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# Subacute sclerosing panecpehaltitis: A rare complication of measles virus

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## Abstract

Subacute Sclerosing Panencephalitis (SSPE) is very rare and fatal progressive disease of the central nervous system caused by the measles virus. It occurs due to defective M protein of the measles virus. It mostly affects children and sometimes young adults. Due to its variable clinical presentation it is often challenging to diagnose SSPE. Clinically it presents as chorioretinits, behavioral changes, cognitive impairment, myoclonic jerks and vision abnormalities. MRI, electroencephalogram and CSF studies helps in diagnosis of SSPE but strong clinical suspicion should be there. In developing countries like India where vaccination is not universally received by all children, measles infection is still endemic. Previous studies have shown that measles is more common in males compared to females.

## Keywords

Subacute sclerosing panencephelitis; SSPE; measles.

## Introduction

Subacute sclerosing panencephalitis is an inflammatory degenerative disease which is preceded by distant past or early life history of measles. But often patient do not have memory of primary measles infection. Rarely, measles immunization can be the cause of SSPE in completely normal children. It has latency period of 4 to 10 years between acute episode of measles and first symptom of SSPE but it can range from 1 month to 27 years. First described in 1993, as inclusion body encephalitis with help of brain biopsies [1]. Dyken has given definitive criteria for diagnosis of SSPE which include (a) clinical presentation, (b) slow wave complexes on EEG, (c) elevated immunoglobulin in CSF, (d) elevated measles antibody and (e) classic brain biopsy findings. It has very fulmitant course and death usually occurs within 5 years of onset [2]. We describe a young adult with changes in behavior and cognitive function.

## Case Presentation

A 22 year old male engineering college student born in low socioeconomic status presented to hospital with chief complain of diplopia, progressive left lower limb weakness that started 2 weeks earlier and change in behavior. Patient became aggressive, goes out bed and try to run out of home which was reported by his father and he was not aware of this changes. Prior to development of this he was in usual state of health with normal cognition. He had frequent falls and decline in cognitive functions. This leads to massive decline in his college performance. Since last 5 days he complains of difficulty in walking due to characteristic jerky movement. Patient had history of fever but exact record was not found. He was admitted to hospital for further evaluation. But in the meantime he developed very high fever and tonic clonic seizure which were treated by sodium valproate. On the third day he collapsed due to development of ventricular tachycardia which was reversed by DC shock. He was intubated and kept on ventilator. Patient developed hyperkalemia and hyponatremia which were treated with appropriate fluids. On fourth day he developed generalized tonic clonic seizure and loss of consciousness which were treated by inj. thiopental. Cognitive changes include loss of recent memory and reduced attention. His speech was intact and there were no delusions or hallucinations. There was no history of rash, generalized weakness, or loss of vision.

At time of his first visit, general examination revealed patient was conscious and normal orientation but with impaired comprehension. He was able to follow simple commands and both pupils were normal in size and reactive to light. There was lower limb weakness with muscle strength of 1/5. He had upward gaze palsy and bilateral lower limb ataxia. All signs of meningeal irritation like nuchal rigidity, brudzinski sign and kernig's sign were absent. His vitals were normal. Examination of cardiovascular, respiratory and gastrointestinal systems were normal. Fundus examination was normal. Motor examination shows bilateral lower limb spasticity with increased deep tendon reflexes. Sensory examination of pain, temperature, pressure and proprioception were intact in whole body. There were no signs of autonomic dysfunction like postural hypotension, loss of bowel and bladder control or loss of thermoregulation.

### Investigations

All blood examinations were turned out to be normal which are listed below

1) Serum ANA profile,

2) Anti brucella IgG and IgM,

3) Autoimmune encephalitis profile,

4) Neuromyleitis optica antibodies- Aqauporin 4 and MOG antibody,

5) Serum Cryptococcus antigen.

MRI shows diffuse hyper intensity in bilateral thalami, postero basal frontal and anteromedial temporal lobe, hippocampus, more on left side. MRI is shown in figure below:

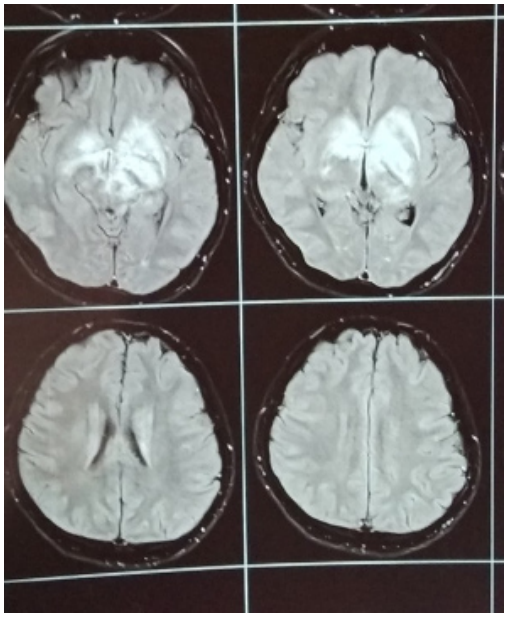

**Figure 1**

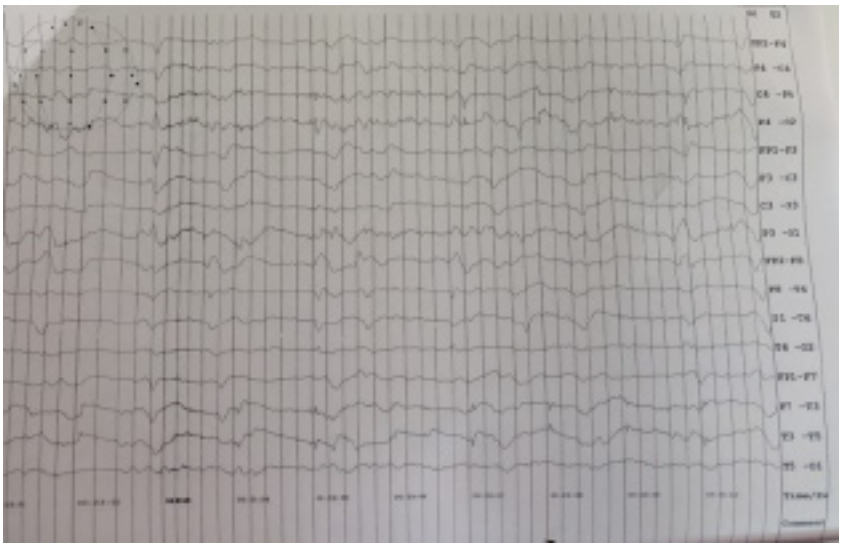

**Figure 2**

CSF studies shows glucose levels of 91 mg/dl, protein level of 55 mg/dl. CSF India ink, gram stain, ZN stain doesn't reveal any organism, and also culture for pyogenic, tubercular and fungal organisms were negative.

| | |
|---|---|
| Japanese encepahalitis virus RT-PCR | Negative |
| Herpes Simplex PCR | Negative |
| Cryptococcus PCR | Negative |
| Measles Antibody IgG | >300 AM/ML (positive if >16.5) |
| Measles Antibody IgM | <0.5 index (positive if >1.1) |
| Adenosine deaminase | 2.1(normal if <10) |

CSF was negative for RT-PCR of herpes simplex virus, Japanese encephalitis virus. CSF has shown high titers of measles antibody. Autoimmune encephalitis panel was also negative. HIV, Hepatitis and Syphilis were negative. EEG shows triphasic waves and slow wave complexes. EEG is shown in (Figure 2). Serum ANA profile and brucella antibodies were negative.

## Treatment and Outcome

The treatment of SSPE is still under research. Management is based on disease modifying agents and symptomatic treatment. Intraventricular or intrathecal interferon and isoprinosine are disease modifying agents. Dose of Isoprinosine is 100 mg/kg/day. Isoprinosine can cause hyperuricemia and renal stones so uric acid levels should be monitored. Dose of natural interferon alfa is 100,000 unit/$m^2$ of body surface area which is increased to 1 million unit/$m^2$ body surface area given five days a week in whole of 6 week regimen. The doses can be repeated upto six times at 2-6 months interval. Today combined regimen of Isoprinosine and interferon alfa is more popular. But due to long duration and expensive treatment, which our patient could not afford only symptomatic treatment was given. Phenytoin, mannitol and sodium valproate were given for seizure control.

Reports have shown that isoprenazine treatment can only prolong the survival [3]. Many different regimens of antivirals and immunomodulators are still under research.

## Discussion

The complications of measles virus infection include [1] Giant cell pneumonitis in lungs mostly in immunocompromised individuals [2] Measles inclusion body encephalitis (MIBE), occurs in patients with defective cellular immunity after acquiring measles infection within 3–6 months [3]. SSPE is a chronic slowly progressive neurodegenerative disease caused by persistent mutant measles virus in neurons and oligodendrocytes. It commonly occurs within 2–10 years after primary infection [4].

SSPE is slow virus disease caused my mutant envelope proteins like M, F and H [1], which are needed for virus budding. Cell mediated immune response will not be able to able to kill virus because no antigen presentation occurs on surface of viral cells. The defective virus thus cannot able to bud out and hence slowly grows into the brain even in the presence of normal immune response. SSPE virus is more neurotropic than normal ones.

In spite of slow course of disease, our patient has developed very rapid deterioration within 6 weeks. Also, he had undergone numerous tests for diagnosis with his previous doctors and all turned out to be in vain. Lack of clinical suspicion has led to late diagnosis. This late diagnosis makes SSPE even more fatal.

Our aim by this case report is to guide treating physician is to consider SSPE in their differential diagnosis because of its atypical and varied presentation. This will help to diagnose it early and reduce unnecessary cost in ruling out other viral and autoimmune etiology. Physician should know all different presentations of the disease. In our case it nearly take 5 months to diagnose this disease because of lack of suspicion by his previous doctors. Another take home point should be SSPE can have adult onset even in twenties. Because most of the cases are reported in teenagers and pediatric population, so there are high chances of missing this in adult patient.

Myoclonus (generalized and focal), seizure (generalized and focal), cognitive defects, weakness, visions defects, extra pyramidal and behavioral problems are common among all various presentations of SSPE. But atypical presentations with regard to clinical scenario, laboratory and electroencephalographic evaluations is big diagnostic challenge. High clinical suspicion should be there for a physician to diagnose the disease. Neonatal and perinatal occurrences are uncommon.

Some clinicians use quantitative ELISA while some uses hem agglutination inhibition assay to detect measles antibody [5]. Some clinicians believed, mere demonstration of measles antibody in CSF is sufficient to clinch diagnosis of SSPE [6]. 10-100 times high titers are expected in SSPE patient's CSF compared to normal. High CSF antibody titers suggests intrathecal synthesis. There is also an evidence that CSF antibody levels may fluctuate during day with total absence in SSPE. Hence to use antibody titer alone for diagnosis is not viable, instead totality of radiologic, clinical and laboratory criteria should be used [7].

SSPE is generally a deadly disease. Often patients may die in few months, but some may remain in a decerebrate state for years

Usually lifelong immunity is given by measles virus infection, but still virus remain sequestered in the brain in spite of normal immune response in patient of SSPE. This raises serious question that whether SSPE occurs due to insufficient immune response.

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