotumour-like presentation in SSPE as an early manifestation is quite unusual. So a high level of suspicion is required to analyse such atypical presentations in SSPE to avoid diagnostic dilemmas.

Learning points

- ▶ Subacute sclerosing panencephalitis (SSPE) may have wide clinical presentation with variable age at the onset and progression which needs to be addressed while management.
- ▶ In developing countries, SSPE is one of the common differential diagnoses in children with or without antecedent measles infection with intellectual disability, myoclonus and variable pyramidal, extrapyramidal and cranial nerve involvement.
- ▶ SSPE may have acute disseminated encephalomyelitis-like presentation which needs high index of suspicion in clinical practice.
- ▶ Increased intracranial pressure in SSPE is not uncommon and may produce false localising sign such as bilateral lateral rectus palsy.

Competing interests None.

Patient consent Obtained.

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