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Unusual presentation of more common disease/injury

Evolution of certain typical and atypical features in a case of subacute sclerosing panencephalitis

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Summary

Subacute sclerosing panencephalitis (SSPE) is a slowly progressive inflammatory disease of the central nervous system caused by a persistent measles virus usually affecting the childhood and adolescent age group. Clinical features at onset are very subtle and non-specific. Certain atypical features can occur at onset or during the course of illness which can be misleading. Neuroimaging features often are non-specific. Features like myoclonic jerks, cognitive decline and typical EEG findings lead to a strong suspicion of SSPE. Here, we describe the stagewise progression of a case of SSPE in a 14-year-old girl who had myoclonic jerks and cognitive decline at onset. During the course of disease, the patient developed cortical vision loss, atypical extrapyramidal features like segmental and hemifacial dystonia ultimately leading to a bedbound vegetative state. EEG showed typical periodic discharges along with positive cerebrospinal fluid serology for measles.

BACKGROUND

Measles infection and its complications are extensively studied. One such complication, subacute sclerosing panencephalitis (SSPE) is a progressive inflammatory disease of the central nervous system caused by a persistent, aberrant measles-virus infection. The incidence of SSPE is very high in India as a result of higher number of measles cases in children, frequent subclinical measles-virus infection and lack of immunisation.[1 2]

SSPE predominantly affects the children and adolescent population. Death usually occurs within 3 years of onset of the disease. 10 per cent of the cases either show a fulminant or prolonged course of the disease.[2] Early diagnosis of SSPE may be difficult since, at the onset, there may be subtle intellectual and behavioural changes that may persist for a few weeks to years without florid features of myoclonus. Also at the onset, there may be atypical features like ataxia and extrapyramidal features, but as the disease progresses, patients develop myoclonus, cognitive decline and typical EEG changes suggestive of SSPE.

Here, we describe the evolution of various typical and atypical clinical features, neuroimaging changes, and stagewise disease progression in a case of SSPE.

CASE PRESENTATION

A 14-year-old girl, previously having myoclonic jerks and cognitive decline for 15 months, presented with insidious onset gradually progressive bilateral painless vision loss. The patient used to collide with objects while walking and had difficulty in visualising faces. The patient developed complete blindness over 2 months so that she could not even perceive light. For the last 2 months, she developed slowness in performing activities more with the right upper and lower limb. She also had gradually progressive difficulty in walking in the form that she used to take short steps and needed support to walk. She developed difficulty in swallowing both solids and liquids along with occasional nasal regurgitation. Patient was bed-bound, completely mute with bladder bowel incontinence during the last 1 month. There was history of abnormal posturing of right upper and lower limb as well as intermittent deviation of neck to the right side with intermittent tonic deviation of angle of mouth to right along with tonic closure of right eye suggestive of right hemifacial dystonia for 1 month. There was no previous history of any major illness. She did not receive any vaccination. There was no significant family history.

The patient was following up in our department. Initially, 15 months ago, she had falls due to myoclonic jerks. Gradually, the frequency of falls increased and she also developed slowly progressive cognitive decline. She was investigated at that time. Her cerebrospinal fluid (CSF) study, MRI brain and EEG were done, and a possibility of progressive myoclonic epilepsy or SSPE was considered. As CSF serology was negative at that time, patient did not fulfil the criteria for SSPE. She was treated with Tab Valproic acid 300 mg two times daily and Tab Clonazepam 0.25 mg two times daily. Patient transiently improved with antiepileptic drugs, but again developed clinical deterioration as mentioned within last few months.

On examination, vitals were stable. General examination was unremarkable. The patient was catheterised with Ryles tube in situ. She was awake, mute, inattentive and spontaneously moving her eyes in all directions. Comprehension was impaired. Detailed higher function examination could not be done. Pupils were of normal size and direct and consensual light reflex was present. She could not fixate her gaze on objects and menace reflex was absent. Fundus examination was normal. Gag reflex was hypoactive. There was lead pipe rigidity in right upper and lower limb along with neck rigidity. Tone was normal in left upper and lower limb.

Figure 1 Photograph showing right hemifacial dystonia.

Intermittent dystonic posturing was seen in right upper and lower limb. There was also the presence of cervical dystonia with rotation as well as tilt of the head to the right along with elevation of right shoulder. Patient had right hemifacial dystonia (figure 1). Detailed power assessment could not be done as the patient was not cooperative. Deep tendon reflex were brisk with flexor plantar response. Frontal lobe release signs were present bilaterally. There were no rest tremors. As she was rigid and mute, formal testing for bradykinesia could not be performed. With these clinical features, a strong possibility of SSPE was considered and patient was investigated accordingly.

INVESTIGATIONS

Her haematological, biochemical parameters like liver, renal functions, blood sugar, thyroid profile, plasma lactate, serum vitamin B12 and homocysteine were in normal range. There was no Kayser-Fleischer ring on slit lamp examination. CSF was acellular with normal proteins except for measles antibody which was significantly elevated in the CSF (value-27.71 NTU(Nova tech unit), >11 NTU is positive)). CSF measles antibody by particulate agglutination test was positive (1:512). Initial MRI brain was normal (figure 2). Imaging this time showed T2 FLAIR (fluid-attenuated inversion recovery) hyperintensities involving the cortex and the subcortical white matter of the parieto occipital region bilaterally (figure 3). There were signal changes noted in right basal ganglia along with internal capsule. Mild cerebral atrophy was noted. EEG initially showed intermittent, generalised non-specific slowing with a normal background activity. EEG this time showed intermittent background slowing along with presence of periodic sharp and slow wave discharges (figure 4). The patient fulfilled 3 of 5 Dyken's criteria this time and was a case of probable SSPE.

TREATMENT

The patient received a first dose of intrathecal interferon 5 million units and is now on tablet valproate 300 mg two times daily. For her extrapyramidal features, she is on Tab Trihexiphenidyl 2 mg three times a day and Tab Pramipexole 0.25 mg three times a day.

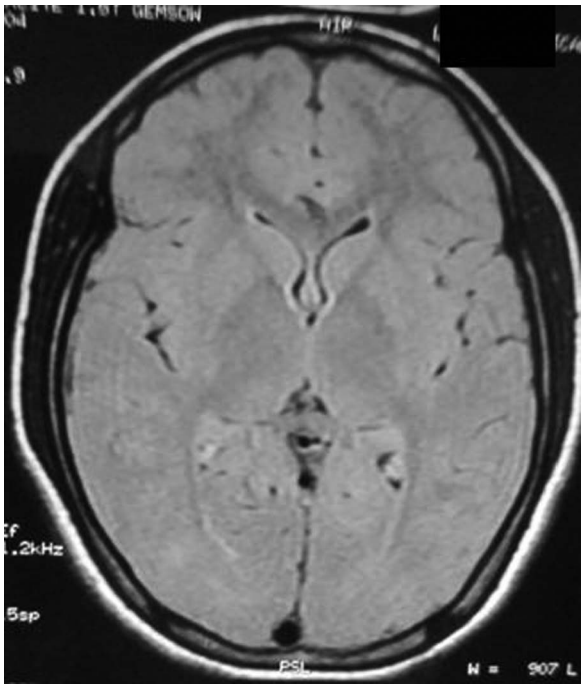

Figure 2 Initial MRI brain T2 fluid-attenuated inversion recovery sequence showing no obvious abnormality.

OUTCOME AND FOLLOW-UP

The patient is still bedridden, mute, catheterised and in a vegetative state. Nutrition is through Ryles tube feeding. She has persistent right appendicular and right cervical and hemifacial dystonia.

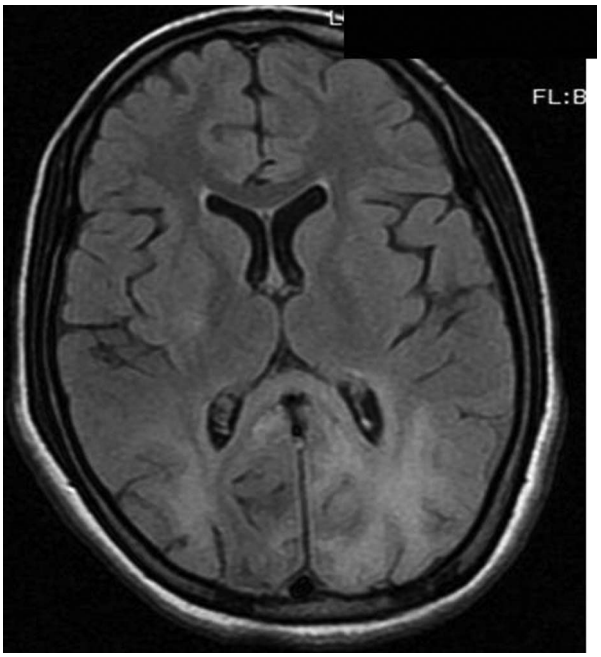

Figure 3 MRI brain T2 fluid-attenuated inversion recovery sequence after vision loss showing parieto-occipital signal changes along with diffuse cerebral atrophy.

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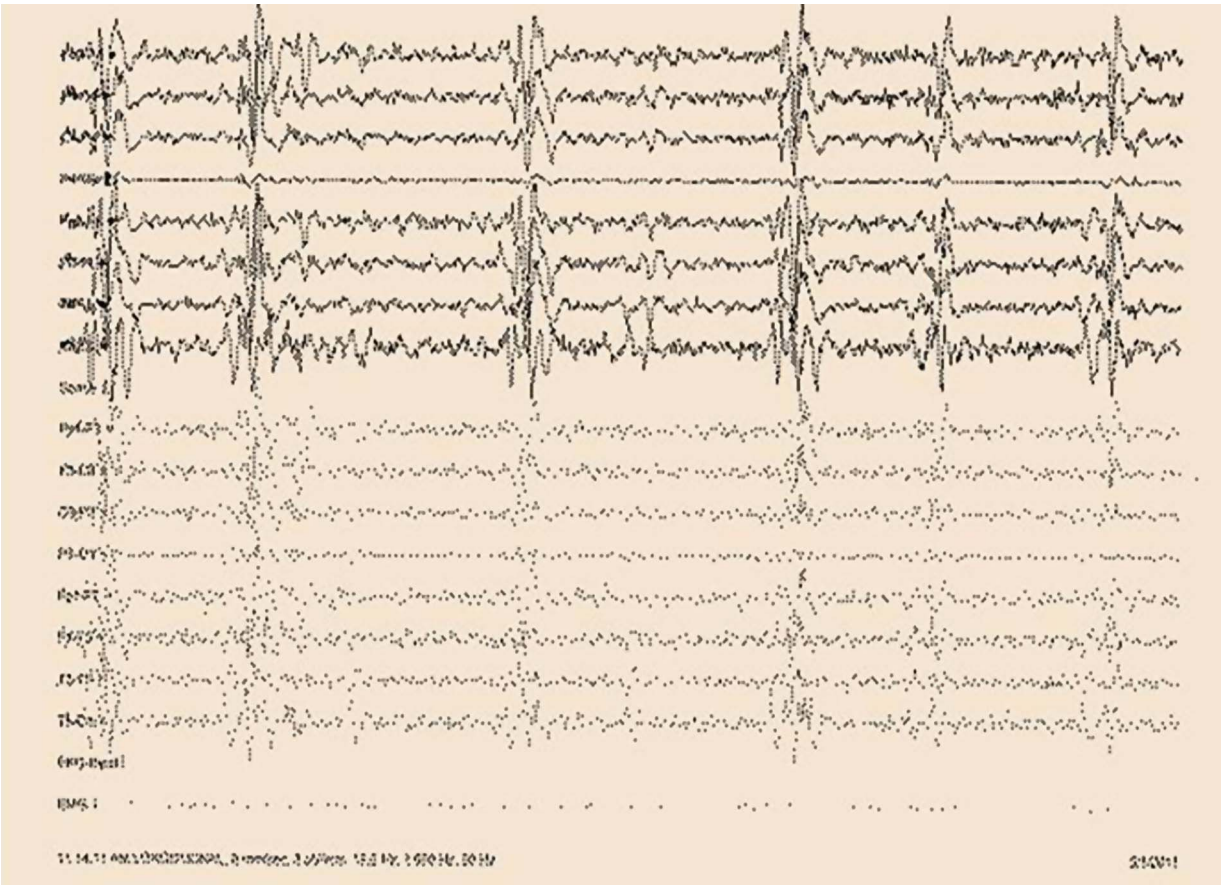

Figure 4 EEG showing periodic discharges.

DISCUSSION

SSPE is a rare, slowly progressive chronic encephalitis involving both the grey and white matter of the brain, caused by a persistent infection by immune-resistant virus. It was first studied by Dawson in 1934 and later elaborated by Van Bogaert who named it SSPE. In 1965, Bouteille[3] demonstrated the presence of viral structures in brain on electron microscopy, and in 1969, measles virus was recovered from a brain of a patient with SSPE.[4] This disease usually presents in the childhood and adolescent age group; however, adult onset cases and case series are reported. Our patient presented in the typical age group of 5–15 years and was not vaccinated against measles. Initial symptoms are very subtle and they may create diagnostic confusion. Initial features include mild intellectual deterioration and behavioural changes without any apparent neurological signs or findings. With the progression of disease, non-specific manifestations evolve into disturbances in motor function and development of periodic stereotyped myoclonic jerks. Myoclonic jerks initially involve the head followed by trunk and limbs.[5] Myoclonus can present as a difficulty in gait, periodic dropping of the head and falling. In the advanced stage of the disease, myoclonus subsides or its frequency decreases. Our case had myoclonic jerks to begin with resulting in falls but gradually, as the disease progressed, frequency of myoclonus decreased. Along the course of the disease, patients frequently develop pyramidal and extrapyramidal features. In advanced stage of the disease, patient has dysphagia, bladder bowel incontinence and is akinetic, mute, rigid and bedridden. Patient usually develops spastic quadriparesis and lands in a vegetative state. In our case also, as the disease progressed over 15 months, patient became mute, inattentive and bedridden with bladder bowel incontinence. Patient also had dysphagia and required Ryles tube for feeding.

Patient had certain atypical extrapyramidal features that are not commonly seen in SSPE which were more troublesome as they caused pain and discomfort to the patient. These were right cervical dystonia, hemifacial dystonia and appendicular dystonia with marked rigidity involving right upper and lower limb. Although extrapyramidal features are common in advanced stage of disease in the form of generalised rigidity, choreoathetoid movements and hemibalismus, only a few patients have dystonia. To date, uncommon presenting features have been described such as tremor, dystonia and hemiparkinsonism.[6] Misra *et al*[7] reported early onset parkinsonian features in two patients. Alexander *et al*[8] also reported a case of myoclonic jerks, spasticity and dystonic posture of right upper limb with generalised seizures in a 17-year-old man who was diagnosed to have SSPE. Dystonia generally in SSPE is appendicular. Hemifacial dystonia has been described with intake of certain drugs[9] but not with SSPE. Cervical dystonia is rare in SSPE. Our patient had a combination of unilateral rigidity, unilateral limb dystonia and same-sided hemifacial and cervical dystonia which is not reported. Dystonias in SSPE are secondary dystonias due to involvement of the basal ganglia especially the

putamen.[10 11] Lesions in the thalamus, cortex, cerebellum and brainstem can produce dystonias. Migratory basal ganglia lesions in SSPE have been reported and axonal spread of virus from the substantia nigra has been implicated in producing parkinsonian symptoms.[12]

Another important system involved in SSPE is the visual pathway. Ocular and visual manifestations are reported in 10–50% of patients, which include cortical blindness, chorioretinitis and optic atrophy. Studies have reported a higher incidence of visual loss amongst patients with adult onset SSPE with age ranging from 20 to 35 years.[13 14] In a study by Khadilkar *et al*,[15] all patients with vision loss had a cortical vision loss secondary to the affection of optic radiation and occipital cortex by measles virus. Visual symptoms involving the anterior pathway usually occur with neurological manifestations, but they may precede neurological manifestation by several years.[16 17] Cortical vision loss usually develops along the course of disease. Our patient had developed cortical vision loss towards the later stage of the disease which progressed over 2 months to complete blindness.

EEG is an important tool for diagnosis in SSPE as EEG findings form one of the diagnostic criteria. The EEG may be normal or show moderate, intermittent non-specific generalised slowing in the initial stages of SSPE. With the appearance of myoclonic jerks, peculiar EEG findings develop in the form of periodic complexes consisting of bilaterally symmetrical, synchronous, high-voltage (200–500 mv) bursts of polyphasic, stereotyped delta waves. Discharges may also include polyspike, spike and wave, sharp and slow wave discharges. Later in the course of disease, the EEG may become increasingly disorganised and show high amplitudes and random dysrhythmic slowing. In terminal stages, the amplitude of waveforms may fall. In our case, EEG initially showed intermittent non-specific generalised slowing which later showed periodic discharges (bilateral synchronus generalised sharp and slow wave duration of 1–1.5 s duration occurring at an interval of 8–9 s).

Neuroimaging is not essential for the diagnosis of SSPE; however, it gives an idea about the extent of disease. Initially, MRI brain may be normal or may show subtle non-specific signal changes involving the white matter. As the disease progresses, signal changes become more conspicuous in the form of ill-defined high signal intensity areas on T2-weighted images in the occipital and parietal subcortical white matter which later become confluent. Brismar *et al*[18] developed a staging system based on neuroimaging findings for SSPE based upon the degree of white matter changes and atrophy. The radiological staging of SSPE may not always exactly correlate with its clinical manifestations, yet sequential MRI may be useful for following the course of the disease.[18] In our case, neuroimaging was normal initially, but MRI brain repeated after 1 year showed parieto-occipital subcortical T2 hyperintense white matter changes correlating with cortical vision loss along with diffuse cerebral atrophy.

Cerebrospinal fluid examination is usually normal. Frequently, it is acellular with normal or a mildly raised protein concentration. The most remarkable feature of the cerebrospinal fluid examination is a markedly raised γ-globulin 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.

Table 1 Stagewise progression of clinical, electroencephalographic and neuroimaging features in this case of SSPE

Duration of disease	Clinical features	EEG	MRI brain	Jabbour stage
3 months	Myoclonic jerks, subtle intellectual changes	Intermittent generalised non-specific slowing	No obvious abnormality	Stage IB
6 months	Myoclonic jerks increased, progressive cognitive decline, language difficulties	Long interval periodic discharges with normal background activity	No obvious abnormality	Stage IIB
9 months	Same features	Short interval periodic discharges	No obvious abnormality	Stage IIB
12 months	Ambulation affected, development of vision loss Myoclonic jerks decreased	Periodic discharges with background slowing	T2 hyperintensities involving parieto-occipital white matter with diffuse cerebral atrophy	Stage IIIA
15 months	Bedridden, mute, inattentive, cervical dystonia, right hemifacial dystonia, hemiparkinsonian features, dysphagia, bladder bowel incontinence	Periodic discharges with background slowing	Same findings	Stage IIIB

SSPE, subacute sclerosing panencephalitis.

Antimeasles antibody titres are also raised in serum as well. Raised antimeasles antibody titres of 1:256 or greater in serum, and 1:4 or greater in cerebrospinal fluid are considered diagnostic of SSPE. In our patient, CSF was acellular, with normal biochemical picture. Measles antibody IgG was significantly raised. Based on the diagnostic criteria proposed by Dyken,[19] our case fulfilled 3 of 5 criteria, thus becoming a probable case of SSPE.

Patient showed stagewise progression of the disease as per Jabbour staging from stage IA to stage IIIb. Table 1 shows the summary of the progression of clinical, neuroimaging and EEG features in this case of SSPE.

Learning points

- Subacute sclerosing panencephalitis is a progressive inflammatory disorder affecting various parts of the central nervous system.
- Typical features are myoclonic jerks, cognitive decline and periodic discharges on EEG.
- It can manifest with atypical features like ataxia, hemiparkinsonism and choreoathetoid movements, dystonia being rare.
- Vision loss is commonly cortical in nature and appears in the later stage of disease.

Competing interests None.

Patient consent Obtained.

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