

# Thinking Measles Unconventionally, SSPE - Why We Must Vaccinate

Dr Nirbheek Sharma<sup>1</sup>, Dr. Divyani Dhole<sup>2</sup>, Dr. Rajesh Rai<sup>3</sup>, Dr. Prithi Inamdar<sup>4</sup>, Dr Neelu Elon<sup>5</sup>

<sup>1,2</sup>Junior Resident, Dr. D. Y. Patil Medical College, Navi Mumbai, India

<sup>3</sup>Professor and Head of Department, Dr. D. Y. Patil Medical College, Navi Mumbai, India

<sup>4</sup>Associate Professor, Dr. D. Y. Patil Medical College, Navi Mumbai, India

<sup>5</sup>Senior Resident, Dr. D. Y. Patil Medical College, Navi Mumbai, India

## 1. Introduction

Measles-related neurological syndromes encompass primary measles encephalitis, acute post-measles encephalitis, measles inclusion-body encephalitis and subacute sclerosing panencephalitis (SSPE). SSPE is a catastrophic consequence of the defective wild-type measles virus with an estimated risk of 4–11/1,00,000 cases worldwide. Effective vaccination campaigns have eliminated measles from the developed countries but developing countries like India incidence rate is 21 cases/million population (1). In 1933 Dawson, for the first time, described a child with progressive mental deterioration and involuntary movements who, at necropsy, was found to have a dominant involvement of grey matter in which neuronal inclusion bodies were abundant [2]. The term SSPE was coined by Greenfield. It is characterized by progressive intellectual deterioration, focal and/or generalized seizures, myoclonus, ataxia, and visual disturbances[3]. Most of the patients die within 1-3 years from onset of symptoms, although spontaneous improvement or stabilization can occur in a small proportion of patients. Measles is primarily disease of childhood with age of onset before 2 years. After a latent period of 6-8 years, it is followed by the onset of progressive neurological symptoms suggestive of SSPE. As a result of subclinical measles infection before the age of 1 year, occasionally, it can be seen in vaccinated children. There is no evidence to suggest that attenuated vaccine virus is responsible for sporadic cases of SSPE. [4,5] Individuals with acquired immunodeficiency syndrome (AIDS) or children whose mothers have AIDS might be at higher risk of a fulminant course and earlier onset of SSPE. [6]

## 2. Case Summary

Here we report a case of a 7-year-old, previously healthy boy presented with myoclonic jerks since past 3 months. Myoclonic jerks heralded the onset of illness following which he had progressive decline in all cortical functions, there was inability to walk, inability to speak and regurgitation of feeds. After 7 days of hospital stay child developed generalized tonic clonic seizures and altered sensorium. There was history of measles at 2 years of age. Birth history was uneventful. Prior to this illness, child was developmentally normal. Child was unimmunized. On examination, Child had emaciated look, severely wasted and stunted with contractures at knee joint and altered

sensorium. Vitals being HR-82/min, RR-16/min, BP-96/40mmg, with GCS of 6/15 on admission. Pallor was present. Child also developed bed sores in buttock area due to prolonged immobilization. No neurocutaneous markers were present.

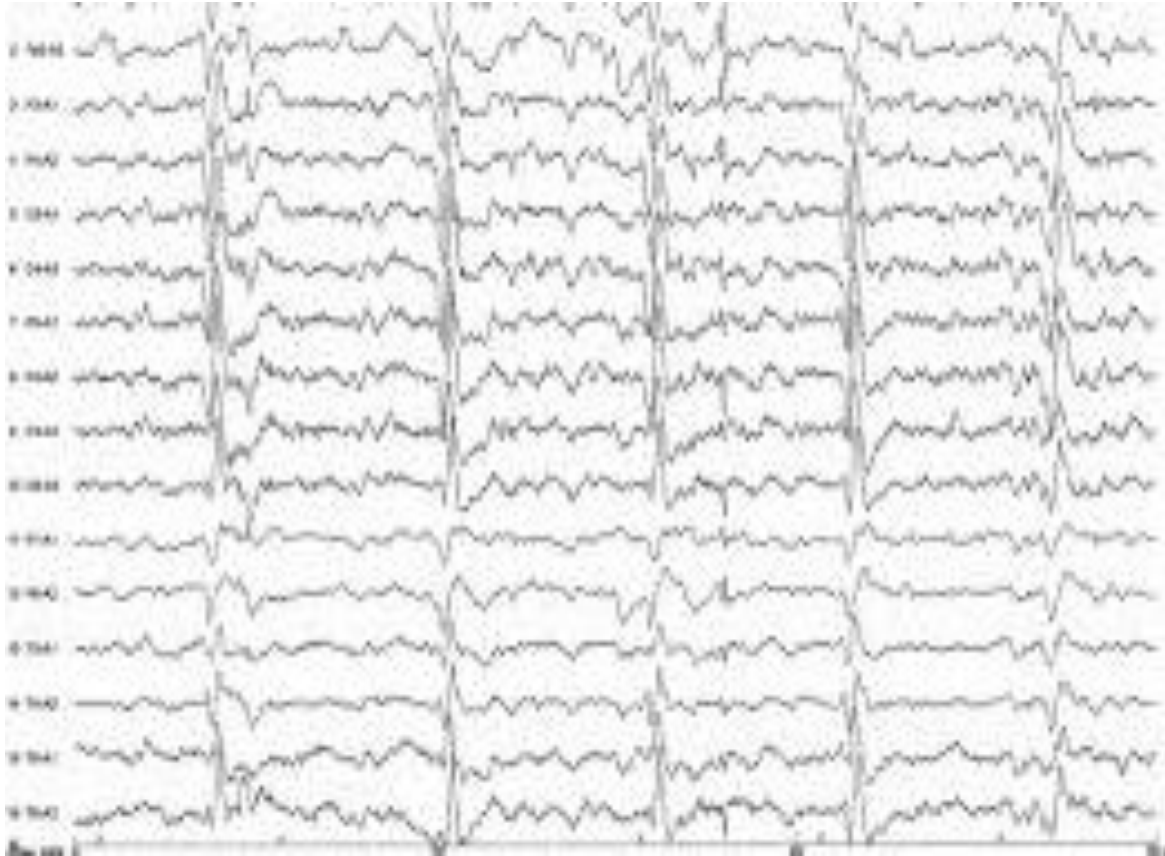
In CNS examination 1) higher mental functions were affected (sensorium, intelligence, speech). 2) There was involvement of 9<sup>th</sup> and 10<sup>th</sup> cranial nerves. Other cranial nerves were normal on examination. 3) There was hypotonia in all four limbs. The power in all the four limbs were grade zero. Deep tendon reflexes were absent. Among the superficial reflexes, abdominal, cremasteric and plantar reflex were absent. Myoclonic jerks were present. 4) The child had sensation to painful stimulus. 5) No cerebellar and meningeal signs were present.

Other systems appeared normal.

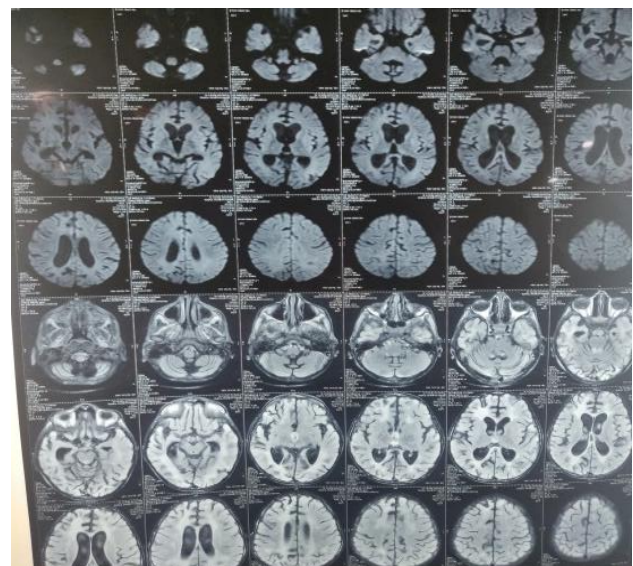
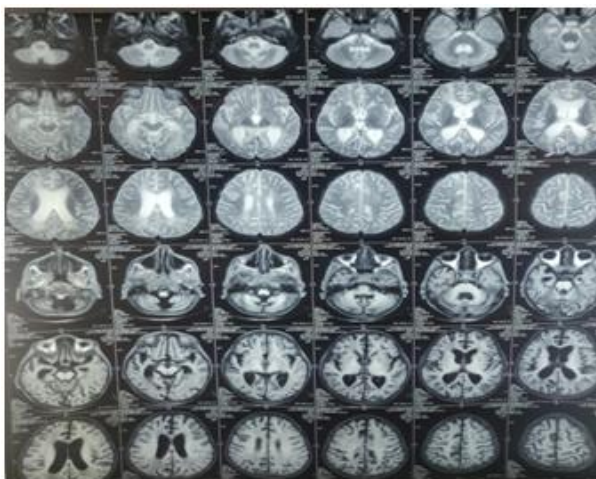


Hemogram was suggestive of microcytic hypochromic anemia and rest biochemical parameters (electrolytes, renal function, liver function) were all normal. The EEG and MRI were suggestive of SSPE which was confirmed by anti-measles antibody (IgG) in high titers in CSF. Child was started on sodium valproate. NGT feeding was given. Water bed and frequent change in position was advised to

present bed sores. Proper nutrition, physiotherapy, occupational therapy and speech therapy further helped in rehabilitation of child. On discharge, patient condition improved, the frequency of myoclonic spasms reduced significantly, child was able to walk with support and sensorium improved.



The EEG was characteristic and revealed bilateral periodic, stereotyped high voltage discharges in central region



MRI Brain revealed asymmetrical white matter hyperintensities in bilateral frontal and parietal lobes with diffuse cerebral and cerebellar atrophy

CSF confirmed anti-measles antibody (IgG) titers in high titers (1:625) reference range 1:256





### 3. Discussion

In India, SSPE is still a common neurodegenerative disorder despite an increase in the measles vaccination. A defective expression of either the matrix, the fusion, or the haemagglutinin proteins of measles virus is responsible for

viral persistence in brain cells and its escape by immune surveillance mechanisms (6). Many studies from all parts of country have been reported with nearly same features [Table 1]. (7,8,9,10,11,12,13,14,15,16,17,18,19)

**Table 1**

Author	No. of cases	Study period	Mean age (years)	M:F	Age of onset >15-20	History of measles %	Measles vaccination %	EEG %	CSF %	Follow-up duration
Lekhra <i>et al.</i> <sup>[9]</sup>	39	1983-1993	11.5±3.5	2.9:1	6	41	41	97.4	79.4	-
Saha <i>et al.</i> <sup>[5]</sup>	82	1983-1987	10	2.4:1	3	70.7	-	100	-	-
Bhat <i>et al.</i> <sup>[10]</sup>	32	1984-1992	6.1	3:1	6	59.3	0	100	88.5	2 months to 5 years
Khare <i>et al.</i> <sup>[11]</sup>	65	1982-1992	-	6:1	-	93.8	0	100	-	-
Prashanth <i>et al.</i> <sup>[12]</sup>	39	1995-2004	20.9±4.9	1.7:1	39	30	-	-	-	11.1±11.4 months
Prashanth <i>et al.</i> <sup>[13]</sup>	268	1995-2004	10.5±3.6	3:1	0	27.9	-	-	-	12.9±23.8 months
Lakshmi <i>et al.</i> <sup>[14]</sup>	33	1989-1992	10	2.3:1	4	42.4	3.3	100	90.9	-
Manayani <i>et al.</i> <sup>[15]</sup>	49	1996-1998	13	2.7:1	-	40	24	83	100	-
Singhal <sup>[16]</sup>	39	1964-1974	11.2	12:1	7	15.7	0	90.5	-	-
Khwaja <i>et al.</i> <sup>[17]</sup>	36	1985-1989	-	6.2:1	8	51.3	0	94.4	36.4	-
Shaikh and Rodrigues <sup>[18]</sup>	32	1984-1989	-	2.5:1	1	91.1	-	90.5	100	-
Mishra <sup>[19]</sup>	114	1992-2001	9.3	3.2:1	-	10.3	3.5	77	100	-
Sonia <i>et al.</i> <sup>[20]</sup>	458	1996-2005	13.3	4.4:1	71	-	-	-	100	-
Khadiikar <i>et al.</i> <sup>[21]</sup>	32	1998-2003	13.4	3:1	4	62.5	35.5	-	-	-
Present study	34	2004-2010	13.4	3.2:1	13	59.9	61.2	100	100	2 years

EEG=Electroencephalographic, CSF=Cerebrospinal fluid, M=Male, F=Female

As per table 1 mean age of presentation was much higher in all the studies except for Bhat et al study where mean age was 6.1 years. Therefore, age of presentation of this case was early as compared to other studies. The diagnosis of SSPE can be reliably established if patient fulfils three of the five criteria given by **Dykencriteria** (20) (table 2).

**Table 2:** Definitive: criteria 5 with three more criteria; probable: three of the five criteria.

Clinical	Progressive, subacute mental deterioration with typical signs like myoclonus
EEG	Periodic, stereotyped, high voltage discharges
Cerebrospinal fluid	Raised gamma globulin or oligoclonal pattern
Measles Antibodies	Raised titre in serum (≥1:256) and/or cerebrospinal fluid (≥1:4)
Brain Biopsy	Suggestive of Panencephalitis

One of the most important limitations in treatment of SSPE is difficulty in recognizing manifestations of disease. Treatments available are very costly and are available only at a few centers. Moreover, these treatments are not curative and only help in buying time for these patients. At present effective measles vaccination seems to be the only solution to problem of this dreaded neurological disorder. (6)

Measles-containing vaccines are a part of the childhood vaccination schedule in all countries. Current World Health Organization (WHO) policy is that “Reaching all children with 2 doses of measles vaccine should be standard for all national immunization programs”

The antiviral drug ribavirin has been tested in animal models of SSPE and was found effective. Recently, this drug has been used in patients with SSPE. Tomoda et al used a combined treatment of high dose intraventricular interferon

alfa along with intravenous ribavirin in two non-responding cases of SSPE.(21) In both the patients no further progression was noted. In one patient the hypertonicity, bladder incontinence, and dysphagia improved three months after starting the combination treatment. Similar, efficacy of high doses of ribavirin and intraventricular interferon alfa has been noted by Hosoya et al in two patients. (22)

#### 4. Conclusion

In short, SSPE is a potentially lethal disease and causes a huge burden both emotionally and financially, affecting not only the family but the country as whole. Furthermore, as this is seen more in the underdeveloped countries, the economic burden to these nations is huge. There is a strong need to improve the vaccination status of countries where the incidence of measles is high as it may be eradicate this devastating condition. This requires a global and political will and ownership by the individual countries.

We must thank Indian government initiative to vaccinate all children between 6months to 15 years with an additional dose of measles vaccine in form of MR campaign held on 27<sup>th</sup> November 2018

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