Abstract: Subacute sclerosing panencephalitis (SSPE) is a rare chronic, progressive demyelinating disease of the Central nervous system (CNS) associated with a chronic non permissive infection of brain tissue with measles virus. The frequency has been estimated at 1 in 100,000 to 500,000 measles cases. We report a 13 year old girl who presented with rapid deterioration of cognition and negative myoclonus involving lower limb and trunk. There is no history of measles or immunisation for measles in the past. The diagnosis of subacute sclerosing pan encephalitis was confirmed provisionally with clinical picture and Electroencephalogram (EEG) studies and later confirmed with cerebrospinal fluid (CSF) studies. We report this case in view of its rare incidence.

Keyword: SSPE, Measles, Negative myoclonus, EEG, CSF antimeasles antibody titre

INTRODUCTION
Sub acute sclerosing panencephalitis (SSPE) is a slowly progressing fatal inflammatory disease of the central nervous system, developing as a sequel to early childhood measles infection\(^1\). Following the original measles infection, the altered intracellular virus remains dormant, only to manifest as SSPE during childhood and adolescence\(^2\). Rarely it may also occur secondarily to measles vaccination. We present a case of sub acute sclerosing pan encephalitis in which there is no previous history of measles or other exanthematous illness. There is also no history for vaccination for measles.

CASE REPORT
13 year old girl presented in the medical outpatient department with complains of progressive deterioration in cognitive function like poor scholastic performance and difficulty in understanding and carry out specific tasks. The cognitive decline was rapid over the past few months. There was also history of involuntary movements in the form of jerks which made her difficult in maintaining her equilibrium while standing or sitting upright for few seconds. History of repeated falls was present. There was no history of seizures or visual, hearing, sphincter disturbances. There was no history of measles or any exanthematous illness in the past. Apart from
oral polio vaccine (OPV), there is no history of immunisation including vaccination for measles. The patient is the only child born to second degree consanguineous parents. On examination she had persistent negative myoclonus in the form of shock like involuntary movement involving trunk and lower limb muscles every few seconds.

Ataxic gait was present. IQ testing done shows moderate mental retardation. Dysarthria was present. There is no weakness of limbs or wasting of muscles or muscle twitching. Fundus examination was normal, no evidence of chorioretinitis or optic atrophy. Her vitals were stable. Routine blood and urine investigation were normal. Computerised Tomography (CT) and Magnetic resonance imaging (MRI) brain showed normal study. Electroencephalogram was taken which shows long interval periodic complexes consisted of bilaterally synchronous and symmetrical high amplitude delta waves repeating every 5 sec with one to one relationship of the negative myoclonic jerks to EEG complexes. Cerebrospinal fluid (CSF) studies were done which showed raised protein levels mainly globulin fraction. CSF sample of this patient was sent to Department of Neurovirology, National Institute of Mental Health And Neuro Sciences (NIMHANS), Bangalore to test for IgG antimeasles antibody. The antimeasles antibody titre was significantly positive (> 1:165) with ELISA. Thus the diagnosis of subacute sclerosing panencephalitis was attained since this patient satisfies four of five criteria put forth by Dyken\textsuperscript{1}. Other differential diagnoses of childhood cognitive deterioration and movement disorders such as Wilson’s disease, childhood SLE, and progressive myoclonic epilepsy (PME) appear unlikely in view of the lack of collaborative clinical, laboratory, and imaging findings. The patient was started on sodium valproate and clonazepam for controlling myoclonus.

There was substantial reduction in myoclonus after starting on anticonvulsants.

**DISCUSSION**

Measles virus causes a wide spectrum of neurologic disease ranging from subclinical involvement and acute measles encephalitis (Post infectious Encephalomyelitis) within days after the onset of a measles exanthem, to chronic subacute sclerosing panencephalitis occurring years after measles infection\textsuperscript{3}. SSPE, also called Dawson disease or subacute inclusion body encephalitis, is a disease caused by a defective measles virus. The relationship between measles and SSPE has been firmly established and measles virus has been isolated from cultured brain cells of patients with SSPE\textsuperscript{4}. Patients with SSPE usually attain measles.
within 2 years of age. The usual incubation period of SSPE following an overt clinical measles infection is 6 to 8 years. Apart from classical clinical presentation, a chronic very slowly progressive form, a fulminant form leading to early death, a stuttering form with remission and relapses and prolonged survival with substantial spontaneous remission have been observed. Recent molecular genetic studies proved that the defective expression of either the matrix (M), the fusion (F), or the hemagglutination (H) proteins may lead to persistence of measles virus in the brain cells under conditions not allowing identification by immune surveillance systems. The altered virus called SSPE virus survives within neurons and glia, replicating by fusion and passed from cell to cell by transsynaptic transmission resulting in cell death, inflammation and gliosis. The main features of the pathology are of a subacute encephalitis affecting grey and white matter to a variable degree and accompanied by diffuse, sometimes marked gliosis. Histologically, the worst affected parts of the cerebral cortex are usually the parietal and temporal lobes, where there is destruction and degeneration of neurones, accumulation of macrophages and chronic inflammatory cells and prominent perivascular cuffing by plasma cells, lymphocytes and other mononuclear cells. In affected areas there is usually marked gliosis. Cowdry type A, Cowdry type B and neurofibrillary tangles are seen diffusely in neurons and oligodendroglia in patients with fatal disease. The introduction of measles vaccination under mass immunisation programs has led to a significant fall in the incidence of measles and SSPE throughout the world. Incidence rates vary from 0.04/million/year in Japan to 2.2 million/year in Middle East countries. The incidence of SSPE declined by at least 90 percent in countries that have practiced widespread immunization with measles vaccine but SSPE still continues to occur sporadically in India. Indeed Radhakrishnan et al observed that with strong coverage of measles vaccination there was substantial fall in SSPE incidence in India between 1996 and 1998. Based on a study of 72 retrospectively collected cases of SSPE through an immunological laboratory at Christian medical college, Vellore, Tamilnadu showed the calculated incidence in India is 2.14/million/year. Among measles cases the frequency has been estimated at 1 in 100,000–500,000 measles cases. Incidence is more among boys, children from lower economic status and those who acquire measles at a lower age. Most frequent age group affected is between 5 to 15 years. Adult onset SSPE has mean age of onset around 21 years. The usual presenting features are cognitive decline and myoclonic jerks. There may be subtle behavioural changes. School performance may deteriorate. The children may appear confused or forgetful. Myoclonic jerks usually involve the head and subsequently the trunk and extremities and typically occur every 5 to 10 seconds and are one of the unique clinical features of the disease. Visual and ocular manifestations include cortical blindness due to diffuse white matter lesions in parietooccipital cortex of the brain, chorioretinitis, papillitis, papilloedema and optic atrophy. Generalised seizures resistant to commonly used anti epileptic medications may occur. Seizures can be disease revealing seizures, occurring before myoclonus or cognitive decline. Our patient presented with features of negative myoclonus which is defined as interruption of tonic muscular activity, time locked to a spike.
on EEG without evidence of antecedent myoclonus. Clinically it appears like a shock like involuntary jerky movement due to sudden brief interruption of muscular activity. Myoclonus specifies the shock-like contraction(s) of a group of muscles, irregular in rhythm and amplitude, and asynchronous, asymmetrical in distribution. Types of myoclonus include: Myoclonus simplex Patients with idiopathic epilepsy may complain of a localized myoclonic jerk or a short burst of myoclonic jerks, occurring particularly on awakening and on the day or two preceding a major generalized seizure, after which these movements cease. One-sided myoclonic jerks are the dominant feature of benign epilepsy with rolandic spikes Diffuse Myoclonus (Myoclonus Multiplex, or Polymyoclonus) Myoclonic jerks involving the muscles diffusely, particularly those of the lower face and proximal segments of the limbs, and the myoclonus persisted for many years, being absent only during sleep. No other neurologic abnormalities accompanied the movement abnormality. Essential Myoclonus appears first in childhood and is of unknown etiology. The myoclonus takes the form of irregular twitches of one or another part of the body, involving groups of muscles, single muscles, or even a portion of a muscle producing abnormal movements like flexion of the arm, jerking backward and forward of head and curving of the trunk Myoclonic Epilepsy Can occur in two forms; a benign idiopathic form called juvenile myoclonic epilepsy or a more serious form where there is remarkable sensitivity of the myoclonus to stimuli of all sorts. Intention, or Action, Myoclonus (Postanoxic) Occurring in a patient who were recovering from hypoxic encephalopathy, these irregular myoclonic jerks occur only during target directed fast (ballistic) movements. Always associated with cerebellar ataxia. Spinal, or Segmental, Myoclonus A repetitive flexion extension myoclonus of the torso aggravated by stretching or action; it has been attributed, on the grounds of its electrophysiologic features, to a spinal origin. Other common clinical features of SSPE are speech disturbance, ataxia and sphincter disturbances. Rarely SSPE may present as extrapyramidal symptoms, Parkinsonian like features, behavioral changes like wandering, behaviour, irritability, adamant behaviour, catatonia. The disease characteristically progresses through the stages of cerebral dysfunction, motor and convulsive phenomenon and deterioration in the state of mute, static and comatose state. At the time of presentation our patient is in stage II of modified Jabbour clinical staging of SSPE. Modified Jabbour clinical staging of SSPE Stage1: Cognitive deterioration and behavioural changes Stage2: Myoclonic jerks, choreoathetosis and gait disturbance Stage3: Decerebrate and decorticate posturing Stage4: Bedridden, flexion posturing of extremities and mutism EEG is highly characteristic and disease specific of all EEG patterns available. The EEG picture is characterised by periodic complexes consisting of bilaterally symmetrical, synchronous, high voltage (200–500 mv) bursts of polyphasic, stereotyped delta waves. Waveforms remain identical in any given lead. These periodic complexes repeat at fairly regular 4–10 second intervals and have 1:1 relationship with myoclonic jerks. CSF may show markedly raised gamma globulin level greater than 20% of total CSF protein. Raised Anti measles antibody titre of 1:256 or greater in serum
1:4 Or greater in CSF is considered to be diagnostic of SSPE. CT and MRI brain is usually non specific. In our patient MRI brain showed normal study.

**Dyken’s diagnostic criteria of SSPE**

- Inexorable cognitive decline and stereotyped myoclonic jerks
- Generalised long-interval periodic complexes in the EEG
- Elevated CSF globulin levels
- Elevated CSF measles antibody titres

Typical histological findings in brain biopsy or autopsy Diagnosis of SSPE requires at least 3 of the above 5 criteria to be fulfilled. Our patient satisfies 4 out of 5 criteria and hence the diagnosis of SSPE is established. Till today there is no treatment which can substantially alter the course of the disease. A combination of oral Isoprinosine and intraventricular interferon alpha appears to influence the course of the disease. But there was no large randomised trial to prove the efficacy of those drugs. Anti-convulsant like clonazepam and sodium valproate is helpful in controlling the myoclonus. SSPE has a relentlessly progressive course resulting in death within 1-3 years after diagnosis. Our patient was started on clonazepam and sodium valproate for controlling negative myoclonus. The patient had substantial improvement with significant reduction in myoclonic jerks.

**References.**


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