

# SUBACUTE SCLEROSING PANENCEPHALITIS

## A CASE REPORT

W. C. TING C. T. TAN

N. C. GONG

### INTRODUCTION

Subacute sclerosing panencephalitis (SSPE) is a progressive fatal disease of the central nervous system. It is rare and commonly affects children and young adults. The disease has characteristic clinical, EEG, measles serology and brain histological features. It is now considered to be caused by measles virus (Connolly, *et al.* 1967). We report here two typical cases seen in the University Hospital, Kuala Lumpur, and also briefly discuss the disease.

### CASE REPORT

#### Case 1

A 14 year old boy from Rawang, Selangor was brought in by his parent with the complaint of unsteadiness in gait and tendency to fall to the left for the last 4 months. During that period, he also developed frequent jerky movement of the left upper and lower limbs and the parents noted progressive deterioration of his mental state. He spoke rarely and often insensibly. He was totally unable to cope with the school work by the time of admission. There was also a change in his personality from a helpful and obedient boy to being sometimes abusive using foul language. A day before admission, he had an episode of generalized tonic clonic convulsion.

There was no history of headache, vomiting or fever. His appetite continued to be fair. He was able to feed and clothe himself. There was no urinary and faecal incontinence. The only significant past history was measles at the age of three years. There was no family history of similar illness.

The father was a construction worker and the mother was a dulang washer.

The patient was not cooperative with the physical examination. He remained quiet most of the time when asked questions. When tested on calculations he was unable to perform more than simple additions. The speech was fluent and he was able to name simple objects. The right optic disc margin was blurred. The other cranial nerves were normal. Myoclonic jerks occurred periodically over the left upper and lower limbs. The left upper limb also showed cog-wheel rigidity. He was able to move all four limbs. The reflexes were equal over both sides with bilateral flexor plantar response. The patient was normal in testing for painful and proprioceptive sensation. He was unsteady with walking, not particularly falling to any side. The BP was 130/80 mmHg. No abnormality was detected in other system.

Investigations showed normal: full blood count, blood urea, glucose, electrolytes, calcium, phosphate and magnesium. Urine microscopy and 25 hours urine copper excretion was also normal. Serum VDRL was negative. The serum antibody titre to measles was raised at 1/128. The ECG, skull xray were normal. Lumbar puncture showed a pressure of 30 cm H<sub>2</sub>O and CSF examination revealed no cells, protein 20 mg%, sugar 61 mg%, no micro-organism and a paretic large gold curve of 321 000000. The CSF antibody titre to measles antigen was raised at 1/32.

Electroencephalogram (Fig. 1) showed that background alpha activity at 9-10 c/s is present posteriorly with 5-6 c/s theta waves. Very high voltage delta waves at 1.5-3 c/sec sometimes with generalised spikes occur symmetrically and synchronously with maximal voltage anteriorly. Intermixed with this are periodic bursts of generalised spike or sharp waves with slow waves occurring every 10-20 seconds with left upper limb jerks and bilateral deltoid electromyogram (EMG) activity. This periodic complex was often followed by a period of suppression in cerebral activities. Photic driving was irregularly seen over both sides.

---

C. T. Tan

MBBS (Melb.) MRCP (UK)

W. C. Ting

MBBS (Sing.), MRCP (UK), MRCP (Ire.), FRACP

N. C. Gong

MBBS (Mal.), M. Med. (Sing.), MRCP (UK)

Department of Medicine, Faculty of Medicine,  
University of Malaya, Kuala Lumpur, Malaysia.

---



Fig. 1 EEG of Case 1. Channels 15, 16 record the EMG activities of right and left deltoid muscles respectively.

### Management

The patient was given clonazepam 1 mg b.d. which reduced his myoclonic jerks substantially. He was also given diphenylhydantoin 200 mg daily for the generalized convulsions. The patients failed to come back for his follow-up.

### Case 2

A 14 year old Chinese student from Temerloh, Pahang, was previously well with normal developmental milestone and average performance in class. About three month before admission, patient was noted to have a gradual onset of progressive jerky movements of right upper limb which later involved the left upper and both lower limbs in a period of a month. These movements were present during wakeful hours but ceased with sleep. At the same time, he was noted to have speech difficulty and progressive intellectual deterioration. He was also noted to smile and laugh inappropriately.

There was no relevant past history of note. There was no definite history of childhood measles and no family history of similar illness. The patient has been looked after by his aunt who was a pig farmer.

On examination, the patient was conscious and alert. His speech consisted only the monosyllables and was often unintelligible. Periodic myoclonic jerks was seen involving all four limbs but more marked on the right arm. There was choreoathetoid

movements noticed in both upper limbs with grimacing of the mouth. The cranial nerves were otherwise normal. The tone was generally increased with non-sustained patellar and ankle clonus. The reflexes were hyperactive with flexor plantar response. He could move all his four limbs. The pin prick sensation was intact; other modalities of sensation could not be tested. The BP was 110/70 mmHg. Other systems were normal.

Investigations showed normal: full blood count, serum urea, electrolyte, glucose, urine microscopy, 24 urine copper excretion and chest x-ray. The serum measles antibody was raised at 1/256. The CSF showed no WBC, RNC, sugar 64 mg%, protein 9 mg% and no micro-organism. CSF VDRL was negative, colloidal gold curve at 1110000000. The CSF measles antibody titre was raised at 1:32.

Electroencephalogram showed asymmetry of the background activities over the two hemisphere although both sides were markedly abnormal (Fig. 2). The right side consisted of beta activity at 16 c/s with delta wave activities at 1½-3 c/s seen mainly anteriorly with intermixed theta range waveforms. The left hemisphere showed little beta range activities. The 1½-3 c/s delta waveform occurred extensively with some theta range activities. Photic driving was also better seen on the right occipital area. Frequent multifocal discharges consisted of spikes and sharp waves were seen. In addition there were



Fig. 2 EEG of Case 2. Channel 15 and 16 record the EMG activities of the right and left deltoid muscles respectively.

periodic stereotyped generalized burst of high voltage delta wave at 1-2 c/s with left sided accentuation occurring every 3-6 seconds. These complexes were accompanied by bilateral EMG activities from both deltoid muscles.

### Management

Clonazepam 1 mg bd was administered. However, patient failed to turn up for follow up.

### DISCUSSION

Subacute sclerosing panencephalitis was first described by Dawson (1933) and later van Bogaert (1945). The former described under the name of subacute inclusion body encephalitis while the latter called it sclerosing leuco-encephalitis. However, the present term is now generally used.

Subacute sclerosing panencephalitis as a slow virus infection from measles is now firmly established. In 1965 (Bouteille *et al.*), the presence of the viral structure resembling viruses in the brain cells of patients with SSPE was demonstrated. Conally *et al.*, (1967) reported markedly increased measles antibody titres in every patient with SSPE so examined.

The mean age of onset is 7.2 years (Jabbour *et al.*, 1972) and the oldest reported was 32 years (Cape *et al.*, 1973). A history of measles is usually but not always found and majority had it before

the age of two. The incidence of the disease is higher in the rural than urban population (Halsey and Modlin, 1976). It is interesting that our two cases are also from the rural environment.

The clinical manifestations resemble a diffuse degenerative disease. The onset is insidious and the disease is progressive. Progressive mental changes and myo-clonic jerks occurring every 5-10 seconds are the early characteristic presentation. Other symptoms and signs include pyramidal and extrapyramidal rigidity, choreoathetosis, regressive speech, drooling, tremor, incoordination of trunk and limbs, convulsions, visual impairment, optic atrophy and choreoretinitis. Jabbour *et al.* (1969) has divided the clinical course into four stages (Fig. 3). Our two patients were in Stage II at the time of presentation. Unfortunately, they defaulted in the follow up.

#### Relative distributions in containers (%)

- Stage I Progressive mental changes.
  - Stage II Motor dysfunction  
Myoclonic jerks  
Convulsions
  - Stage III Rigidity  
Progressive decerebration and coma
- Death ← --- Arrest (Stage IV)

Fig. 3. Clinical course of subacute sclerosing panencephalitis (Bellman *et al.*, 1978).

Death is usually due to vasomotor failure or supervening infection. Most patients die in 3 to 24 months from the onset of illness but some cases of recovery or arrest of the disease has been reported.

Raised serum antibody titre to measles is a useful simple and confirmatory test. The antibody levels are usually well above those seen in convalescent phase of the acute measles and above those of measles encephalitis. The measles antibody is usually demonstrable in spinal fluid; usually at a lower titre than in the serum. There is often no pleocytosis in CSF, the protein and glucose are normal. The colloidal goldcurve may show a first zone rise. An enormous relative increase in gammaglobulin in the spinal fluid is a typical finding, more specific is a oligoclonal gammopathy, both in serum and in spinal fluid, presenting in the form of M-gradients in the cathodal field in electrophoresis.

The EEG usually show diffuse dysrhythmia with slowing of the background activities. The characteristic feature is the presence of periodic generalized high amplitude slow wave complexes synchronous with the myoclonic jerks (Markand & Panszi, 1975). The severity of the EEG changes is not a reliable indicator for the prognosis.

The brain at autopsy is frequently normal in weight and gross appearance. Microscopically, there is widespread in neuronal loss, glial sclerosis, perivascular infiltration with mononuclear cells. Acidophilic intranuclear inclusion bodies are found in both neurone and glial cells but vary greatly in number. It is not necessary to perform a brain biopsy to make a diagnosis.

The pathogenesis is still not clearly understood. Byrington and Johnson (1975) found that intracerebral injection of mantly SSPE strain into Hamsters produce a chronic encephalitis if injected into weaning animals of 21-22 days of age. In contrast, newborn and adult animals died from an acute encephalitis unless immunosuppressed. The finding suggest the age factor in the entry of measles virus that is important; perhaps related to the immaturity of the brain or immune system. This correlates well with the clinical observation that SSPE patients usually contact their primary measles illness below two years old.

Treatment has been unsatisfactory. Steroids in high doses (Parker, *et al.*), antiviral agents (Freeman,

1969, Haslam, *et al.*, 1970) and interferon inducers (Leavitt *et al.*, 1971) have been generally unsuccessful. Clonazepam may reduce myoclonic jerks.

Modlin (1976) has found that the risk of SSPE following measles vaccination is 0.4 to 1.3 cases/10<sup>6</sup> population versus the risk following natural measles of 5.2 to 9.7 cases/10<sup>6</sup> population. Thus, immunization seem to have a partial protective effect. Furthermore, it is hoped that when the population becomes completely immunized against measles virus; measles and subsequently SSPE will completely disappear.

## SUMMARY

Two Malaysian boys of Chinese origin who satisfy the necessary criteria of subacute sclerosing panencephalitis are reported. A brief description of the symptomatology, epidemiology, laboratory finding, pathology, pathogenesis and treatment of the illness was also given.

## ACKNOWLEDGEMENT

We wish to thank Puan Rohani for typing the manuscript.

## REFERENCES

- Bellman, M.H., Dick, G. (1978) Subacute sclerosing panencephalitis, *Postgraduate Med. J.*, 54, 587-590.
- Bouteille, M., Fontaine, C., Vendrenne, C. and Delarus, J. (1965), Sur un cas d'encephalite subaigue a inclusions. Etude anatomoclinique at ultrastructurale, *Rev. neurol.*, 118, 454-458.
- Byrington, D.P. and Johnson, K.P. (1972) Experimental subacute sclerosing panencephalitis in the hamster - correlation of age with chronic inclusion-cell encephalitis, *J. Infec. Dis.* 126, 18-26.
- Byrington, D.P. and Johnson, K.P. (1975) Subacute sclerosing panencephalitis virus in immunosuppressed adult hamster, *Lab. Invest.*, 32, 91-97.
- Cape, C., Martinez, A., Robertson, J.T., Hamilton, R., Jabbour, J.T. (1973) Adult onset of subacute sclerosing panencephalitis, *Arch. Neurol. (Chic.)*, 28, 124-127.
- Conolly, J.H., Allen, I., Hurwitz, L.J. and Millar, J.H.S.D. (1967), Measles virus antibody and antigen in subacute sclerosing panencephalitis, *Lancet*, 1, 542-544.
- Dawson, J.R. (1933) Cellular inclusions in cerebral lesion of lethargic encephalitis, *Amer. J. Path.*, 9, 7-15.
- Freeman, J.M. (1969) Treatment of Dawson's encephalitis with 5-bromo-2'-deoxyuridine, *Arch. Neuro.*, 21, 431-434.
- Halsey, N.A. and Modlin, J.F. (1976) Subacute sclerosing panencephalitis. Epidemiologic data on 375 retrospective cases and a preliminary report on a case control study. Presented at 25th Annual EIS Conference, April 5-9.

- Haslam, R.H.A., McQuillen, M.P. and Clark, D.B. (1969) Amantidine therapy in subacute sclerosing encephalitis, *Neurology*, 19, 1080-1086.
- Jabbour, J.T., Garcia, J.H., Lemmi, H., Ragland, J., Duenas, D.A. and Sever, J.L. (1969) Subacute sclerosing panencephalitis. A multidisciplinary study of eight cases, *J. Amer. Med. Ass.*, 207, 2248-2254.
- Leavitt, T.J., Merigan, T.C. and Freeman, J.M. (1971) Haemolytic uraemic like syndrome following polycarboxylate interferon induction, *Amer. J. Dis. Child.*, 121, 43-47.
- Markand, P.N., Panszi, J.G. (1975) The electroencephalogram in subacute sclerosing panencephalitis, *Arch. Neurology*, 32, 719-726.
- Modlin, J.F., Jabbour, J.T., White, J.T. and Halsey, N.A. (1976) Epidemiologic studies of measles, measles vaccine, and subacute sclerosing panencephalitis, *Paediatrics*, 59, 505.
- Parker, J.C., Klintworth, G.K., Graham, D.G., Griffith, J.F. (1970) Uncommon morphologic features in subacute sclerosing panencephalities (SSPE), *Amer. J. Path.*, 61, 275-291.
- Van Bogaert, L. (1945) Une leucoencephalite sclerosante subargue, *J. Neurol. Neurosurg. Psychiat.*, 8, 101-120.