Subacute sclerosing panencephalitis presenting as neuromyelitis optica

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SUMMARY

Subacute sclerosing panencephalitis (SSPE) is a slowly progressing inflammatory and degenerative disorder of the brain caused by a mutant measles virus. The diagnosis of SSPE is based on characteristic clinical and EEG findings (periodic complexes) and demonstration of elevated antibody titres against measles in cerebrospinal fluid. SSPE can have atypical clinical features at the onset. The authors here report a case of a 3-year-old child who presented with vision loss followed 15 months later by quadriparesis with bladder involvement. These clinical features resembled that of neuromyelitis optica. However, as the disease progressed, appearance of myoclonic jerks, periodic discharges on EEG and positive cerebrospinal fluid serology for measles led to the final diagnosis of SSPE.

BACKGROUND

Subacute sclerosing panencephalitis (SSPE) is a devastating neurodegenerative disorder caused by persistent measles virus infection affecting childhood and early adolescence.[1] SSPE is an uncommon disease in developed countries but is still a major concern in developing countries. The occipital cortex is involved initially which usually results in cortical vision loss. Visual abnormalities can also occur due to involvement of optic nerve and retina. The spinal cord is uncommonly affected in SSPE and, if affected, the involvement is usually late along with brainstem involvement. Usual clinical picture of SSPE consists of myoclonus and progressive cognitive decline progressing to a mute, bedridden and incontinent state finally leading to death.[2] Atypical features like ataxia, dystonia, tremors and hemiparkinsonian features have been reported. Here, we report an interesting case of SSPE which initially had involvement of optic nerve and spinal cord simulating that of NMO. Later on, SSPE was diagnosed based on myoclonic jerks, typical EEG findings and cerebrospinal fluid (CSF) serology.

CASE PRESENTATION

A 3-year-old female child presented with history of fever, cough and cold 15 days prior to admission. Fever was moderate to high grade not associated with chills or any skin rash, and it lasted for 8–9 days. In total, 5–6 days after the onset of fever, the patient developed rapidly progressive quadriparesis along with bladder involvement and became bed bound in a few days. There was no history of any eye deviation, facial deviation, dysphagia or dysphonia. The patient's parents gave history of a previous episode of bilateral vision loss 15 months ago which was most probably acute in onset, rapidly progressed over a few days to complete blindness. There has been no improvement in vision since then. Milestones were achieved normally and the child was not vaccinated. Family history was not significant.

On examination, vitals were stable. General examination did not reveal any abnormality. The child was conscious but irritable. Light perception was absent. The patient could not fixate gaze on objects. The pupils were bilateral mid-dilated, very sluggishly reacting to light and the fundus was suggestive of bilateral primary optic atrophy (the disc margins were well defined, chalky white disc with attenuation of vessels crossing the disc margin). There was hypotonia in all the four limbs with inability to hold the neck. The child could barely move limbs in the bed and appeared as a floppy baby. Deep tendon reflexes were hypoactive with extensor plantars. Clinically, a possibility of acute disseminated encephalomyelitis or cervical myelitis was considered. However, previous episode of vision loss leading to optic atrophy and now an episode of myelitis led to a strong suspicion of neuromyelitis optica (NMO).

INVESTIGATIONS

Haematological parameters, biochemical parameters like renal, liver functions, electrolytes, plasma lactate and thyroid profile were within normal limits. The CSF picture showed a total of 20 cells with lymphocytic predominance and mildly raised proteins. CSF virology for Dengue, Herpes simplex and measles was negative.

Fundus photograph (figure 1): bilateral optic atrophy.

MRI brain (figure 2): MRI brain showed no obvious abnormality.

MRI cervical spine (figure 3 A,B): cervical spine showing ill-defined T2 hyperintense signal changes extending from C2 to C6 suggestive of longitudinally extensive transverse myelitis along with mild expansion of the cervical cord.

MRI cervical spine T2 axial section (figure 4): ill-defined T2 hyperintensities within the spinal cord.

EEG was suggestive of intermittent slowing. There were no epileptiform discharges.

TREATMENT

The patient received IV methylprednisolone along with supportive care.

OUTCOME AND FOLLOW-UP

After 2 months, there was mild improvement in power. The patient developed multifocal and

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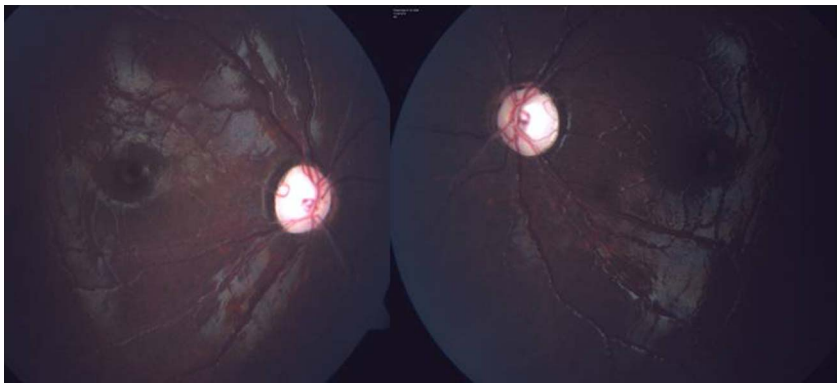

Figure 1 Fundus photograph showing bilateral optic atrophy.

generalised myoclonic jerks involving the limbs and trunk. EEG now showed periodic high-amplitude sharp-and-slow wave discharges of duration 0.5–1 s occurring every 4–5 s along with background slowing (figure 5). CSF IgG measles was positive with titre of 22.3 NTU (>11 considered positive) and measles antibody by particulate agglutination test was 1 : 512 (positive >1 : 128). Presence of myoclonic jerks, periodic discharges on EEG and significantly elevated CSF measles antibody led to the diagnosis of a probable case of SSPE as per Dyken's criteria. Syrup valproate (200 mg/5 ml) 2.5 ml TDS was started and the patient received first dose of intrathecal interferon (5 MU). The patient still continues to have myoclonic jerks with no further improvement.

DISCUSSION

SSPE, a disorder of the central nervous system with grave prognosis is a slow virus infection caused by defective measles virus usually affecting the childhood age group. The clinical features consist of personality and behavioural changes and worsening school performance, followed by myoclonic seizures, paresis, dyspraxias, memory impairment, language difficulties, blindness and eventually obtundation, stupor and coma.[3]

Our patient initially had an episode of optic neuritis followed by cervical myelitis leading to a strong suspicion of NMO.

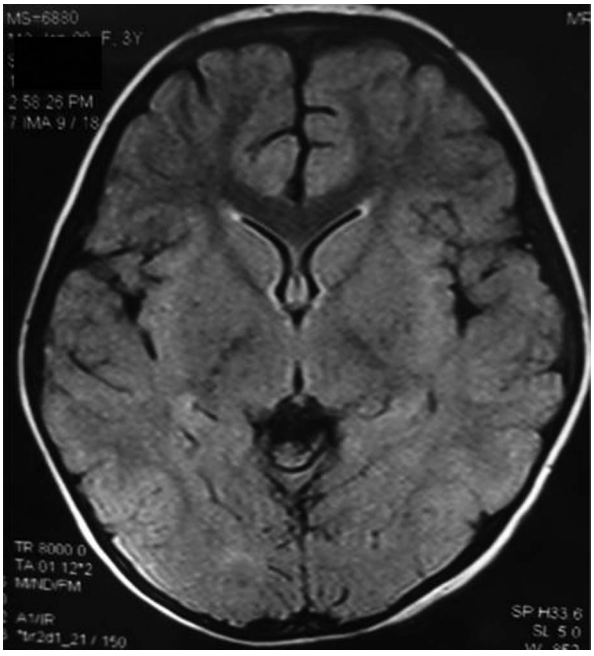

Figure 2 MRI brain T2 FLAIR sequence showing no obvious abnormality.

NMO (Devic's disease) is an inflammatory, demyelinating syndrome of the central nervous system, which is characterised by severe attacks of optic neuritis and myelitis, which, unlike the attacks in multiple sclerosis, commonly spare the brain in the early stages.[4] There can be unilateral optic neuritis, a longer interattack interval (months or years), and a relapsing course.[5 6] A viral prodrome precedes the onset of the disease in 30–50% of cases.[7] In our case, quadriparesis was preceded by a viral illness and it occurred 15 months after an episode of vision loss. Occurrence of bilateral simultaneous optic neuritis or sequential optic neuritis in rapid succession is more suggestive of NMO. In our case, vision loss was bilateral and severe resulting in complete blindness with optic atrophy.

Spinal cord involvement usually presents in the form of complete transverse myelitis with an almost symmetrical sensory level and sphincter dysfunction.[4] Spinal cord lesions usually extend over three or more vertebral segments.[7] Normal brain MRI is initially present in 55–84% of patients with NMO.[8] CSF findings with a lymphomononuclear pleocytosis >50 cells/mm^3 and lack of oligoclonal bands may be indicative of, but not specific for, NMO. Visual evoked potentials (VEP) are frequently abnormal. In our case, MRI brain did not show any obvious abnormality with CSF showing an inflammatory picture. MRI cervical spine was suggestive of longitudinally extensive transverse myelitis. VEP did not show any recordable waveforms. Presence of NMO-IgG/AQP4 (aquaporin 4) antibodies supports the diagnosis of NMO (level A) and is a prognostic marker for high-risk syndromes. Even with the most sensitive assays, 10–25% of patients clinically diagnosed with NMO are seronegative for NMO-IgG.

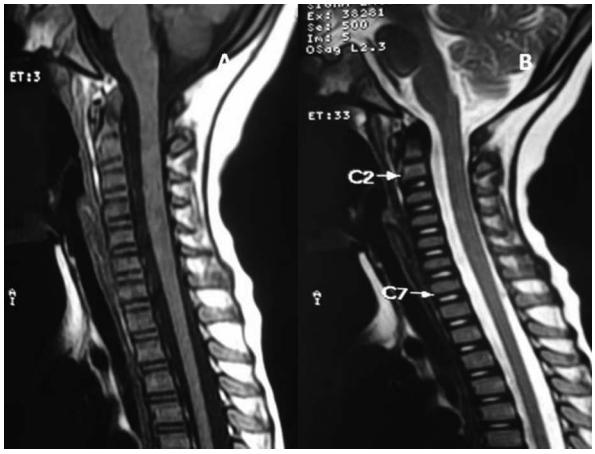

Figure 3 (A) T1 sagittal view showing mild cervical cord expansion (B) T2 sagittal view showing ill-defined signal changes extending from C2 to C6.

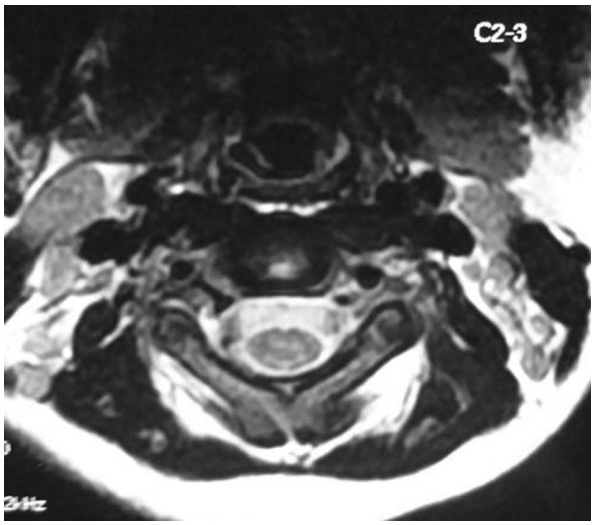

Figure 4 MRI cervical spine T2 axial view shows ill-defined T2 hyperintensities.

In our case, NMO-IgG was negative. Clinical findings were similar to that of NMO at the onset; however, the patient developed myoclonic jerks during follow-up with EEG showing periodic discharges. These two features are very typical of SSPE and form two of the diagnostic criteria proposed by Dyken.

Ocular and visual manifestations are reported in 10–50% of patients of SSPE.[1] These include papilledema, papillitis, optic atrophy, chorioretinitis and cortical blindness. These may precede neurological involvement in 10% of patients.[9] A study by SH Green on ophthalmological findings in SSPE stated that ophthalmological features may present before marked neurological signs are present, and SSPE must be considered in the differential diagnosis of children with retinitis, oedema of the optic disc, optic atrophy, or more complex disorders of visuomotor function.[10] The virus directly affects the optic nerve, retina and choroid resulting in optic neuritis, retinitis and chorioretinitis, respectively. In our case, to begin with, the patient had vision loss due to optic neuritis which preceded the development of motor features.

Motor features in our case included quadriparesis followed by myoclonic jerks. SSPE is known to present initially with certain atypical features. Arora *et al*[11] reported a case of a 16-year-old teenager diagnosed as ADEM with MRI s/o non-specific signal changes in brain and cervical spinal cord. The patient did not respond to steroids and later died. Brain biopsy confirmed the diagnosis of SSPE. Another report by Comert *et al*[12] reported a case of SSPE presenting as spastic quadriparesis following febrile illness. Involvement of the spinal cord is rare in SSPE. Histopathological and immunological studies on autopsy cases have demonstrated the involvement of the spinal cord.[13 14] A case of adult onset SSPE has been reported with cervical cord signal changes on MRI.[15] Presence of spinal cord signal changes on MRI calls for extensive medical and laboratory diagnosis to rule out other diseases. As the disease progresses, typical features like myoclonic jerks increase the suspicion of SSPE. The diagnosis of SSPE is established by the demonstration of characteristic periodic EEG complexes in most of the patients. Our case showed periodic sharp-and-slow wave discharges. CSF examination is mandatory in SSPE. The most remarkable feature of CSF examination is a markedly raised gammaglobulin level, which is usually greater than 20% of total cerebrospinal fluid protein. Raised titres of antimeasles antibodies in the cerebrospinal fluid are diagnostic of SSPE. In our case, CSF measles IgG was significantly raised and diagnosis of SSPE was ascertained.

Learning points

- Initial manifiestations of subacute sclerosing panencephalitis (SSPE) can be quiet varied.
- However, as the disease progresses, typical manifestations lead to diagnosis.
- This case to begin with had atypical features simulating that of neuromyelitis optica but as the disease progressed, characteristic myoclonic jerks and EEG findings alongwith cerebrospinal fluid serology confirmed the diagnosis of SSPE.
- Involvement of spinal cord is rare in SSPE and needs extensive work up to rule out other illnesses like infectious or postinfectious transverse myelitis and inflammatory disorders like neuromyelitis optica.
- In the childhood age group, with optic atrophy and progressive neurological deterioration, possibility of SSPE should be considered and investigated promptly, so that early treatment can slow down the progression of disease and improve the quality of life.

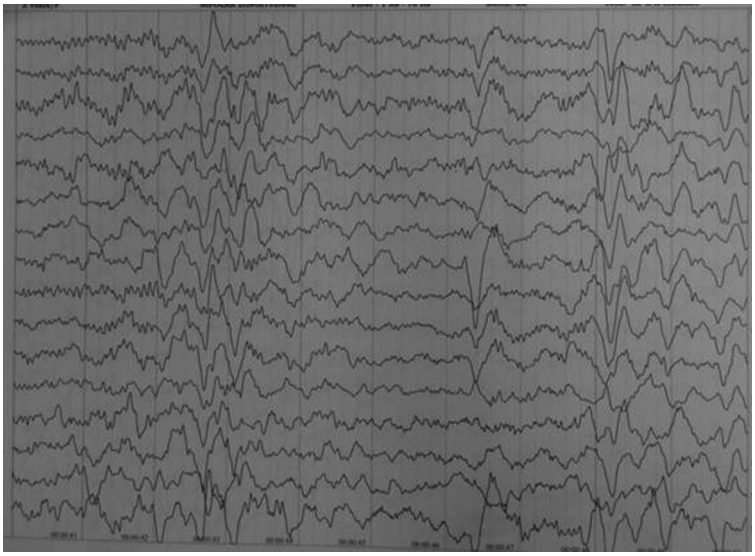

Figure 5 EEG showing periodic discharges.

Competing interests None.

Patient consent Obtained.

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