

PREVALENCE OF SSPE: A SEROLOGICAL STUDY

A. Kapil
S. Broor
P. Seth

ABSTRACT

The presence of measles antibodies in serum and cerebrospinal fluid (CSF) of 340 samples from children clinically suspected of subacute sclerosing panencephalitis (SSPE) were studied. One hundred and thirty eight (40%) of these children had SSPE based on the serological evidence. The mean age group of children affected was 8.2 years. The M : F ratio was 5 : 1. The titres of antibodies ranged from 1 : 2 to 1 : 32 in the CSF and from 1 : 16 to 1 : 512 in the serum.

Key words: Measles, Subacute sclerosing panencephalitis.

Subacute sclerosing panencephalitis (SSPE) is a slowly progressive inflammatory disorder of the central nervous system (CNS). It is a complication of measles virus infection(1). The diagnosis of SSPE is based on the isolation of virus from the brain biopsy(2), presence of raised antibodies in serum and cerebrospinal fluid (CSF)(3-5), presence of specific antibody to nucleocapsid and envelope structures of measles virus in CSF and serum(6), or by immunofluorescence(7).

Various sero-surveys conducted in India have reported a high prevalence of SSPE based on detection of measles antibodies in serum and CSF of the affected children(8-10). The present study was conducted to assess the prevalence of SSPE in children based on the serological evidence.

Material and Methods

Three hundred and forty clinically suspected cases of SSPE whose samples were sent to our laboratory for detection of measles antibodies during the period January 1985 to January 1991 were included in the study. Both serum and CSF samples collected simultaneously were sent from 286 children and in 33 and 16 subjects, only CSF and serum samples, respectively, were sent. The control samples consisted of 196 CSF samples from clinically suspected cases of viral encephalitis or meningoencephalitis and in 144 of these serum samples were also included. The serum and CSF samples were stored at -20°C till the time of testing.

Complement Fixation test (CFT) was done on all the samples to study the complement fixing antibodies to measles virus by the standard accepted techniques(11). Measles antigen for CFT was prepared in our laboratory by propagating the Shwartz vaccine strain of Measles virus in Vero Cell

From the Department of Microbiology, All India Institute of Medical Sciences, New Delhi 110 029.

Reprint requests: Dr. Arti Kapil, E-48, Ansari Nagar, New Delhi 110 029.

Received for publication: September 11, 1991;

Accepted: January 25, 1992

lines(11). The antigen was titrated and stored at -70°C . The complement for CFT was prepared from pooled guinea pig serum by standard technique(12). Hemolysin for CFT was raised in the rabbits by standard technique(11). It was titrated and stored at -70°C .

Results

Three hundred and forty cases of clinically suspected SSPE whose samples were sent to our laboratory were studied. Based on the presence of complement fixing antibodies in the CSF or serum, 136 patients were found positive, having the serological evidence of measles virus infection. The mean age group affected was 8.2 years. Males were affected more commonly as compared to females (ratio being 5 : 1). Titres in CSF ranged from 1 : 2 to 1 : 32 (*Table I*) whereas the serum titres ranged from 1 : 16 to 1 : 512 (*Table II*). In the control group, the titres of measles antibodies in serum ranged from 1 : 8 to 1 : 16 whereas the CSF samples were negative for measles antibodies. The titres in controls were significantly lower than those in the adults.

The serum : CSF ratio ranged from 64 : 1 to 2 : 1 in positive samples (*Table III*). Samples of CSF in 7 cases were found

TABLE I—CSF Titres of Measles Antibodies in Patients and Controls

| Titres | Patients | Controls |
|----------|----------|----------|
| < 1 : 2 | 0 | 196 |
| 1 : 2 | 38 | 0 |
| 1 : 4 | 37 | 0 |
| 1 : 8 | 32 | 0 |
| 1 : 16 | 24 | 0 |
| 1 : 32 | 6 | 0 |
| > 1 : 32 | 1 | 0 |
| Total | 138 | 196 |

TABLE II—Serum Titres for Measles Antibodies in Patients and Controls

| Titres | Patients | Control |
|---------|----------|---------|
| < 1 : 8 | 0 | 108 |
| 1 : 8 | 0 | 32 |
| 1 : 16 | 9 | 4 |
| 1 : 32 | 21 | 0 |
| 1 : 64 | 24 | 0 |
| 1 : 128 | 25 | 0 |
| 1 : 256 | 27 | 0 |
| 1 : 512 | 13 | 0 |
| Total | 119 | 144 |

anti-complementary and hence were not included. Excluded are also 16 patients in whom only serum samples were sent.

Discussion

Measles virus infection is endemic in our country as reported earlier(13-16). The data on SSPE from India is limited. In the present study, the prevalence of SSPE has been studied in the clinically suspected cases referred to our laboratory for measles serology from various parts of India.

One of the diagnostic criterion for SSPE is the presence of measles antibodies in serum and CSF of the patients(4). It has been shown that immunoglobulins found in the CSF of these patients are locally synthesised in the brain and do not cross the blood brain barrier because the infection does not involve the meninges(1,16,17).

In the present study, it was found that 138 out of 340 clinically suspected patients had serological evidence of measles virus infection of CNS by CFT. The serum : CSF ratio was high. The serum CSF ratio of poliomyelitis has been studied in normal subjects and has been shown to be 505 : 1(18).

TABLE III—Serum : CSF Ratio in SSPE Cases

| Total | Serum : CSF ratios | | | | | |
|-------|--------------------|-------|-------|--------|--------|--------|
| | 2 : 1 | 4 : 1 | 8 : 1 | 16 : 1 | 32 : 1 | 64 : 1 |
| 129 | 6 | 10 | 27 | 47 | 34 | 5 |

No report has yet provided a baseline ratio for measles antibody in the serum and CSF of the normal population(19). The mere presence of measles antibodies in the CSF, therefore, appears to be diagnostic.

Various serological studies reported earlier from India are from a small number of patients(8-10). Broor *et al.* studied 17 cases of SSPE in Chandigarh for the presence of measles hemagglutinating antibodies in serum and CSF sample(9). A high antibodies titre was detected in the serum (1 : 64 to 1 : 1024) and CSF (1 : 4 to 1 : 128). In all their control subjects, CSF antibodies were <1 : 2 and serum antibodies ranged from 1 : 2 to 1 : 128.

In another report by Khare *et al.* from Delhi, 47 patients of SSPE were studied(10), 63.9% of these patients gave history of measles in the first two years of life. Only one patient had history of immunization against measles. The hemagglutinating antibodies to measles virus ranged from 1 : 8 to 1 : 2048 in serum and 1 : 4 to 1 : 256 in the CSF of the patients. In the control group, it ranged from 1 : 2 to 1 : 128 in serum and 0 to 1 : 2 in CSF. Incidence of SSPE from other countries has been reported to be 0.5-1 case per million population(20). These are mainly from the developed countries where measles immunization programme started much earlier.

This study indicates the problem of SSPE in India but it is not possible to comment upon the incidence of the disease as the present study is a hospital based study.

A prospective study is required in a general population to establish the incidence of SSPE, which would also reveal the impact of National Measles Immunization Programme in India.

Acknowledgements

The authors are thankful to Mrs. P. Thaney for the technical help and to all the clinicians for sending the samples.

REFERENCES

1. Pringle CR, Health RB. Paramyxoviridae. In: Principles of Bacteriology, Virology and Immunity, 8th edn. Eds Collier LH, Timbury MC. London, Edward Arnold, 1990, pp 273-279.
2. Horta Barosa K, Sever J, Zeman W. Subacute sclerosing panencephalitis; Isolation of a measles virus from a brain biopsy. Nature 1969, 221: 974-979.
3. Polna I, Yszkowski J, Kulezyeki J, Szesesniak A, Abramowicz H. Prevalence of measles antibodies in patients with SSPE in Poland in the years 1971-1978. J Neurol 1980, 224: 145-149.
4. Connolly JH, Allen IV, Hurwitz LJ, Miller JHO. Measles virus antibody and antigen in SSPE. Lancet 1967, 1: 542-549.
5. Polna I, Cendrowski W. Serological studies on the etiological role of measles like virus in SSPE. J Neurol 1977, 216: 301-307.
6. Vandvik B, Norrby E. Oligoclonal ISG antibody response in the CNS to different measles virus antigen in SSPE. Proc Natl Acad Sci 1973, 70: 1060-1065.

7. Dayan AD, Stokes MI. Immunofluorescent detection of measles virus antigens in CSF cells in SSPE. *Lancet* 1971, 1: 891-892.
8. Broor S, Pal SR, Banerjee AK, *et al.* Virological and pathological study of SSPE. *Indian J Med Res* 1975, 63: 671-674.
9. Broor S, Pal SR, Banerjee AK, *et al.* SSPE in Chandigarh. *Indian J Med Res* 1979, 70: 536-540.
10. Khare S, Kumari S, Sehgal S. Seroepidemiology of SSPE in Delhi. *Indian J Med Res* 1990, 91: 94-98.
11. Lennette EH, Schmidt NJ. Measles virus. *In: Diagnostic Procedures for Viral, Rickettsial and Chlamydial Infections*, 5th edn. Am Public Hlth Association Inc, 1979, pp 665-669.
12. Burrell CJ, Worrwick DA, Marmien BP. Serodiagnosis of virus infections. *In: Practical Medical Microbiology*, 13th edn. Eds Collee JG, Duguid JP, Fraser Ali, Marmon BP. Edinburgh, Churchill Livingstone, 1989, pp 831-841.
13. Broor S, Pal SR, Banerjee AK, Chitkara NL, Choudhury S. Seroepidemiological study of measles virus infection in and around Chandigarh. *Indian J Med Res* 1976, 64: 1740-1748.
14. Pereira SM, Beiyamin V. Measles in a south Indian community. *Trop Geogr Med* 1972, 24: 124-129.
15. Salunka SR, Natu M. Epidemiological investigation of a measles outbreak in Anjiwala. *Indian Pediatr* 1977, 14: 519-524.
16. Cutler RW, Merler E, Flammerstad JP. Production of antibody by the CNS in SSPE. *Neurology* 1968, 18: 129-132.
17. Tourtelotte WW, Parker JA, Hernden RM, Cuadros CV. SSPE: Brain immunoglobulin-G, measles antibody and albumin. *Neurology* 1968, 18: 117-119.
18. Clarke JK, Danie DS, Dick GWA. Viral antibody in CSF and serum of multiple sclerosis patients. *Brain* 1965, 88: 953-959.
19. Schultze HE, Heremans JF. Molecular biology of human proteins. *J Med Micro* 1966, 1: 735-739.
20. Jabbour JJT, Duenas DA, Server JL, Kroebbs HM, Horta-Barbosa LE. Epidemiology of SSPE: A report of the SSPE registry. *J Am Med Assoc* 1972, 220: 959-965.

NOTES AND NEWS

CME PROGRAMME ON PREVENTION AND CONTROL OF NOSOCOMIAL INFECTION IN HOSPITALIZED PATIENTS

Under the scheme for Continuing Medical Education with the Medical Council of India, approved by the Ministry of Health and Family Welfare, Government of India, a Continuing Medical Education Programme on 'Prevention and Control of Nosocomial Infection in Hospitalized Patients' is to be held at Christian Medical College, Vellore from October 29-31, 1992, in collaboration with American Association of Physicians from India and USA.

The Organizing Secretary is Dr. M.K. Lalitha, Professor of Microbiology, Christian Medical College, Vellore.