

Subacute sclerosing panencephalitis

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Summary

Subacute sclerosing panencephalitis (SSPE) is now considered to be caused by measles virus. There are four diagnostic criteria, namely the clinical picture, a characteristic EEG, serology of serum and CSF and brain histology. A register of cases in the U.K. has been kept since 1971, and up to September, 1977, ninety-six patients have been reported. The male/female ratio is 2 : 1. The disease most commonly affects children between the ages of nine and eleven years who usually have had measles at a very early age. The average delay between the measles infection and onset of SSPE was 6.8 years and of the thirty-four patients known to have died the average survival time was 1.2 years. There are still many questions about the pathogenesis and epidemiology of SSPE that have yet to be answered.

Introduction

By 1950, subacute inclusion body encephalitis of Dawson and subacute sclerosing leuco-encephalitis of van Bogaert were considered to be descriptions of the same disease and the term subacute sclerosing panencephalitis was introduced to cover them both.

Although Dawson (1933) had suggested a viral aetiology, the association with measles was not found until 1967, when Connolly *et al.* (1967) demonstrated very high levels of measles antibody in the serum and cerebro-spinal fluid of patients with SSPE and showed the presence of measles antigen in their brains by fluorescent antibody staining.

Other evidence incriminating measles includes the finding on electron microscopy of structures very like the nucleocapsids of a paramyxovirus (Tellez-Nagel and Harter, 1966) and the isolation by cultivation of an agent very similar to measles virus (Horta-Barbosa *et al.*, 1969).

Diagnosis

In order to diagnose SSPE four criteria have to be considered as follows.

Clinical course

This has been arbitrarily divided into several stages (Fig. 1). The first stage is characterized by an insidious onset of dementia and changes in behaviour and the child often presents because of a deteriorating school performance. Progression to the second stage is marked by motor dysfunction with both pyramidal and extrapyramidal signs. Myoclonic jerks are often present and convulsions may occur. In the third stage the patient becomes progressively decerebrate with increasing rigidity and a declining level of consciousness. Death usually occurs fairly rapidly but may be delayed several months or even years. This has been called a fourth stage but is really just a temporary arrest in the inexorable progress of the disease.

- Stage I. Progressive mental changes.
- Stage II. Motor dysfunction.
Myoclonic jerks.
Convulsions.
- Stage III. Rigidity.
Progressive decerebration and coma.



FIG. 1. Clinical course of subacute sclerosing panencephalitis.

Electro-encephalogram (Fig. 2).

This characteristically shows high voltage slow wave complexes across all leads. They occur regularly at 3.5- to 20-sec intervals and are often synchronous with the myoclonic jerks.

Measles serology

This is essential. The most important single diagnostic criterion for SSPE is the finding of a low CSF : serum ratio of measles antibody. In normal control patients this is between 1/200 and 1/500 (Clarke, Dane and Dick, 1965). Although increased

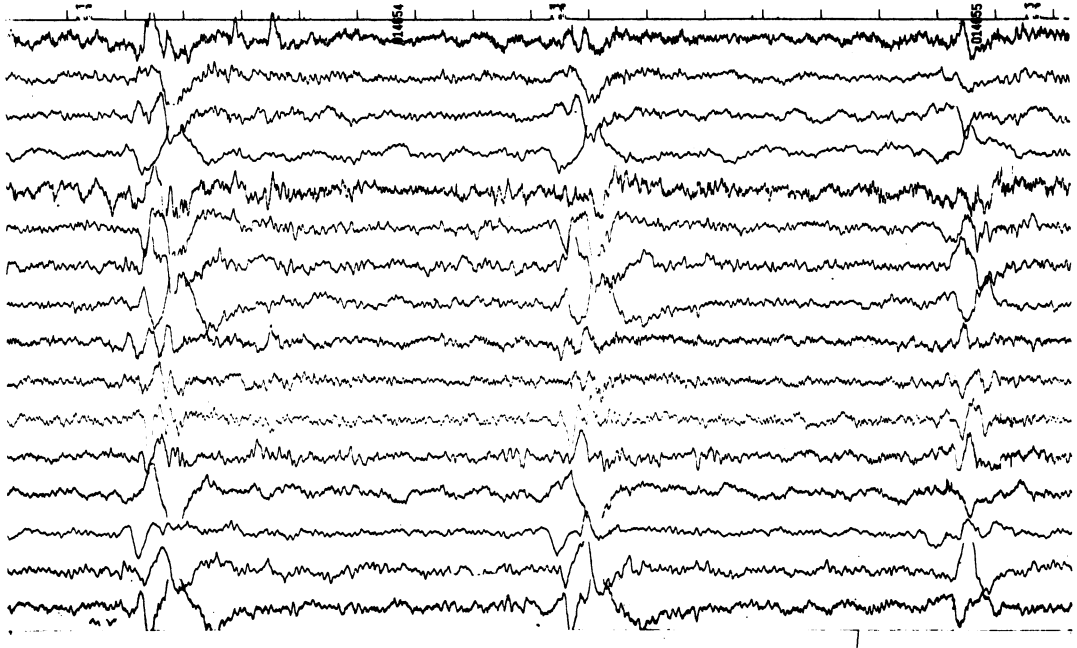


FIG. 2. EEG in subacute sclerosing panencephalitis

permeability of the blood/brain barrier occurs in some other inflammatory conditions (Sherwin *et al.*, 1963) the CSF antibody levels do not reach the values seen in SSPE, and the CSF : serum ratio remains high.

Brain histology

This is the least important criterion and it is not necessary to perform a brain biopsy in order to make a diagnosis of SSPE.

Register of cases of subacute sclerosing panencephalitis

Some of the SSPE cases observed by G.D. in Belfast followed an unusually mild epidemic of measles. This raised the question of whether an avirulent vaccine virus could perhaps act in the same way and be more likely to cause SSPE than could a virulent wild virus. The Joint Committee on Vaccination and Immunization asked G.D. to set up a register of cases of SSPE in the U.K., and notifications were requested from paediatricians, neurologists and infectious disease specialists throughout the country.

The following data have been collected during the period 1971 to September, 1977.

Sex

Sixty-four males have been reported and thirty-two females – giving a male to female ratio of 2 : 1.

Age of onset of SSPE (Fig. 3)

This was known in ninety-three cases and the average was 9.8 years. The youngest patient was aged 3 years and the oldest 27 years.

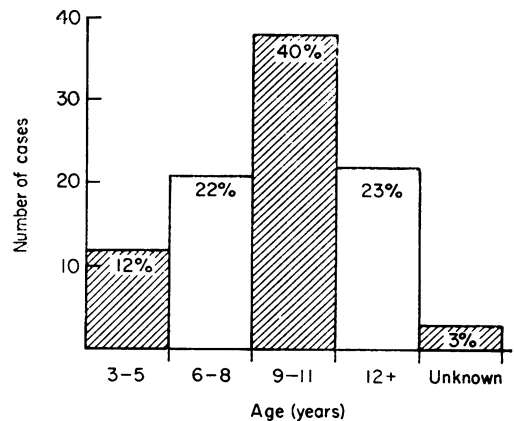


FIG. 3. Age of onset of subacute sclerosing panencephalitis (average 9.8 years).

Year of onset of SSPE (Fig. 4)

There has been little difference in the number of cases presenting each year since 1971, when the Register began to ask for notifications. The current low figure for 1977 reflects the long delay between the appearance of the first symptoms of the disease and the diagnosis being made.

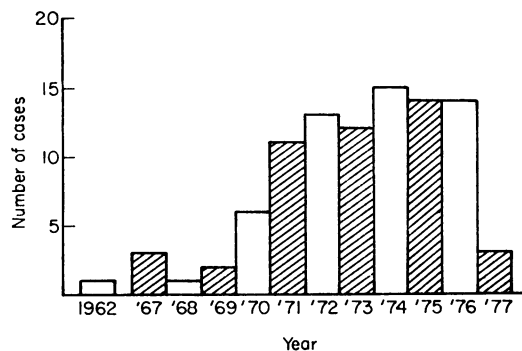


FIG. 4. Year of onset of subacute sclerosing panencephalitis.

Age at time of measles infection (Fig. 5)

There was a positive history of measles in ninety-two cases; in seventeen, the parents could not remember the date and in four cases, measles infection was definitely denied. Three of the last group of children had received live measles vaccine. The notable feature is the young age at which the patients have their attack of measles – 48% had been infected before their second birthday.

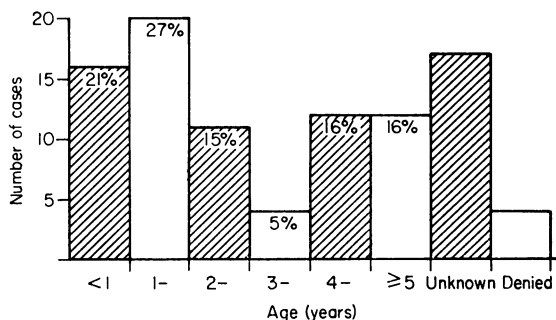


FIG. 5. Age at time of measles infection.

Delay between measles and onset of SSPE (Fig. 6)

The average delay was 6.8 years and the range was from 1.5 years to 18 years.

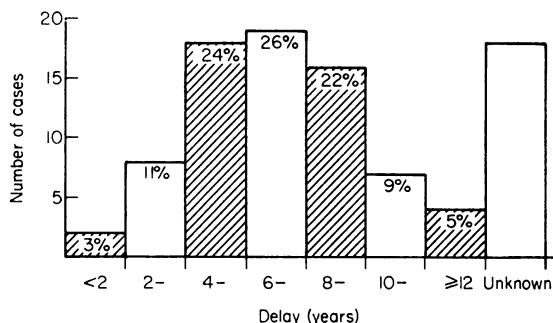


FIG. 6. Delay between measles and onset of subacute sclerosing panencephalitis (average 6.8 years).

Survival time (Fig. 7)

The date of death is known for thirty-four cases and the mean period from the onset of their disease to death is 1.2 years. Sixty-one per cent of these patients had died within one year; however, the present figures may be biased, as the Register has been collecting data for a relatively short time and some of the longer surviving patients have not yet died and are therefore not included.

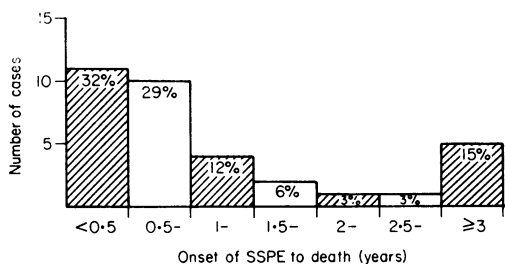


FIG. 7. Survival time in subacute sclerosing panencephalitis (average 1.2 years).

Epidemiology

Some of the cases were imported from overseas but it appears that the incidence of indigenous cases in recent years is approximately 0.2/10⁶ of the total population, or about 1/10⁶ of the child population.

Although there are three cases associated with measles vaccine there is no evidence that there is a serious risk of SSPE following vaccination. A review of a larger number of cases was recently reported from the U.S.A. by Modlin *et al.* (1977) showing that SSPE follows measles vaccine at a rate of 0.5 to 1.1 cases/10⁶ doses of vaccine issued. The rate following natural measles is between five and ten cases/10⁶ infections – thus having a risk between five and twenty times greater than that following the vaccine.

There are many epidemiological mysteries about SSPE. Racial predispositions have been suggested, for instance, in Southern Africa it has been found to affect predominantly non-whites (McDonald, Kipps and Leary, 1974), whereas in the U.S.A. it is more common in the white population (Detels *et al.*, 1973). Rural/urban differences were also found in the U.S.A. and affected children have more often been exposed to pet birds, fowl and pigeons. Why do children who develop SSPE have their measles infection so early in life? A large family size has been suggested as a possible factor and this was found in a study conducted in Israel (Soffer *et al.*, 1976). Siblings are frequently infected with measles simultaneously but familial cases of SSPE are rare.

In order to try to answer some of these questions the World Health Organization has set up a study

group to look at the international epidemiology of SSPE to which the U.K. data will be contributed.

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