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Neurology

CLINICAL PRESENTATION OF SUBACUTE SCLEROSING PANENCEPHALITIS : A CASE SERIES

KEY WORDS: SSPE, myoclonus, electroencephalogram

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ABSTRACT

Subacute sclerosing panencephalitis (SSPE) is a potentially lethal neuroinflammatory disorder of brain due to mutated measles virus. The involvement of SSPE includes multiple domains of brain networking resulting into multiple clinical entities including cognition, behavior, consciousness, movements, speech, and locomotion. A total of 6 cases were chosen from 29 cases of SSPE with neurological complication which were presented in the Department of Neurology from December 2021 to August 2023. We present here with salient clinical, radiological and electroencephalogram features of these cases. The main objective of this case series is to help clinicians to identify different neurological manifestation of SSPE. In addition, the importance of myoclonus, seizure and electroencephalogram in the diagnosis of SSPE is further emphasized.

INTRODUCTION

Subacute sclerosing panencephalitis (SSPE) is a progressive demyelinating disease of the brain caused by infection of a mutant strain of the measles virus with significant morbidity and mortality.[1] Its incidence varies depending on the country and ranges 4–11 cases per million population per year.[2] The exact pathogenesis of SSPE is not known. The spectrum of neurological manifestations in SSPE includes altered sensorium, cognitive decline, behavioural abnormalities, movement disorders, seizure, progressive focal neurological defiicits.[3] The diagnosis of SSPE is based on criteria proposed by Dyken and staging is performed by modified Jabbour classification.[4,5] In this case series, we tried to describe the important clinical presentations of SSPE and attempt to highlight the need for its early detection and management.

MATERIAL AND METHOD

During the period from December 2021 to August 2023, there were a total of about 29 cases of Subacute sclerosing panencephalitis. In this case review, we present a total of six cases of SSPE to highlight the varied neurological presentation with a review of literature for the same.

The clinical details of the cases have been obtained from prospective analysis of the patients who were referred to or admitted at the Neurology Department, BRD MC, Gorakhpur.

The diagnosis of SSPE was made according to Dyken criteria.[4]

In all patients, we analyzed the detailed history and performed complete neurological examination, brain magnetic resonance imaging (MRI), electroencephalogram (EEG) and cerebrospinal fluid (CSF) measles IgM and IgG titres with IgG index.

Case Descriptions

Case-1:

A 15-year-old boy presented with intermittent fever for 60 days, altered sensorium for 14 days, vomitting, generalized tonic-clonic seizure with intermittent jerky movements of left upper limb. His vaccination status was naïve. He was febrile with a Glasgow Coma Scale (GCS) of E2V2M4 and Kernig's sign positive. He had segmental myoclonus with decerebrate rigidity, and bilateral extensor plantar response. He was diagnosed clinically as subacute meningo-encephalitis and further work-up. His brain MRI showed T2/FLAIR hyper-intense fronto-parietal cortical lesions of right side. (Figure-1A) EEG showed rhythmic fast periodic high-amplitude generalized discharges. (Figure-2A) His CSF examination showed 40 cells, all lymphocytes, elevated protein, normal sugar with measles IgM titre of 15 NTU and IgG of 15.5 NTU. He was diagnosed as stage III SSPE and started on intra-thecal interferon therapy, levetiracetam (500mg twice daily), and supportive therapy. At 6-months follow-up, patient sensorium did not improve but he was seizure-free.

Case-2:

An 18-year-old female presented with a history of cognitive decline of 18 months, followed by abnormal jerky movements of body for 1 month. Her vaccination status was incomplete. The patient was having GCS of 14 (E4V4M6) without meningeal signs and cranial nerve function. There was presence of intermittent sudden jerky movement of whole body in the form of myoclonus. Her CSF examination showed having 15 cells (all lymphocytes) with mildly elevated protein and normal sugar with measles IgG titres of 15 NTU. MRI brain was showing T2/FLAIR hyper-intense lesions in parieto-occipital sub-cortex symmetrically. (Figure-1B) Her EEG showed slow Rademecker's complexes. (Figure-2B) She was diagnosed as stage II SSPE and started on interferon therapy. She succumbed over a period of 1 year.

Case-3:

A 10-year-old boy presented with fever for 2 months and multiple episodes of focal seizure for 1 month with behavioral abnormality in the form of agitation and aggressiveness. His vaccination status was partial. His GCS was E2V3M5 with monoplegia of right upper limb. EEG showed intermittent focal spike and wave discharges. (Figure-2c) CSF showed 20 cells (all lymphocytes) with elevated protein and normal sugar with IgM measles titres of 13.5 NTU. MRI brain showed asymmetric T2/FLAIR cortical hyperintense lesions involving the left frontal lobe. (Figure-1C) He was diagnosed as stage II SSPE and treated with interferon therapy and valproate therapy 300mg twice daily dosing. He is presently under follow-up for 5 months and seizure-free with improved GCS.

Case-4:

A 25-year-old male presented with behavioural abnormality for 5 years, jerky movement of left side of body for 3 years,

slowness of activities for 2 years, cognitive impairment for 8 months and progressive difficulty in speaking for 3 months. He was not vaccinated ever. Presently he is bedbound and does not speak on verbal command, but vocalizes with incomprehensible low-volume sound on painful stimulation. His nervous system examination showed presence of primitive reflexes, generalized rigidity, hyper-reflexia, plantar extensors, with mutism. His brain MRI showed generalized cortical atrophic changes with diffuse posterior predominant subcortical T2/FLAIR hyperintense signal changes.(Figure-1D) His EEG showed diffuse delta slowing. His CSF showed 12 cells (all lymphocytes), elevated protein, normal glucose with strong measles IgG titre of 23 NTU. He was diagnosed as stage IV SSPE in akinetic mutism state and treated with interferon, valproate (1 gram twice daily), clonazepam (1g thrice daily), levo-dopa carbidopa (100/25mg thrice daily) and supportive therapy. He succumbed over 2 months.

Case-5:

A 19-year-old boy presented with episodes of repetitive clapping followed by abnormal jerky movement of body with swaying back for 2 years. There was history of scholastic decline for last 1 year. He was fully vaccinated as per his age. His GCS was 15 with presence of stereotypy followed by negative myoclonus. His brain MRI showed right-sided parieto-occipital subcortical hyperintense signal changes. (Figure-1E) His EEG was positive for Rademecker's complexes. His CSF was normal for routine examination but measles IgG index was 1.6. He was diagnosed as stage II SSPE and treated with interferon therapy, clonazepam (0.5mg twice daily) which showed clinical improvement for myoclonus and stereotype over 2 months of follow-up.

Case-6:

A 24-year-girl presented with difficulty in walking in the form of swaying for 2 years, aggressive behavior for 1 and ½ year, with new-onset episodes of falling backward. Her birth and development history was normal. She was vaccination-naïve status. She was admitted in different hospitals and worked-up for autoimmune encephalitis, lupus, vasculitis but was found to be sero-negative. There was no significant family history. Her nervous system examination revealed cerebellar ataxia and negative myoclonus. Her brain MRI showed focal T2/FLAIR parietal gliotic changes.(Figure-1F) Her EEG showed generalized periodic complexes. Her CSF IgG titres were elevated for measles (16 NTU). She was treated with interferon therapy, quetiapine (50 mg daily), clonazepam (0.5mg thrice daily) and vitamin E (400mg twice daily). She was stable at 2 months of follow-up.

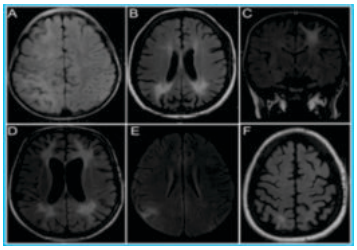

Figure-1: MRI of brain in SSPE patients.

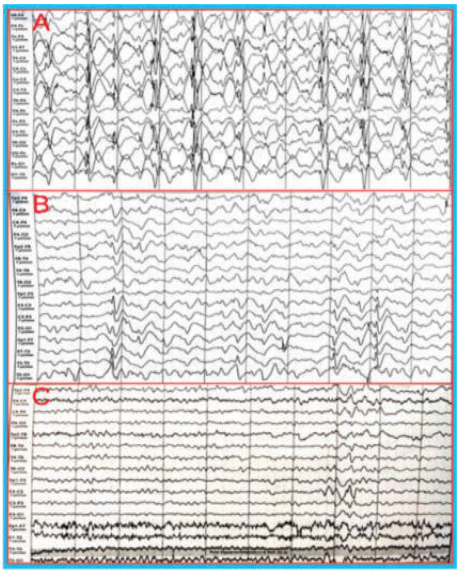

Figure-2: Electroencephalogram in SSPE patients

Table – 1 Clinical, radiological and electroencephalogram profile in SSPE patients (n=6)

Serial Number	Age (years), Sex	Symptom	Duration Stage (S)	EEG	MRI	Out come
1.	15, M	Fever, altered sensorium, GTCS, myoclonus	60 days S-II	T2/FLAIR hyper-intense fronto-parietal cortical lesions of right side	Fast rhythmic periodic high-amplitude generalized discharges	Seziure-free at 6 months follow-up, rest no improvement.
2.	18, F	Cognitive decline, myoclonus	14 months S-II	Symmetric T2/FLAIR hyper-intense subcortical lesions in parieto-occipital	Slow Rademecker's complexes	Died over 1 year
3.	10, M	Fever, focal seizure, behavioural abnormality, altered sensorium	2 months S-II	Asymmetric T2/FLAIR cortical hyperintense lesions involving the left frontal lobe	Intermittent focal spike and wave discharges.	Seizure-free with improved sensorium at 5 months follow-up
4.	25, M	Behavioural abnormality, myoclonus, slowness, cognitve impairment, progressive difficulty in speaking	5 years S-IV	Generalized cortical atrophic changes with diffuse posterior-predominant subcortical T2/FLAIR hyperintense signal changes	Diffuse delta slowing	Died over 2 months.
5.	19, M	Repeated clapping and myoclonus	2 years S-II	Right-sided parieto-occipital subcortical T2/FLAIR hyperintense signal changes.	Rademecker's complexes	Clinical improvement for myoclonus and stereotypy over 2 months of follow-up

6.	24, F	Swaying aggressive behavior and new-onset falls (myoclonus)	2 years S-II	Focal T2/FLAIR parietal gliotic changes	Generalized periodic complexes	Stable at 2 months of follow-up.

Note: M, male; F, female; S, stage; FLAIR, Fluid attenuation inversion recovery sequence; EEG, electroencephalogram; MRI, magnetic resonance imaging.

DISCUSSION

In this case series, we tried to describe the different observed neurological manifestations of SSPE patients. (Table-1) The most prominent characteristics in these cases was the presence of myoclonus and EEG changes. SSPE is an eventually progressive neuro-inflammatory disorder of brain affecting both white and grey matter with seemingly high morbidity and mortality.

The clinical spectrum includes cognitive impairment, altered sensorium, behavioural/mental abnormalities, movement disorders (myoclonus, chorea, dystonia, parkinsonism), ataxia, abnormal posturing (decerebrate/decorticate), loss of all cortical functions, akinetic mutism and coma.[6] A plethora of movement disorders in combination can be encountered in SSPE.[7] In this case series, we highlighted the occurrence of SSPE in the form of meningoencephalitis, dementia with myoclonus, psychosis with myoclonus, fulminant akinetic mutism, stereotypy with myoclonus and ataxia with myoclonus. Previous studies have emphasized on the importance of movement disorders in the recognition of SSPE.[8,9,10,11] Epilepsy is also an important feature of SSPE recognition.[12]

Autoimmune encephalitis, progressive myoclonic epilepsy, progressive myoclonic encephalopathies and neuro degenerative disorders are important differentials. Treatment includes intra-thecal interferon alpha-2a, Isoprinosine and ribavirin, with supportive therapy (clonazepam, valproate, levetiracetam and oxcarbamazepine for myoclonus).[13] Vaccination is known to prevent SSPE, but there are a few patient reports despite vaccination.[14]

Despite the best possible therapies available to curb morbidity in SSPE, there is presently no drug to hault the disease progression or prevent mortality.

CONCLUSION

SSPE is an established, yet an emerging tropical inflammatory disease with protean neurological manifestations. The exact aetio-immunopathogenesis is not well explored. Myoclonus is an important entity in SSPE. The expanding clinical spectrum of SSPE lacks therapeutic exploration at present. A greater awareness of vivid manifestations of SSPE can lead to early diagnosis.

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