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Clinical and Laboratory Profile of Twenty Cases of Subacute Sclerosing Panencephalitis

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Summary

Objective: To observe the clinical presentation and laboratory profiles of subacute sclerosing panencephalitis (SSPE) patients.

Design: An observational study.

Setting: Department of Paediatrics, Bangabandhu Sheikh Mujib Medical University, Dhaka.

Study period: November 2003 to October 2006.

Subjects : Twenty clinically diagnosed patients of SSPE.

Results: Male: Female ratio was 4:1. Mean age was 7.45 years. Eighty percent had past history of measles and 87% of them had measles before 2 years of age. Twenty percent had history of vaccination against measles. Common presenting symptoms were myoclonic jerks (100%), altered speech (90%), progressive cognitive deterioration and behavioral change (85%). EEG findings showed periodic discharge in 95% cases and measles specific antibody IgG was positive in CSF in 100% cases. Neuroimaging findings were hyper intense signals in white matter in 35.71% and cortical atrophy in 14.3% cases.

Conclusion: Myoclonic jerks, altered speech and progressive mental deterioration were the main presenting features and measles specific antibody in CSF was present in all cases. History of measles before 2 years of age was present in most of the cases.

Key words: *SSPE, measles, seizures.*

Introduction

Subacute sclerosing panencephalitis (SSPE) is a subacute inflammatory and degenerative disease of central nervous system[1]. It is a rare progressive neurological disorder of childhood and early adolescence[2-4]. It has been known to develop after measles infection, though the exact pathogenesis is still not fully known [5-8].

Typically it presents with myoclonus, behavioural changes and dementia progressing to a mute, bed ridden and incontinent state finally leading to death.

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The most remarkable feature of the cerebrospinal fluid examination is markedly raised gamma globulin level. IgG and IgM fraction to measles virus on oligoclonal electrophoresis with normal cell count and normal or mildly raised total protein in CSF is diagnostic of SSPE[9,10]. IgG and IgM antibodies to measles virus are not normally found in unconcentrated CSF. IgM antibody against measles virus can also be demonstrated in serum and this also favour the diagnosis. Usually the ratio of antibody content in CSF is higher in comparison to serum. Electroencephalography (EEG) in initial stage shows slowing with characteristic episodes of "suppression –burst" pattern of high amplitude slow and sharp waves recurring periodically. Computed tomography (CT scan) of brain is usually normal in early stages but cerebral atrophy appears later[11]. The probable diagnosis of SSPE can be done on the basis of clinical

features, CSF findings and EEG features. For definitive diagnosis, brain biopsy is needed. Other neurodegenerative disorders, progressive myoclonic epilepsy and other differential diagnoses are excluded by typical clinical features, cerebrospinal fluid changes, EEG and neuroimaging findings[12].

This study was carried out to observe the clinical presentation and to find out the available investigation profile of 20 cases of SSPE.

Materials and Methods

This observational study was carried out in the Paediatric department of Bangabandhu Sheikh Mujib Medical University (BSMMU), from November 2003 to October 2006. During the period 20 cases of SSPE were diagnosed clinically.

The diagnosis was based on history that includes age of onset, duration of illness, history of measles and measles vaccination, presenting symptoms like myoclonus, cognitive decline, behavioural changes, seizures, loss of vision and sphincter dysfunction. Physical examination includes abnormalities of higher mental functions, ophthalmological examination findings, motor and sensory deficits. Specific investigations includes CSF and serum study with measles specific antibodies in CSF and plasma. Positive IgM antibodies in serum and either IgG or IgM or both in CSF were taken as diagnostic criteria of SSPE. EEG was done in all cases for finding out typical changes of SSPE. Neuroimaging (MRI and/or CT) was done in 14 patients. Six patients could not afford it. Though brain biopsy could be definitive but it was not possible is our setting. However, diagnosis was based on a combination of clinical features of SSPE and supported by measles specific antibody titers in CSF and in serum, periodic discharges in EEG and neuroimaging findings. The findings were recorded on a previously prepared standard data collection form. The features in studied cases are analyzed.

Results

A total of 20 cases of SSPE were included in this study. Sixteen (80%) of these patients were male and four (20%) were female. Male female ratio was 4:1. Eighteen patients (90%) came from rural areas and nineteen patients (95%) were of poor socioeconomic background. The age of onset of SSPE ranged from 3.5 years to 10.2 years with a mean age of onset of 6.9 years. Maximum number of patients (60%) had onset between the age group of 6-8 years. The age at presentation varied from 4 years to 11 years with a mean age of 7.45 years. Maximum number of patients (55%) also presented between the age group of 6-8 years (Table-I). In this study sixteen patients (80%) had past history of measles, among them 14 (87%) had measles before 2 years of age and 4 (20%) were vaccinated against measles (Table-II). Duration between measles / measles vaccine and onset of SSPE was 2.5 years to 4 years in three patients (15%), 5 years to 8 years in sixteen patients (80%) and 9 years in only one patient (5%) (Table-III). In this study the mean time of interval between measles/ measles vaccine and onset of SSPE was 5.85 years (range 2.5 - 9 years).

Table - I

Age of onset and presentation in studied cases (n=20)

Age (years)	Onset Number (%)	Presentation Number (%)
3.5 - 5	3 (15)	4 (20)
6 - 8	12 (60)	11 (55)
9 - 11	5 (25)	5 (25)

Presenting symptoms were mild intellectual or cognitive deterioration, deterioration of school performance and behavioral changes in 85% cases without any apparent neurological signs. Later disturbance of motor function and development of periodic stereotyped myoclonic jerks (100%), frequent fall (90%). Myoclonic jerks initially involved head and subsequently trunk and limbs. Muscular contraction was followed by 1-2 seconds of relaxation and disappeared during sleep. Besides myoclonic jerks, which were the part of diagnostic criteria, involuntary movements (75%), speech impairments (90%) and difficulty in standing (50%) were present. Three patients (15%) presented with visual loss (Table-IV).

Table - II

Past history of measles or Measles vaccines (n=20)

Past history	Number	Percentage
Measles	16	80
Measles vaccine	4	20

In CSF study the antimeasles antibody was found in 100% cases. Among them IgG was positive in all the

cases and IgM was found in 75% cases. Simultaneously, serum antibody titers of measles were high. IgG was found in 15 (75%) cases and IgM in 10 (50%) cases. CSF protein was mildly elevated in 4 (20%) cases.

Table - III

Duration between measles / measles vaccine and onset of SSPE (n = 20)

Duration in years	Number	Percentage
2.5 - 4	3	15
5 - 8	16	80
> 9	1	5

Table - IV

Clinical presentation of the studied SSPE patients (n = 20)

Clinical presentation	Number	%
Behavioural change		
Decreased attention span and of school performance	17	85
Motor function		
Myoclonic jerks	20	100
Frequent fall	18	90
Difficulty in standing & gait	10	50
Diskinetic movement	15	75
Speech impairment		
Slurred speech	10	50
Loss of speech	8	40
Autonomic dysfunction		
Urine incontinence	8	40
Stool incontinence	6	30
Impairment of consciousness		
Semiconsciousness	4	20
Unconsciousness	3	15
Neurological signs		
Spasticity	11	55
Convulsion	4	20
Decorticate rigidity	2	10
Ophthalmic involvement		
Loss of vision	3	15

EEG was done in 20 (100%) patients. Among them typical periodic synchronous discharge and/or suppression burst pattern (Fig.-1) with poor normal rhythmic activities were noted in 19 (95%) cases and slow waves was found in one case (5%) (Table - V).

Table - V

CSF, serological and EEG findings of the patients (n = 20)

Investigation	No	%
Anti measles antibody in CSF		
Ig G positive	20	100
Ig M positive	15	75
Anti measles antibody in serum		
Ig G Positive	15	75
Ig M Positive	10	50
EEG		
Periodic discharge	19	95
Slow waves	1	5

Out of 20 patients MRI / CT scan of brain were done in 14 patients. Six (42.84%) patients had normal imaging, 5 (35.71%) had hyperintense signals (T_2 weighted MRI) mainly in the cortical & sub cortical area of parieto occipital, temporal and frontal region (Fig.-2). One patient had hyper intense signals in basal ganglia. Two patients (14.28%) had cortical atrophy in CT/ MRI of brain (Table-VI).

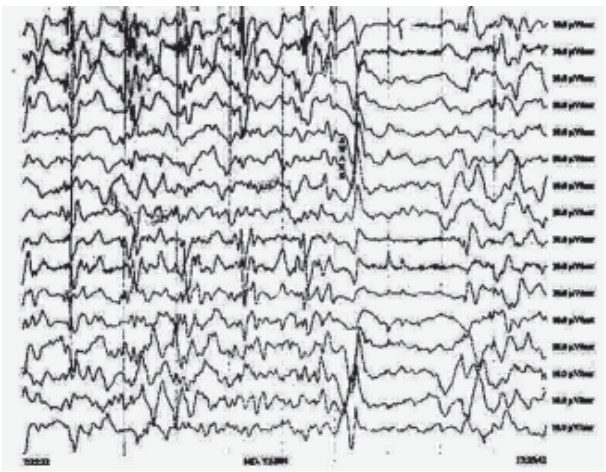

Fig.-1 : *EEG of SSPE Patient showing periodic discharge over frontal & temporal area.*

Table - VI
Neuroimaging findings of the patients (n = 14)

Imaging finding	Number	%
Magnetic resonance imaging		
Normal	3	21.4
White matter hyper intense signals	5	35.7
Cortical atrophy	2	14.3
Basal ganglia involvement	1	7.1
Computed tomography (n=5)		
Normal	3	21.4
Cortical atrophy	2	14.3

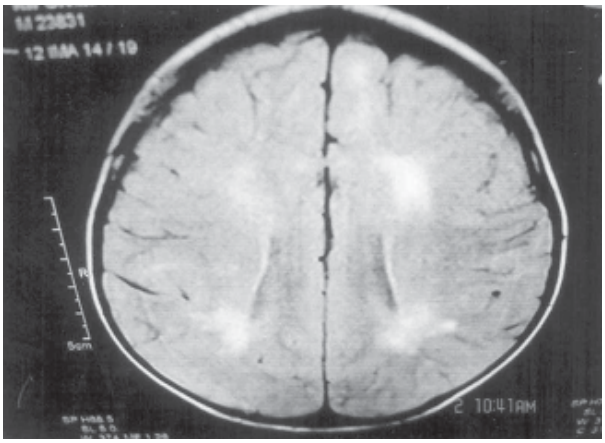

Fig.-2: *MRI of brain showing hyperintense signals in both parieto-occipital area*

Discussion

SSPE is a chronic inflammatory neurodegenerative disease of central nervous system in children following measles infection which is invariably fatal[1]. The age of onset of symptoms is in between 5 and 15 years of age with the mean age being 10 years[12]. The age of onset in this study was 3.5 years to 10.2 years with the mean age of 6.9 years which is lower than the finding (13.4 years) of one study[13], but consistent with Charle's study (7.9 years)[14]. This finding is keeping with the fact that globally the average age of SSPE is increasing due to better vaccination coverage. The duration between measles/measles vaccine and onset of SSPE varied from 2.5 years to 9 years with a mean of 5.8 years which is lower than the study by Zaidi (7-13 years)[15] but consistent with Charles et al (6.2 years)[14].

In this study only 4 patients were vaccinated against measles and developed SSPE. Studies suggest that SSPE among the vaccinated group may be due to malnutrition of children in the developing countries, different type of measles virus strain in the environment, subclinical measles infection prior to measles vaccination and faulty storage (cold chain) of the vaccine[13,18].

In the present study, only 20% patients were vaccinated against measles. So the lack of vaccination coverage might be the cause of lower age of onset of SSPE. Vaccine against measles do not cause SSPE. Because the DNA sequence of antimeasles vaccine is different from those that of measles virus which causes SSPE[16,17].

In this study preponderance of male was found as found by Jahan et al[19]. Previously it was thought that the social circumstances were related to this disparity[20]. However, those studies were done long ago, and those social issues have much changed over the past. So this observation is difficult to explain by only social issues. It might be related to hormonal influences[8,21].

In this study myoclonic jerks were present in all cases (100%), which is consistent with other studies [13,19]. Cognitive decline was present in 85% cases, which was 81 % in study by Satish at el[13]. Three patients presented with uncommon symptoms like loss of vision, though the incidence of vision loss is more in adult onset SSPE with the age of 20-35 years[22]. Vision loss in two patients were due to white matter lesion in parieto-occipital region and one patient had optic atrophy. This finding correlate with another study, where vision loss was in 21% cases[13]. Thus at all ages vision loss is an important feature of SSPE.

Four (20%) patients developed convulsion during the course of the disease. The seizure was generalized tonic clonic in nature and did not respond to any antiepileptic drugs. Kissani et al[23] showed documented epilepsy in 2% cases in a series of thirty patients. Ozturk et al[24] had seven (19.4%) patients with seizure in their series of 36 patients. The incidence of seizure in the present study is higher in comparison to the studies mentioned above, this might be due to delay in presentation in the present study.

Elevated titer of measles antibody both in serum and cerebrospinal fluid was found in maximum cases, which was consistent with the other studies[12,13,19]. In EEG typical 'suppression burst' finding was present in 95% patients, which matched with other studies[13,19,25]. The features of neuro imaging abnormalities in white matter, gray matter and basal ganglia were consistent with other studies[19,26].

Conclusion

Child presenting with myoclonic jerk of recent onset who is coming from poor socioeconomic status and was not vaccinated against measels or had measels before 2 years of age, one should consider the diagnosis of SSPE. Investigations like CSF and serum anitbody to measles virus may further help in the diagnosis.

References

1. Dyken PR. Subacute sclerosing panencephalitis. Current status. Neurol Clin 1985; 3: 179-96.
2. Hoppen T, Jacobi G, Rister M. Subacute sclerosing panencephalitis. Clin Padiatr 2003; 215: 268-69.
3. Modlin JF, Jabbour JT, Witte JJ, Halseyna NA. Epidemiologic studies of measles, measles vaccine and subacute sclerosing panencephalitis. Pediatrics 1977; 59: 505 -12.
4. Modlin JF, Halsey NA, Eddins DL. Epidemiology of subacute sclerosing panencephalitis. Pediatrics 1979; 94: 231-36.
5. Schneider Schaulies J, Niewiesk S, Schneider Schaulies S,Ter Meulen V. Measles in the CNS: the role of viral and host factors for the establishment and the maintenance of a persistent infection. J Neurovirol 1999; 5: 613-22.
6. Schneider Schaulies S, Ter Meulen V. Pathogenic aspects of measles virus infection. Arch Virol supple 1999; 15: 139-58.
7. Bonthius DJ, Stanek N, Grose. Subacute sclerosing panencephalitis a measles complication in an interationally adopted child. Emerging Infections Diseases 2002; 6: 377-81.
8. Dyken PR . Neuroprogressive disease of post infectious origin: a review of a resurging subacute sclerosing panencephalitis (SSPE). Ment Retard Dev Disabil Res Rev 2001; 7: 217-25.
9. Mehta PD, Kane A, Thormer M. Quantification of measles virus specific immunoglobulin in serum, CSF and brain extract from patients with subacute sclerosing panencephalitis. J Immunol 1977; 118: 2254-61.
10. Reiber H, Lange P. Quantification of virus specific antibodies in cerebrospinal fluid and serum: Sensitive and specific detection of antibody synthesis in brain. Clin Chem 1991; 37: 1153-60.
11. Modi GH, Campbell BP. Subacute sclerosing panencephalitis. Changes on CT scan during acute relapse. Neuroradiology 1996; 38: 636-40.
12. Garg RK. Subacute sclerosing panencephalitis. Postgrad Med J 2002; 78: 63-70.
13. Khadilkar SV, Patil SG, Kulkarni KS. A study of SSPE: Early clinical features. J Pediatr Neurol 2004; 2: 73-77.
14. Charles SM, Joyee MM, Toshiaki T, Kenji M, Ryuta K. Clinical Presentation of subacute sclerosing panencephalitis in Papua New Guinea. Tropical Medicine & International Health. 2003; 8: 219-27.
15. Zaidi AKM, Goldman DA. Infectious Diseases. In: Kligman RM, Behrman RE, Jenson HB, Stanton BF, editors. Nelson Textbook of Pediatrics. 18th ed. Philadelphia: WB Saunders company; 2007. P. 1334-35.
16. Norrby E, Kristensson K. Measlecs virus in the Brain. Brain Res Bull 1997; 44: 213-20.
17. Jin L, Beard S, Hunjan R, Brown DW, Miller E. Characterization of measles virus strain causing SSPE: a study of 11 cases. J Neurovirol 2002; 8: 335-44.
18. Zilber N, Kahana E. Environmental risk factors for Subacute Sclerosing Panencephalitis (SSPE). Acta Neurol Scand 1998; 98: 49-54.
19. Jahan A, Azam M, Begum D, Parveen M, Khan NZ. Subacute Sclerosing Panencephalitis (SSPE) – a study of 6 cases. Dhaka Shishu Hospital Journal 2002;18: 59-62.

20. Singhal BS, Wadia NH, Vibhakar BB, Dastur DK. Subacute sclerosing pancephalitis. Neurol India 1974; 22: 87-94.

21. Zeman W, Kolar O. Reflections on etiology and pathogenesis of subacute sclerosing panencephalitis. Neurology 1968; 18: 1-7.

22. Green SH, Wirtschaftir J. Opthalmoscopic findings in subacute sclerosing panencephalitis. Br J Ophthalmol 1973; 57: 780-87.

23. Kissani N, Ouzzani R, Belaidi H, Ouahabi H, Chkili T. Epileptic seizures and epilepsy in Subacute Sclerosing Panencephalitis (report of 30 cases). Neurophysiol Clin 2001; 31: 398-405.

24. Ozturk A, Gurses C, Baykan B, Gokyigit A. Subacute Sclerosing Panencephalitis: clinical and magnetic resonance imaging evaluation of 36 patients. J Child Neurol 2002; 17: 25-29.

25. Kuroiwa Y, Celesia G. Clinical significance of periodic EEG patterns. Arch Neurol 1980; 37: 15-20.

26. Brismar J, Gascon GG, Vonsteyern KV, Bohlega S. Subacute Sclerosing Panencephalitis: evaluation with CT and MRI. Am J Neuroradiol 1996; 17: 761-72.