

Subacute Sclerosing Panencephalitis

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Summary:

Subacute sclerosing panencephalitis (SSPE) is chronic progressive encephalitis of childhood and young adolescent due to persistent measles virus infection. This case illustrates a 14 year old girl presented with short history of intellectual decline, abnormal behavior, myoclonus and altered consciousness with suggestive neuroimaging mimicking metachromatic leucodystrophy. Subsequently she was

diagnosed to be a case of Subacute sclerosing panencephalitis (SSPE) on the basis of Electroencephalography (EEG) and Cerebrospinal fluid(CSF) measles antibody titer.

KeyWords: *Subacute sclerosing panencephalitis, Measles, Metachromatic leucodystrophy.*

(J Bangladesh Coll Phys Surg 2019; 37: 205-208)

DOI: <http://dx.doi.org/10.3329/jbcps.v37i4.43352>

Background:

Subacute sclerosing panencephalitis (SSPE) was first described by Dawson in 1933-1934 as sub acute inclusion encephalitis. It is a rare progressive, invariably fatal long term complication of measles infection. The latency period between acute measles and first symptoms of SSPE is usually

4 to 10 years but ranges from 1 month to 27 years.¹ It is characterized 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.² Although SSPE affects mostly children younger than 12 years, interestingly, there is a considerable increase in the number of adult cases of SSPE.^{3,4} It has a progressive and fulminant course that results in death within 5 years of onset.⁵ 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 atypical presentation along with nonspecific laboratory or electrophysiological values. We describe a young girl with short history of intellectual decline, myoclonic jerks, altered consciousness with neuroradiological

findings mimicking metachromatic leucodystrophy the unusual association of SSPE.

Case Presentation:

14 year old girl, born of consanguinity with normal birth and development, was a student of class IV, hailing from Norshingdhi, presenting with the complaints of abnormal behaviour for three months, involuntary movements of limbs for one and half months and altered consciousness for 14 days. She had low grade fever for 2 months which was never documented. At first, her behavioral disturbances started with irrelevant talk, gradually became aggressive and violent, deteriorating in academic performance, she left schooling due to inattentiveness, inability to remember her studies and reduced activities in her daily life. Few days later, she began to have cognitive impairment; she could not recognize her family members except her mother. She then developed rapid, sudden myoclonic jerks of all limbs persisting for few seconds, increased in frequency for one and half months. There was no history of generalized seizures, limb weakness, gait abnormalities, behavioural problems or altered sensorium. It was not associated with tongue bite, bowel bladder incontinence, loss of consciousness, post ictal confusion or headache and vomiting. The patient developed altered consciousness for last 14 days and became bed ridden. There was no history of cough, hemoptysis, jaundice and contact with tuberculosis patient. Also no previous event of birth trauma or head injury. Family history was unremarkable. There was no previous history of measles infection. Vaccination status of measles was doubtful.

General physical examinations revealed that patient was ill-looking, disoriented and unable to co-operate. She had repeated myoclonic jerks involving all four limbs. Her vital parameters were normal.

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Received: 1 April, 2018

Accepted: 8 June, 2019

On neurological examination, her state of consciousness according to Glasgow Coma Scale is E3+V3+M4=10/15, disoriented with irrelevant talks and there were no signs of meningeal irritation. Her cranial nerves could not be evaluated properly, fundoscopy was normal. Motor system examination showed increased tone, exaggerated tendon reflexes with bilateral planter extensor. Sensory and cerebellar functions could not be elicited. Slit lamp examination of eyes revealed no KF ring. Examination of other systems revealed no abnormality.

Investigations:

The routine blood examinations revealed no abnormality. Liver Function Test is normal. 24 hour Urinary copper <20.0mcg/l (>100 mcg/l in Wilson's disease), concentration of ceruloplasmin 29 mg/dl (20-35 mg/dl). MRI brain revealed T1WI iso, T2WI and FLAIR hyperintense irregular lesions in both frontal and periventricular region. No restricted diffusion was seen in DWI. Lesions were suggestive of metachromatic leucodystrophy at both frontal and periventricular region.(Figure-1)

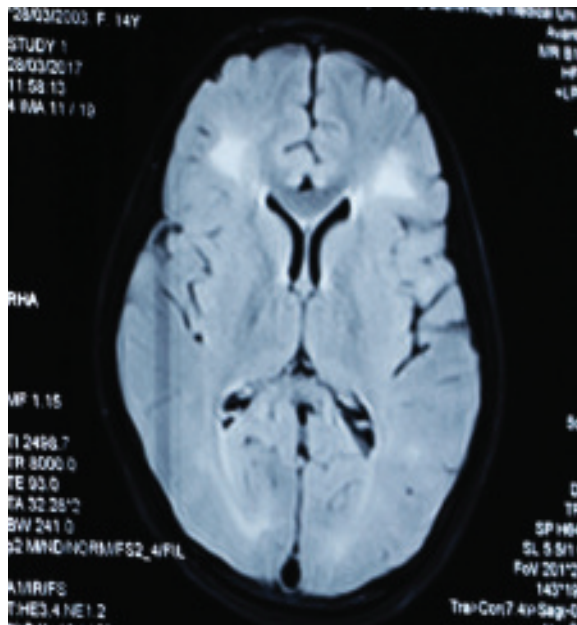


Fig.-1: MRI of Brain with contrast showing metachromatic leucodystrophy at both frontal and periventricular region.

EEG revealed frequent periodic bursts of spikes and slow waves from the background at regular intervals, suggestive of Subacute Sclerosing Panencephalitis. (Figure-2)



Fig.-2: EEG showing periodic outbursts of slow waves, suggestive of Subacute Sclerosing Panencephalitis.

Cerebrospinal fluid(CSF) studies showed that colour is watery and clear, CSF sugar was 89 mg/dL; protein was 75.10 mg/dL with acellular back ground. CSF Gram stain, Ziehl-Neelsen stain, and culture for pyogenic, tubercular and fungal organisms were negative. Gene Xpert for detection of Mycobacterium tuberculosis was negative. CSF measles immunoglobulin G antibody was positive in high titre. Screening for HIV, neurosyphilis, hepatitis B and C were negative. Brain biopsy was not done as they denied such invasive investigations.

Treatment

No specific treatment was given. Only supportive treatment as airway support, maintenance of circulation by intravenous fluid, hydration and nutrition maintenance by nasogastric tube feeding. Care of bladder-by catheterization, care of bowel by laxative for constipation, care of skin and oral hygiene. Anticonvulsant: Sodium valproate was given for her involuntary movement and Clonazepam was used for sedation.

Outcome And Follow-Up

The patient's condition remained unchanged on symptomatic treatment and patient was discharged on request. Eventually, her condition was progressively deteriorated.

Discussion:

Diagnostic criteria of SSPE are

1. Clinical Progressive, subacute mental deterioration with typical signs like myoclonus
2. EEG Periodic, stereotyped, high voltage discharges
3. Cerebrospinal fluid :Increased gammaglobulin or oligoclonal pattern
4. Measles antibodies: Increased titre in serum (>1:256) and/or cerebrospinal fluid (>1:4)
5. Brain biopsy suggestive of panencephalitis

Definitive: criteria 5 with three more criteria; probable: three of the five criteria.⁶

The initial symptoms are usually subtle and include mild intellectual deterioration and behavioral changes without any apparent neurological signs or findings. Parents and teachers may notice progressive deterioration in scholastic performance. As disease advances non-specific manifestations evolve into disturbances in motor function and development of periodic stereotyped myoclonic jerks. It initially involve the head and subsequently trunk and limbs may not be obvious early in the disease but can be elicited by the patient standing with feet together and arms held forward and then watching for periodic dropping of the head, neck, trunk, or arm; these are often concomitant with contraction of facial musculature and slow eye blinks, it does not interfere with consciousness. Patients may, frequently, develop pyramidal and extrapyramidal signs. Myoclonus can present as a difficulty in gait, periodic dropping of the head, and falling. Few patients may develop ataxia, dystonia, and dyskinesia. Generalized tonic-clonic seizures and partial seizures may also occur.⁶⁻⁸ In advanced stages of the disease, patients become quadriparetic, spasticity increases, and myoclonus may decrease or disappear. There is autonomic failure with loss of thermoregulation leading to marked temperature fluctuations. There is progressive deterioration of sensorium to a comatose state and ultimately the patient becomes vegetative. Decerebrate and decorticate rigidity appear, breathing becomes noisy and irregular. At this stage, patients frequently die due to hyperpyrexia, cardiovascular collapse, or hypothalamic disturbances.⁹ CSF examination is usually normal. Frequently, it is acellular with normal or a mildly raised protein concentration. The most remarkable

feature of CSF examination is a markedly raised gammaglobulin level, which is usually greater than 20% of total cerebrospinal fluid protein. Because of the large increase of intrathecal synthesis of IgG, CSF IgG concentration ranges from 10–54 µg/dl compared with 5–10 µg/dl in normal children.^{10,11} Reverse transcriptase polymerase chain reaction technique and brain biopsy might be useful in confirming the diagnosis in SSPE with negative CSF findings.¹²

Our patient presented with the complaints of abnormal behavior, myoclonus and cognitive impairment. Once myoclonus is evident the clinical diagnosis is seldom a problem. However, subtle behavioural changes at an early stage of disease are frequently missed by relatives. Many such patients are often treated by a psychiatrist at this stage. In some cases myoclonus is not present; atonia may be present but can be overlooked.¹³ MRI is more sensitive in detecting white matter abnormalities. In the early stages of the disease, cerebral MRI shows lesions usually involving parieto-occipital cortico-subcortical regions asymmetrically. In time, symmetric periventricular white matter changes become more prominent. However, more recently Aydin et al.¹⁴ described that MRI findings could be normal with SSPE. The diagnosis is based upon typical cerebrospinal fluid changes and a characteristic electroencephalography pattern. The diagnosis of SSPE can be reliably established if patient fulfils three of the five criteria given by Dyken.⁶

Conclusion:

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. Diagnosis is especially problematic in adult patients with SSPE; differential diagnoses are also different. Treatments available are very costly and are available only at a few centers in the world. Moreover, these treatments are not curative and only help in buying time for these patients.

Conflict of interest: None.

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