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Clinical and Neuroimaging Changes of Subacute Sclerosing Panencephalitis – Experience 30 Cases in Tertiary Care Center in Bangladesh

Gopen Kumar Kundu and M. Monir Hossain

ABSTRACT

Background: **Subacute sclersing panencephalitis (SSPE) is a very rare progressive, fatal neurodegenerative disease of the control nervous system of childhood and early adolescence. It is a slow virus disease caused by persistent defective measles virus infection of the brain**

Objective: **To see the clinical andneuro-imaging findings in children with Subacute sclerosing panencephalitis.**

Methods: **This retrospective study was conducted at Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, a tertiary care premier Postgraduate Medical Institution in Bangladesh. Thirty (30) Subacute sclerosing panencephalitis (SSPE) children were evaluated at paediatric neurology ward during the period January 2010 to December 2017. Diagnosis was based on typical clinical characteristic features, the presence of periodic discharges on EEG, demonstration of raised antibody titer against measles in the plasma and cerebrospinal fluid Detected by ELISA in all patients.**

Results: **Total number of studied children were 30. Mean age was 10.2±3.1 year and Male female ratio was 5:1. Most of the patient arrived from poor socio-economic (83.33%) background of rural area (66.67%) of Bangladesh. Among them 46.67% had history of measles infection during early childhood. Progressive deterioration of school performance (50%), gait disturbance (70%), myoclonus (83%) dysarthria (43%) and Ocular manifestations like optic atrophy & papilledema (83.33%) were the main presenting feature of our studied children. All of the patients (100%) showed positive measles specific antibody IgG in CSF and On electroencephalographic findings showed periodic burst suppression in 90.90% cases. Most of the children (56.6%) were in stage II category and other 3.3%, 33.3%,6.6%, were stage I, stage III, stage IV category respectively. Neuroimaging study showed abnormalities in 45.83% cases included periventricular white matter hyper intense signal changes, cortical atrophy and ischaemic change.**

Conclusion: **In our study most of the SSPE patient were in stage II.About half of the patient had history of measles infection during early childhood. Neuroimaging abnormalities found in about half of the cases and majority cases were in stage II. Common neuroimaging abnormalities were periventricular white matter hyper intense signal changes and cortical atrophy.**

Keywords: subacute sclersing panencephalitis (SSPE), measles, myoclonic jerk.

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I. Introduction

Subacute sclersing panencephalitis (SSPE) is a very rare progressive, fatal neurodegenerative disease of the control nervous system of childhood and early adolescence. It is a slow virus disease caused by persistent infection of the brain by a mutated form of the measles virus acquired earlier in life that results from a complex and poorly understood interaction between the host's immune system and measles virus. SSPE was described first by Dawson [1] in 1934, in an individual with rapidly progressive encephalitis. Later, van Bogart [2] described another individual with the same clinical

presentation but is whom the disease exhibited a more gradual course in 1945. The latency period between measles virus infection and first symptoms of SSPE is usually 4 to 10 years but ranges from 1 month to 27 years [3].

Evidence was provided that the true incidence of SSPE is approximately 4-11 cases per 100000 cases of measles [4]. Developed countries such as USA have been reported an incidence of 6.5-11 cases per 100,000 acute measles infections [5]. But the prevalence of SSPE is nearly 20-per 100,000 when measles occurs under 1 year of age versus 1 per 100,000 for infections after 5 years of age [6]. The SSPE incidence may differ geographically and may change over time. A higher incidence et SSPE has noted in boys, although primary measles infection shows no such sex disparity [7]. The incidence is higher among rural children, children with two or more siblings, and children with mental retardation. It is also more common in children with a lower birth order and in children living in overcrowded environments [8]-[11].

Other factors, also Identified as risk factors for SSPE may modify the course of acute measles infection – for example, a close temporal relationship of measles with another viral infection such as Epstein- Barr virus or parainfluenza type-1 virus. Widespread immunization has produced greater than 90% reduction in the incidence of SSPE in developed nations [12].

When the disease occurs in vaccinated children, it is thought to result from a subclinical measles infection that occurred before the age of 1 year, when immunization is usually begun. There is no evidence to suggest that attenuated vaccine virus is responsible for sporadic cases of SSPE [13].

SSPE is caused by the intra cerebral spread of measles virus leading to a destruction of neurons. The brain tissue of SSPE cases has been examined by molecular methods, and wild type measles virus strains have been identified but there was no similarity of vaccine strains [14]. However, the exact pathogenesis of SSPE is still unclear. Immaturity of the immune system and of the central nervous system is thought to play a role when SSPE develops after an early acute measles infection [15]-[17].

The clinical course of SSPE varies considerably in symptoms, duration, and intensity. Typically, four stages of disease are observed in SSPE beginning with changes in personality and behavior as well as failure in school. The second stage is characterized by massive, repetitive, and frequent myoclonic jerks, seizures and dementia. During the third stage rigidity, extra pyramidal symptoms, and progressive unresponsiveness develop. The last stage is characterized by coma, a vegetative state, autonomic failure or akinetic mutism. The survival period after onset of symptoms is typically between one to three years [18], [19].

SSPE causes a slow, progressive decline in cognitive function but, fulminant course is not uncommon [20]-[22]. Brain biopsies or postmortem histopathological examination show evidence of astro-gliosis, neuronal loss, degeneration of dendrites, demyelination, neurofibrillary tangles, and infiltration of inflammatory cells. The diagnosis is based upon typical clinical characteristics, the presence of periodic discharges on EEG, demonstration of raised antibody titer against measles in the plasma and cerebrospinal fluid. Treatment of SSPE is mainly supportive and usually lifelong. Specific therapy with immune modulators has been tried but is still controversial [23]. A combination of oral Isoprinosine and intraventricular interferon alfa appears to be the best effective treatment. Patients responding to treatment need to receive it lifelong. Effective immunization against measles is the only solution presently available to the problem of this dreaded disease.

SSPE is still endemic in many developing countries, where measles vaccination in early infancy has not yet reached the World Health Organization's goal of greater than 80% coverage [24].

In Bangladesh, there is no notification or central documentation of SSPE cases. Therefore, information regarding the absolute number of SSPE cases or the SSPE incidence is lacking. So, this retrospective study of SSPE cases out to get an insight at the disease in the population of Bangladesh.

II. Method and Materials

This retrospective study was conducted at Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, a tertiary care premier Postgraduate Medical Institution in Bangladesh. Thirty (30) Subacute sclerosing panencephalitis (SSPE) children were evaluated at paediatric neurology ward during the period January 2010 to December 2017. Diagnosis was based on typical clinical characteristic features of progressive cognitive and/or behavioral changes, myoclonus the presence of periodic discharges on EEG, demonstration of raised antibody titer against measles in the plasma and cerebrospinal fluid detected by ELISA in all patients. Analysis for oligoclonal band in CSF was not carried out. We have not performed any specific test to determine disruption of the blood-brain barrier. Thirty children had above at first symptom onset were considered to have onset SSPE and their data regarding measles vaccination, any history of measles, age at onset of symptoms and diagnosis, presenting symptoms, initial diagnosis, clinical staging, course of the disease, electroencephalographic changes, and measles anti body status were recorded. Data were collected in structured data collection sheets. Statistical analysis was done by SPSS 7.

III. Results

After merging the SSPE cases, 30 unique SSPE cases that were diagnosed in BSMMU during 2010 to 2016 were identified.

TABLE I: Distribution of Studied Cases by Demographic Characteristics (N=30)

Age	5-10 Years	≥11 Years	Total
	18 (60%)	12 (40%)	30 (100%)
Sex	Male	Female	
	24 (80%)	06 (20%)	30 (100%)
	Mal: Female	5:1	
Inhabitant	Rural	Urban	
	20(66.67%)	10 (33.33%)	30 (100%)
Economic Status	Poor	Middle class	
	25 (83.33%)	5 (16.67%)	30 (100%)
H/O measles	Present	Absent	
	14(46.67%)	16(53.33%)	30 (100%)

Table I showed 24 (80%) of the 30 children with SSPE were male and 6 (20%) were female and male female ratio was 5:1. A total of 18 (60%) children's age were within 5 to10 years and 12 (40%) were11 or more than 11 years and their mean age was 10.2±3.1 year. Out of these thirty, 20 (66.67%) children were arrived from rural area of different parts of the country and 10 (33.33%) were from urban area. Majority of the patients (83.33%) were from poor socio-economic background.

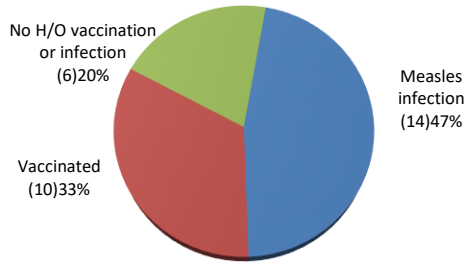

Fig. 1. History of measles infection and vaccination among study population (n=30). Showed out of 30 children, 14 (46.67%) had history of measles infection during early childhood, 10 (33.33%) immunized against measles vaccine through EPI programme and 6 (20%) children had no history of immunization or measles infection. All (100%) of the patients showed positive measles specific antibody IgG in CSF.

TABLE II: DISTRIBUTION OF STUDIED CASES BY CLINICAL PRESENTATION(N=30)

	Features	Number	(%)
Clinical presentation	Deterioration of school performance	15	50%
	Gait disturbance	21	70%
	Myoclonic jerks	25	83%
	Dysarthria	13	43%

Table II showed clinical presentation of 30 SSPE studied children. The behavioral and cognitive symptoms consisted of poor academic performance, forgetfulness, recent change in personality, dullness, and apathy. Progressive deterioration of school performance occurred 15 (50%) children. Twenty one patients (70%) had gait disturbance and falls probably due to myoclonus and 13 (43%) children developed dysarthria. The presenting manifestations were myoclonus 25 (83%) children. No patient had status epilepticus or other form of epilepsy.

TABLE III: OPHTHALMOLOGICAL ASSESSMENT OF STUDIED CASES (N=30)

	Features	Number	(%)
Ophthalmological Abnormalities	Normal	5	16.67%
	Abnormal: Optic atrophy (24), Papilloedema (1)	25	83.33%

Table III showed Ophthalmological abnormalities like optic atrophy, papilloedema. It was found 25 (83.33%) children. Rest of five (16.67%) children were normal in eye evaluation.

TABLE IV: DISTRIBUTION OF STUDIED CASES BY STAGING(N=30)

Staging	Number	Percentage (%)
Stage-1	1	3.3
Stage-II	17	56.6
Stage-III	10	33.3
Stage-IV	2	6.6

Table IV showed clinical staging of our studied children. Most of the children (56.6%) were in stage II category and other 3.3%, 33.3%,6.6%, were stage I, stage III, stage IV category, respectively.

TABLE V: DISTRIBUTION OF STUDIED CASES BY EEG FINDING (N=22)

EEG	Number	(%)
Normal	2	9.09
Abnormal:Periodic complexes	20	90.90

Table V showed, characteristic EEG picture with periodic complexes, consisting of bilaterally symmetrical, high voltage burst (200-500 uV) delta waves, appearing at 4-10 sec interval and have 1:1 relationship with myoclonic jerks of 90.90% children and 9.09% were normal EEG finding.

TABLE VI: DISTRIBUTION OF STUDIED CASES(N-24) BY NEURO-IMAGING (MRI)

Findings	Number	(%)
Normal	13	54.17%
Abnormal	11	45.83%
• Cortical atrophy	3	12.50%
• Hyperintense signal in white matter	5	20.83%
• Ischaemic change	3	12.50%

Magnetic resonance imaging (MRI) studies were carried out during the course of initial period of hospitalization (Table VI).

MRI was done in 24 children after the onset of symptoms. Thirteen patients (54.17%) had normal MRI. In the remaining 11 patients (45.83%), the MRI abnormalities included focal or diffuse white matter hyper intense signal changes was observed on T2 sequences in five patients (20.83%), cortical atrophy of varying degrees in the three patients (12.5%) and ischaemic change three patients (12.5%).

IV. DISCUSSION

SSPE is common neurodegenerative disorder in Bangladesh despite increase in measles vaccination. Studies regarding SSPE in our country very few, however, may case report and few articles have been reported with nearly same features. Though expanded programme on immunization (EPI) is very much successful in Bangladesh but measles is still persisting and common in Bangladesh, 47% 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 I). Although measles infection is equally common in both sexes, higher incidence (male/female ratio) has been noted in boys in our study similar to study by Prashant et al. [12]. 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.

TABLE VII: CLINICAL COMPARISON OF SSPE OF PATIENTS OF PRESENT STUDY WITH OTHER SEVERAL STUDY

Author	No. of Cases	Study period	Mean age (years)	Male : Female	H/O measles (%)
Saha et al [5]	82	83-87	10.0	2.4:1	70.7
Bhat et al [10]	32	84-92	6.1	3:1	79.3
Prosanto et al [12]	39	95-2004	20.9±4	1.7:1	30
Sonia et al [20]	498	96-2005	13.3	4.4:1	-
Present study	30	2010-2017	10.2±3.1	5:1	46

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 though exposure to aerosols but also through direct contact with larger droplets [23], [24]. In present study shows similar clinical picture. Mean age of onset of SSPE is in second decade in most of the studies while in study Saha et al, mean age was 10, which was compatible of our study (10.2±3.1 year). The clinical presentation of adult onset from childhood onset as personality change and ophthalmic manifestations are common presenting features. In the present commonest features are myoclonus, behavior, and ophthalmic symptoms.

As compared to pre-immunization, there has 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 its association with low-socioeconomic status. The presence of SSPE in vaccinated patients indicates either previous subclinical infection prior to measles vaccination or poor maintains of cold chain for vaccine transport [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.

Against measles is the only answer to this progressive fatal neurodegerative disorder.

V. Conclusion

In our study most of the SSPE patient were in stage II. About half of the patient had history of measles infection during early childhood. Neuroimaging abnormalities found in about half of the cases and majority cases were in stage II. Common neuroimaging abnormalities were periventricular white matter hyper intense signal changes and cortical atrophy.

Limitation

The data was a one-point source data and so could not evaluate the trends over time.

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Author Contributions

Conceived and designed the study, collected data, and analyzed the data: Dr Gopen Kumar Kundu. Clinical Help: Dr Md Monir Hossain.

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