Original Article

Subacute sclerosing panencephalitis: A clinical appraisal

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Abstract

Introduction: Subacute sclerosing panencephalitis (SSPE) is a rare chronic, progressive encephalitis affecting primarily children and young adults, caused by a persistent infection of immune resistant measles virus. The aim of the present study is to describe the clinical profile and natural history of patients with SSPE. **Methods:** We collected data of patients with SSPE during 2004-2010 who fulfilled Dyken's criteria. We analyzed demographical, clinical, electrophysiological, and imaging features. **Results:** Study included 34 patients, 26 (76.5%) males with age of onset from 3 to 31 years. Twenty one patients were below 15 years of age formed childhood SSPE and 13 above 15 years of age constituted adult onset group. 85.3% had low-socioeconomic status. Eleven received measles vaccination and seven were unvaccinated. 59.9% patients had measles history. Most common presenting symptom was scholastic backwardness (52.5%) followed by seizures (23.5%). Three patients each had cortical blindness, macular degeneration, decreased visual acuity, and optic atrophy. Electroencephalographic (EEG) showed long interval periodic complexes and cerebrospinal fluid anti-measles antibody was positive in all. Magnetic resonance imaging was done in 70.5% with was abnormal in 52.5%. Mean incubation period of SSPE after measles was 9.6 years. The follow-up duration was 1-10 years, (average of 2 years). Only one patient died from available data of follow-up, 9 were stable and 10 deteriorated in the form of progression of staging. **Conclusion:** SSPE is common in low-socioeconomic status. The profile of adult onset did not differ from childhood onset SSPE, except for a longer interval between measles infection and presence of the ophthalmic symptom as presenting feature in adult onset group.

Key Words

Measles, myoclonus, subacute sclerosing panencephalitis

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Introduction

Subacute sclerosing panencephalitis (SSPE) is a rare progressive demyelinating disease of the central nervous system associated with a chronic infection of brain tissue with measles virus, most commonly seen in children and young adults.[1] It is also called as Dawson's encephalitis after Dawson who first described it.[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.

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SSPE generally follows the prevalence of measles in a population. The incidence rate in the USA in 1960 was 0.61 cases/million persons younger than 20 year. By 1980, the rate had fallen to 0.06 cases/million.[4] Incidence is still high in developing countries though variable, in India estimated incidence by Saha *et al*.[5] was 21/million population while an annual incidence of 1.5/million was reported in the Middle East.[6] 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. The measles vaccine has changed the epidemiology of measles dramatically from the erstwhile worldwide distribution to a rare disorder in developed countries. 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.[6,7] 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.[8]

The aim of the present study is to describe the clinical profile and natural history of patients with SSPE after improvement in measles vaccination and to see any change in clinical characteristics.

Methods

We abstracted data of patients with SSPE during 2004-2010 who fulfilled Dyken's criteria. The diagnosis of SSPE can be established, if the patient fulfills any three of the following five criteria:[3] (1) Typical clinical presentation with progressive intellectual deterioration with signs of myoclonus; (2) characteristic electroencephalographic (EEG) pattern; (3) elevated cerebrospinal fluid (CSF) globulin levels; (4) elevated CSF measles antibody titers; and (5) brain biopsy suggestive of measles. We analyzed demographical, clinical, electrophysiological, and imaging features.

Results

There were 34 patients, 26 (76.5%) males and 8 (23.5%) females. Minimum age of onset was 3 years and maximum age was 31 years. Only two patients were below 5 years of age and 13 patients were above 15 years of age. 85.3% were from low-socioeconomic status. Out of 34 patients vaccination data was available in 18 patients of whom 11 were vaccinated and 7 were not vaccinated, remaining patients were unsure about vaccination status. 59.9% patients had history of measles while 41.1% did not. Most common presenting symptom was scholastic backwardness in 52.5% followed by seizures in 23.5% in which myoclonic seizures was most common presentation. Fundus examination was abnormal in 20.6%, in the form of macular involvement, optic atrophy, and retinal hemorrhages. Three patients had cortical blindness, three patients had macular degeneration, three patients had decreased visual acuity, and three had optic atrophy. The mean age of onset of measles was 3.3 years in childhood and 5.0 years in adult onset SSPE group. The mean age of onset of symptoms was 10.4 years in childhood onset (<15 years) while 19.3 years in adult onset. Mean incubation period of SSPE after measles was 9.6 years (childhood onset 5.9 and adult onset 14.9). The most common presenting symptom was scholastic decline in childhood group, while in the adult onset group, six patients presented with either cognitive or behavioral changes, four had ophthalmic symptoms, and three had myoclonus at onset. None of childhood onset patient presented with ophthalmic symptom. The average follow-up in adult onset group was 3.1 years compared to 1.5 years in childhood onset group. EEG showed long interval periodic complexes in all. CSF anti-measles antibody was positive in all. At the time of diagnosis, all patients were in stage II. Computed tomography scan of the head done in 17.6% of the patients was normal. Magnetic resonance imaging was done in 24 (70.5%) patients with 52.5% having abnormalities. Most common abnormality was hyper-intensities involving gray as well as white matter in parieto-occipital area followed by fronto-parietal area. The follow-up duration was 1-10 years (average of 2 years). Twenty patients were followed up for more than 2 years of which eight patients were for more than 3 years with maximum duration of follow-up was 10 years. One patient had fulminant course and died within 9 months of onset of symptom. Nine patients were stable and 10 deteriorated in the form of progression of staging. Age of onset of SSPE and measles vaccination status was statistically insignificant.

Discussion

In India, SSPE is still common neurodegenerative disorder despite increase in measles vaccination. Population based studies are very few, however, many studies from all parts of country have been reported with nearly same features [Table 1]. As measles is still common in India, 60% patient had measles history in present study, consistent with 40-60% in previous studies in contrast to studies before widespread measles immunization (90%)[9-21] [Table 1]. Although measles infection is equally common in both sexes, higher incidence (male/female ratio 3:1) has been noted in boys, in childhood onset SSPE.[22] This may be attributed to increased risk of being intensively exposed within the home for boys as compared to girls as per Aaby *et al*.[22] In adult onset SSPE, the gender distribution is reported to be equal, however, in our cohort, there was a preponderance of males (9 males and 2 females), similar to study by Prashant *et al*.[12]

Table 1: Epidemiological and clinical characteristics of patients with subacute sclerosing panencephalitis in India

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 *et al*.[9]	39	1983-1993	11.5±3.5	2.9:1	6	41	41	97.4	79.4	-
Saha *et al*.[5]	82	1983-1987	10	2.4:1	3	70.7	-	100		-
Bhat *et al*.[10]	32	1984-1992	6.1	3:1	6	59.3	0	100	88.5	2 months to 5 years
Khare *et al*.[11]	65	1982-1992	-	6:1	-	93.8	0	100	-	-
Prashanth *et al*.[12]	39	1995-2004	20.9±4.9	1.7:1	39	30	-	-	-	11.1±11.4 months
Prashanth *et al*.[13]	268	1995-2004	10.5±3.6	3:1	0	27.9	-	-		12.9±23.8 months
Lakshmi *et al*.[14]	33	1989-1992	10	2.3:1	4	42.4	3.3	100	90.9	-
Manayani *et al*.[15]	49	1996-1998	13	2.7:1		40	24	83	100	-
Singhal[16]	39	1964-1974	11.2	12:1	7	15.7	0	90.5		-
Khwaja *et al*.[17]	36	1985-1989	-	6.2:1	8	51.3	0	94.4	36.4	-
Shaikh and Rodrigues[18]	32	1984-1989	-	2.5:1	1	91.1	-	90.5	100	-
Mishra[19]	114	1992-2001	9.3	3.2:1		10.3	3.5	77	100	-
Sonia *et al*.[20]	458	1996-2005	13.3	4.4:1	71	-	-	-	100	-
Khadilkar *et al*.[21]	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

The incidence is high among children from lower- socioeconomic levels, large family size, and rural area as measles virus is transmitted by respiratory secretions, predominantly through exposure to aerosols but also through direct contact with larger droplets.[23,24] Mean age of onset of SSPE is in early second decade in most of the studies while in study by Bhat *et al*. it was 6.1 year. There are very few adult onset SSPE cases in literature, largest series of 39 patient by Prashant *et al*.,[12] followed by present study (13 patients) consisting 38.2% of cohort. The study by Sonia *et al*.[20] consisted of 71 adult patients but data of only four patients is available. The findings of that study are also comparable with study by Prashant *et al*. and present study. In the study by Prashant *et al*. mean age of onset of symptom in adult onset SSPE was 20.9 years similar to 19.3 years in our study. The clinical presentation of adult onset differs from childhood onset as, personality change and ophthalmic manifestations are common presenting features.[25,26] In the present series, six patients presented with either cognitive or behavioral changes, four had ophthalmic symptoms, and three had myoclonus at onset.

Follow-up data is very scarce with maximum follow-up being 5 years in study though some individual case reports have Long duration follow-up. The course of adult onset SSPE is generally postulated to have an aggressive course but Singer *et al*.[26] reported higher rate of spontaneous remission and favorable response to disease modifying agents in adult onset group. In present study, the average follow-up in adult onset group was 3.1 years compared to 1.5 years in childhood onset group, so it is not possible to comment on the length of patient survival. As compared to pre-immunization, there has been no significant change in the mean age of presentation in patients of SSPE. It has increased to 13 years from around 10 years.[12,19,20] The preponderance of male patients continues, though less prominent as well as its association with low-socioeconomic status. The presence of SSPE in vaccinated patients indicates either previous subclinical infection prior to measles vaccination or poor maintenance of cold chain.[12,19,20] SSPE is a devastating disorder that deserves elimination through the immunization of all children worldwide. These observations are of public health significance as effective immunization against measles is the only answer to this progressive fatal neurodegerative disorder.

Conclusion

SSPE is common in low-socioeconomic status. The profile of adult onset did not differ from childhood onset SSPE, except for a longer interval between measles infection and presence of the ophthalmic symptom as presenting feature in adult onset group.

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