Subacute Sclerosing Panencephalitis in the Cape Province

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SUMMARY

An account is given of an apparently high incidence of subacute sclerosing panencephalitis of measles in children admitted to the Red Cross Children's Hospital and Groote Schuur Hospital during the past 2 years.

The condition, although well known, was rarely diagnosed at these hospitals before the end of 1970. Since then, 15 confirmed cases have been seen over a 22-month period, representing a much higher incidence of the disease than reported from other parts of the world.

All the children were non-White and 75% were boys. None had received measles vaccine.

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The bizarre and rare disease of children, adolescents and young adults between the ages of 2 and 20 years, subacute sclerosing panencephalitis (SSPE), has a predilection for males. The cardinal features are a progessive intellectual deterioration associated with episodes of myoclonic spasms. The mental regression is at first insidious but in the older child there is a gradual falling-off in his school performance. This regression is usually the first indication that something is wrong, but in some instances the onset of the disease is heralded by convulsions or by disturbances of gait due to ataxia or hypertonicity, and is followed later by mental deterioration. As the disease progresses, speech disorders are common and dysarthria may go on to complete mutism; the intermittent myoclonic jerking becomes more general and eventually involves the whole body with increased hypertonicity and limitation of movement. The child becomes completely demented and commonly goes into a state of opisthotonus, which lasts until death.

The average duration of the illness is about one year, but death may occur within a few months of the onset of symptoms. However, there are reports that SSPE may follow a more chronic course,[1] and an occasional recovery has been claimed.[2,3] So far no drugs, including corticosteroids and antiviral agents,[4] have proved to be helpful in the management of these cases.

In Table I the findings in our 15 patients are listed. All patients exhibited mental deterioration and myoclonic movements. Speech disorders were common and there were 8 cases of mutism among those so affected. Just under half the patients showed hypertonicity and convulsions.

TABLE I. CLINICAL DATA IN 15 PATIENTS WITH SSPE

Age range	:	3 - 13 years
Race	:	9 Coloured, 6 Bantu
Sex ratio	:	11 males : 4 females
Measles before 2 years of age	:	6 of 9 where information is available

Intellectual deterioration:	15/15
Myoclonic jerking:	15/15
Speech disturbance:	13/15
Mutism:	8/15
Hypertonicity:	7/15
Convulsions:	6/15
Typical or highly-suggestive EEG:	11/15
Paretic colloidal gold curve:	10/13
Measles CF antibody levels in serum:	512 - 8192
Measles CF antibody levels in CSF:	12 - 128

DIAGNOSTIC CRITERIA

A clinical diagnosis of SSPE is supported by electroencephalography, estimation of the globulins in the cerebrospinal fluid and demonstration of measles antibodies in high titre in both serum and CSF. Where biopsy or post-mortem specimens are available, histology, electron microscopy, the demonstration of viral antigen by fluorescent antibody and even virus isolation have helped to confirm the association of this disease with measles.

Electro-encephalography

The EEG in SSPE is characteristic and shows periodic bursts of high-amplitude slow waves which coincide with the myoclonic episodes.[5] It is claimed that if enough tracings are made during the illness, the characteristic pattern will always be seen. In our series it was, in most cases, only possible to take a single tracing from each of the 15 patients, but in 11 instances the results were typical or highly suggestive.

Globulins in the CSF

In a patient with SSPE, the CSF protein content and cell counts are usually within normal limits, but there is

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an increase in globulins with a first-zone (paretic) type response in the Lange colloidal gold test. The latter test was performed in 13 of our patients and 10 showed a positive result.

Demonstration of Measles Antibodies in Serum and CSF

The most important of the readily available laboratory investigations in SSPE is the demonstration of measles antibodies in high titre in both serum and CSF.[6]

In the encephalitis of acute measles, high levels of measles antibodies are found in the serum, but in the CSF, if present at all, they are usually demonstrable only in the undiluted or half-diluted fluid. By contrast, in the CSF of SSPE patients the antibody levels detected by complement fixation with measles antigen are always elevated and may rise as high as 256.

In our series, measles antibody was demonstrated in the CSF of all 15 patients and it varied in titre from 12 to 128 with a geometric mean of 41. The complement-fixing measles antibody in the sera of the 15 SSPE patients was generally high, and varied from 512 to 8 192 with a geometric mean of 3 497. In 4 of these patients more than one serum sample was received and in these the antibody levels had not fallen over periods of 2 - 5 months.

The complement-fixing measles antibody titre in the serum of patients with acute measles is usually high, but after the recovery period the serum antibody level falls rapidly. In SSPE, however, the serum antibody levels remain high and may even rise;[7] when these fall, this occurs slowly, in contrast to the sharp falling-off after acute measles.[8]

Brain Biopsy

For completeness, it is important to note that histological examination of biopsy material from a case of SSPE may show a panencephalitis characterised by perivascular infiltrations of inflammatory cells and the presence of inclusion bodies in neuronal and glial cells.[9] Fluorescent antibody techniques will demonstrate measles antigen within the cells in the biopsy material,[9,10] and electron microscopy may show inside the affected cells tubular structures similar to those of the nucleoprotein of paramyxoviruses.[10,11] In a number of laboratories a virus has been isolated from the brain,[12-14] but the ultimate characterisation of the strain of virus recovered has still to be reported.

EPIDEMIOLOGY

In sharp contrast to our experience over the previous 15 years we have seen 15 cases of SSPE during a recent 22-month period. The patients came from a population of 6,7 million living in widely scattered areas of the Cape Province, and which include the homeland territories of the Transkei and Ciskei. This gives an annual incidence rate for the Cape Province of at least 1,2/million of the population. The significance of this estimate may be better appreciated when compared with the reported incidence rates in other countries, which are shown in Table II. It will be seen that the rate for the Cape Province is astonishingly high, and even allowing for undoubted under-reporting, a feature mentioned in the paper from Finland,[15] this is still 3 times greater than in Finland and 10 times greater than in the USA.

TABLE II. COMPARATIVE INCIDENCE OF SSPE

Country	Period	No. of cases	Cases of SSPE/ million/year
USA[15]	10 years	219	0,12
Finland[17]	10 years	20	0,4 - 0,5
Great Britain[16] ...	10 years	20	?
South Africa (Cape Province only) ...	22 months	15	1,2

It is believed that these 15 patients do not represent the total number of cases of SSPE in the Cape Province. The area is served by the teaching hospitals of another medical school besides our own, as well as by several large regional hospitals and many smaller ones. As yet, we have little information about any patients with SSPE who may have been admitted to these centres during the period under review. Further, the disease is not notifiable. Thus the true incidence for the whole of the Cape Province may be considerably higher than our present estimate suggests. On the other hand, patients with clinical diagnostic problems are frequently referred to our Cape Town teaching hospitals for consultation, and such patients come from the whole of the Province. It is also possible that some practitioners in other hospitals are aware of our interest in SSPE and accordingly have directed their patients to us.

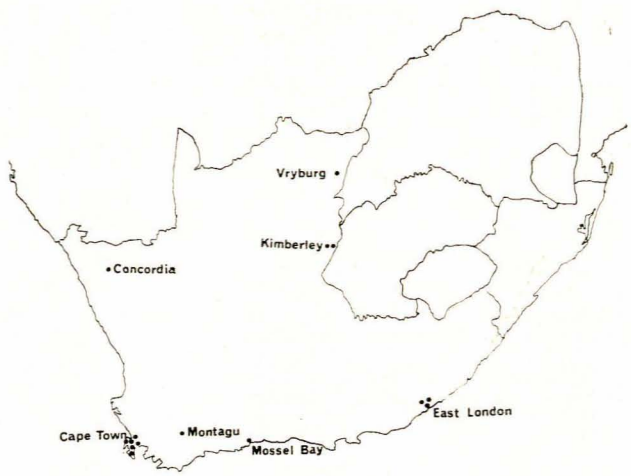

Fig. 1. Regional distribution of 15 cases of SSPE in the Cape Province.

Fig. 1 indicates the distribution of the places of residence of the 15 patients; the clusters around Cape Town and

East London probably reflect the presence of specialist hospitals serving large surrounding areas. No information or figures regarding SSPE in other provinces of the Republic, South West Africa or Rhodesia are presently available to us.

Our 15 patients varied in age from 3 to 11 years, with a preponderance of 11 boys to 4 girls. This gives a ratio of 2,8 : 1 which is very similar to that in the USA of 3,3 : 1 recorded by Jabbour *et al.*,[16] and 2,0 : 1 by Dick.[17]

All of our 15 patients were non-White, 9 being Coloured and 6 Bantu. Nearly all were from underprivileged sections of their communities and from families of low economic status. It was not always easy to establish an accurate clinical history for each child prior to the onset of the manifestation of SSPE. There was, however, a recorded history of preceding measles infection in 9 patients, and in 6 of these the infection occurred before the end of the second year of life. This early age of first infection is noted in several reports from other countries. In the series reported by Jabbour and his colleagues,[16] 55% of the patients had had measles before the age of 2 years.

In our series there is no indication that the first infection with measles was related to an epidemic year or to a period of high epidemicity of a neurovirulent strain of measles virus, as the first infections in the 9 patients giving a history of previous measles were spread over a period of 9 years. There is no information available regarding the severity or otherwise of the antecedent attack of measles. None of the patients had received either inactivated or live measles virus vaccine.

DISCUSSION

This 22-month experience with SSPE in the Cape Province draws attention to 15 children under 13 years of age from a total population of 6,7 million giving a high incidence rate of 1,2 million/year. As they were all either Coloured or Bantu patients, the disease can no longer be regarded as rare in this section of the population of the Cape Province.

It is not yet possible to say with certainty that these observations indicate a recent real increase in the incidence of this syndrome. Where serious or fatal complications of an otherwise relatively benign virus disease appear to occur in one area more frequently than in others, it is important to gather all the relevant available epidemiological, social and serological data which may lead to a better understanding of the geographical distribution of the cases and of the pathogenesis of the disease.

Several workers have indicated that the viruses isolated from the brains of patients with SSPE have features which distinguish them from the common wild-type measles virus in tissue culture, and that attenuated or atypical strains may be responsible for the lesions in the central nervous system. With this thought in mind, the widespread use of live attenuated measles virus vaccine demands very careful scrutiny for some years to come. Although vaccination against measles may prove to be effective in many countries, its use in the population groups in which we have seen an undue number of patients with SSPE may require special consideration before being applied as a general public health measure. It is essential to know that these children are not in some way immunologically deficient to the extent that they are incapable of reacting effectively to measles virus infection as most of the world's children are able to do.

In our series of patients none had received inactivated or live measles virus vaccine. Despite what is said in the previous paragraph, it is hoped that it will be shown that early vaccination of these population groups will also protect them from these disastrous late consequences of the first infection with measles virus.

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