Case Report

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Subacute Sclerosing Panencephalitis with Subclinical Infection

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Abstract

Subacute Sclerosing Panencephalitis (SSPE) is a chronic complication of measles. It is a neurodegenerative disorder characterized by cognitive and memory deterioration, behaviour abnormalities, involuntary movements and repetitive myoclonic jerks and a steady motor decline. We report a case of a 7-year-old girl with subacute sclerosing panencephalitis presenting with myoclonic jerks, regression of motor milestones and speech. The child was not immunised for measles. Magnetic resonance imaging revealed multiple variable-sized ill-defined T2W and FLAIR hyperintense areas are seen involving the white matter of the bilateral fronto-parietal lobes. Electroencephalograph findings and CSF analysis confirmed the diagnosis of subacute sclerosing panencephalitis.

Keywords: Subacute Sclerosing Panencephalitis, Neurodegenerative, Myoclonic Jerks

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Introduction

Subacute Sclerosing Panencephalitis (SSPE) is a neurodegenerative disorder due to a persistent infection with a mutated wild measles virus that is harboured intracellularly in the central nervous system for several years.[1,2] After 7-10 years the virus regains virulence and attacks the cells in the central nervous system resulting in inflammation and cell death, leading to a neurodegenerative process. Measles at an early age favours the development of SSPE. Measles is still a common communicable disease, particularly in Africa and Asia. As per the recent WHO report, 7 million people were found to be affected with measles in 2016.[3–5] Approximately, 38% of Indian children fail to receive the basic immunization in the first year of life.[6] Approximately 50% of the global measles-associated deaths occur in India.[7,8] The pathogenesis of SSPE remains difficult to interpret, factors involved are defective measles virus and interaction with a defective or immature immune system. The virus isolated from brain tissue of patients with SSPE lacks the matrix or M protein one of the 6 structural proteins. Clinical manifestation begins insidiously 7-13 years after primary measles infection.

We discuss a 7-year old girl with SSPE presenting with myoclonic jerks, regression of motor milestones and speech. The diagnosis was confirmed by elevated anti-measles antibodies titres in CSF and periodic complexes on an electroencephalogram.

Case Report

A 7-year-old girl born of the non-consanguineous marriage, presented with myoclonic jerks since 1year and regression of motor milestones and speech since 1month. The patient developed jerky movements of head each occurring at an interval of 5-10 mins. This lasted for a year which gradually involved upper limbs and lower limbs for one month. There was a regression of motor-milestones and speech. Currently, she can stand with support and can speak 2-3 word phrases. These abnormal movements resulted in clumsiness, incoordination and difficulty in performing daily activities. There was no history of visual or hearing disturbance. She had not been immunised for measles. Birth history was normal. Development of the child was normal till 6 years of age.

On examination, she was conscious, oriented to person. She has slurred speech with small phrases comprising of 2-3 words. She has a periodic brief, sudden, myoclonic jerks resulting in imbalance and frequent falls. Sensory, motor system and cranial nerve examination were normal. Fundoscopy was normal.

Electroencephalogram showed large-amplitude periodic complexes, these periodic complexes repeat at fairly regular 4–10 second intervals and have 1:1 relationship with myoclonic jerks [Figure 1], magnetic resonance imaging (MRI) showed multiple variable-sized ill-defined T2W and FLAIR hyperintense areas are seen involving the white matter of the bilateral fronto-parietal lobes [Figure 2], No restriction on diffusion-weighted images or blooming on gradient images is noted. No enhancement is seen in the post-contrast study. Anti-measles antibodies titres were elevated in both blood and CSF [Table 1]. With these findings a diagnosis of SSPE is confirmed most likely Stage II. Tablet valproic acid and Tablet Clobazam was started to control myoclonic jerks. Occupational therapy was started to aid the child in feeding and Physiotherapy was started to prevent contractures as the child was bedridden, immunization advice was given and she was discharged on oral Valproic acid (36mg/kg/day) in two divided doses and Tablet Clobazam (10mg/day). Other drugs like Isoprinosine, interferons are not prescribed due to financial constraints.

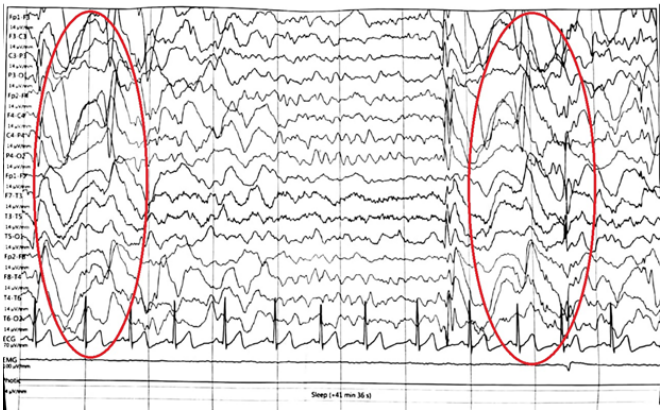

Figure 1: EEG showing periodic complexes

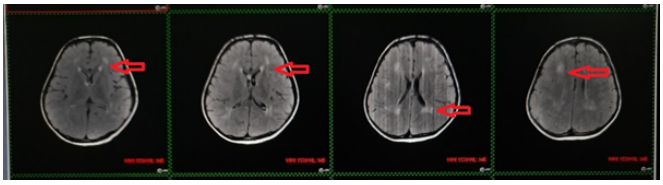

Figure 2: MRI showing hyper-intense areas involving white matter.

Table 1:

Investigation	Observed value	Unit	Biological reference interval
Serum IgG measles	10250	U/ml	
CSF IgG measles	15000	U/ml	
Serum total IgG	2040	mg/dl	700-1600
CSF total IgG	16.3	mg/dl	0-3.4
CSF/serum Quotient reference	5.8		Normal <1.3 Equivocal 1.3-1.5 Positive >1.5

Discussion

We discuss a case of SSPE with myoclonic jerks and white matter hyperintensities of bilateral fronto-parietal lobes classifying it as a stage 2 disease. The clinical course of the disease can be classified into 4 stages. The initial phase (stage 1) is characterised by irritability, reduced attention span, poor scholastic performance and temper tantrums. In the 2^{nd} stage, involuntary movements and repetitive myoclonic jerks appear but the consciousness is maintained. In the 3^{rd} stage, involuntary movements disappear and are replaced by choreoathetosis, immobility, dystonia and lead pipe rigidity due to involvement of basal ganglia. The sensorium deteriorates into dementia, stupor and then coma. In the 4^{th} stage, vital centres located in the brainstem get involved and soon death ensues. In acute fulminant SSPE the disease progression is rapidly leading to death within three months of the diagnosis. In the series of Risk and Haddad, approximately 10% of patients had such a fulminant course.[8–10] In acute fulminant SSPE various stages of the disease cannot be recognised. Ocular and visual manifestations are reported in 10%–50% of patients, which include cortical blindness, chorioretinitis, and optic atrophy.[11] Visual symptoms usually occur along with neurological manifestations but they may precede neurological manifestation by several years.[12,13] Park et al, in a patient presenting with chorioretinitis, have demonstrated numerous filamentous, microtubular, and intranuclear viral inclusions in the nuclear layers of retina consistent with the measles virus.[14]

Subacute Sclerosing Panencephalitis is diagnosed on the basis of typical clinical features and at least one of the following supporting findings 1. Presence of periodic complexes in electroencephalograph, 2.Elevated anti-measles IgG in CSF and serum, 3.Typical histologic features in brain biopsy specimen and/or isolation of virus or viral antigen from brain tissue. There is no definitive cure for SSPE although many drugs have been tried with conflicting results. Amantadine is an anti-RNA agent, very well absorbed from the gastrointestinal tract, and crosses the blood-brain barrier, but the response to treatment

in few cases of SSPE is disappointing.[9] In isolated reports, interferon beta plus Inosiplex intravenous immunoglobulin plasmapharesis, and corticosteroids have been tried with variable results.[10,11] The average survival is 1-3 years since the onset of symptoms. Incidence of SSPE has decreased in nations with good measles vaccination coverage.

SSPE can have an atypical presentation with generalised choreoathetosis and bilateral putamenal hyperintensities in stage 1 of the disease. Choreoathetosis if present usually manifests in advanced stages of the disease along with rigidity, motor and cognitive impairment. Radiographic findings are a normal MRI or subtle, multifocal subcortical changes in stage 1; periventricular and subcortical white matter involvement in stage 2; cortical, subcortical, periventricular, and corpus callosum involvement and brain atrophy in stage 3; cortical, subcortical, brain stem, and cerebellar involvement and brain atrophy in stage IV of SSPE.

Measles vaccination reduces the risk of measles infection and SSPE.[1] Because infants infected with measles are at highest risk for SSPE, it is important to protect them by vaccination and herd immunity.[3] Some cases have no known history of febrile rash illness, but the SSPE diagnosis indicates a subclinical or mild form of infection.[1] SSPE diagnosis during pregnancy has been reported in the literature, suggesting that the altered immune system during pregnancy might permit the virus, if present, to replicate in the central nervous system[4]. SSPE is generally a simple diagnosis to make, requiring only CSF antibody testing that can be performed in public health and clinical laboratories.[3]

Conclusion

In conclusion, SSPE which is a chronic complication of measles infection is a devastating neurodegenerative condition, the clinical presentation of our case was with myoclonic jerks, regression of speech and motor milestones. The child was not immunised for measles, she had no evidence of prior measles infection. CSF revealed elevated anti-measles antibodies titres and EEG showed periodic complexes thus confirming the diagnosis of SSPE. Management of SSPE is primarily supportive. Isoprinosine clinical trials with or without interferon use suggest significant benefit. Clobazam and valproic acid are of significant benefit in the control of myoclonic jerks in the early stages of illness.

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