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SUBACUTE SCLEROSING PAN-ENCEPHALITIS

A REVIEW OF 17 CASES WITH SPECIAL REFERENCE TO CLINICAL DIAGNOSTIC CRITERIA

BY

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The purpose of this communication is to review 17 cases of subacute sclerosing pan-encephalitis and to draw attention to a clinical feature which we believe to be pathognomonic.

Greenfield (1950) united under this term those forms of subacute encephalitis previously described by Dawson (1933, 1934), Van Bogaert (1945), Pette and Döring (1939), Brain, Greenfield, and Russell (1948), and Lhermitte (1950).

Study of our patients reveals (1) that certain clinical features are usually present which, when recognized, indicate the diagnosis; (2) that certain investigations (electroencephalogram and the Lange colloidal gold curve in the spinal fluid) are of equal diagnostic value; and (3) that some clinical features (particularly those of raised intracranial pressure and focal or lateralized neurological signs such as hemiplegia) can involve the risk of misdiagnosis.

Review of the Main Features

The clinical evolution of this disease has been well reviewed by Foley and Williams (1953). The first symptoms in this series were usually intellectual deterioration and degradation of personality. Less often episodic staggering, clumsiness (symmetrical or lateralized), or some other kind of seizure, or

TABLE
DETAILS OF 17 CASES OF

Case No.	Age (yr.) at Onset and Sex	Early Staggering Episodes	Episodic Spasms	Ocular Symptoms	Focal or Lateralized Symptoms	Lange Curve (C.S.F.)
1	6 M	–	Obvious 5 mth. from onset	Nystagmus (horizontal)	Clumsy left limbs	3221000000
2	13½ M	+	Obvious 6 mth. from onset	Papilloedema	—	5543210000
3	11 F	–	—	–	Left hemiplegia	5555543210
4	10 F	+	Obvious 1 mth. from onset	—	—	5555543210
5	10 M	+	Obvious 2 mth. from onset	—	Right hemiparesis	5432110000
6	10 M	Unknown	Obvious 9 mth. from onset	—	Right hemiplegia	5555432110
7	7 F	–	Obvious 1 yr. from onset	Optic neuritis produced transient blindness	—	5554321000
8	13 M	–	Detected in right fingers 3 mth. from onset (later obvious)	Sudden blindness at onset; disc margins blurred	Left hemiplegia after stroke at 2 years	5332100000
9	11 M	–	Detected in right fingers 1 mth. from onset	Nystagmus (horizontal)	—	5543300000
10	8½ M	–	Detected in right big toe (never elsewhere) 5 mth. from onset	Nystagmus (horizontal)	—	5555532100
11	10 M	+	Obvious 3 mth. from onset	—	—	1111000000
12	10 F	–	Detected in fingers and toes 3 wk. from onset	—	—	5444321000
13	15 M	+	Obvious 3 mth. from onset	—	—	5432200000
14	12½ F	+	Detected in left fingers 3 mth. from onset	—	Left hemiparesis	5555432110
15	10½ F	+	—	Papilloedema	—	5554321100
16	5½ F	+	Epilepsy partialis continuans gave place to typical repetitive spasms	—	Left hemiparesis	4332100000
17	5 M	+	Obvious 3 mth. from onset	—	Right hemiplegia	5532110000

transient blindness or occasional headache was the first symptom. *Grand mal* fits (generalized or with focal features) occurred in 4 patients (Cases 1, 8, 9, 10), and focal myoclonic jerking in the form of epilepsy partialis was continuous in 3 patients (Cases 3, 16, 17). Unusual kinds of seizure took the form of occasional irregular sudden or explosive momentary flinging of the arms above the head where they remained 'frozen' for several seconds before relaxing (Case 15); and periodic stereotype movement sequences lasting some 90 seconds in which the left elbow would gradually flex during the crescendo phase and extend during the diminuendo, quivering of the left hand ending the motor act (Case 13). The commonest kind of seizure was a short periodic, repetitive spasm seen in all but two patients (Cases 3 and 15). These spasms are described in some detail below.

As a rule, spastic quadriplegia eventually develops; but focal neurological deficits such as incoordination, tremulousness, and hemiplegia may appear long before the terminal stage is reached.

A paretic Lange colloid gold curve in the spinal fluid is an almost constant finding in this disease (Szliwowski and Cumings, 1961) and was present in all our cases.

Characteristic high-voltage paroxysms of slow waves occurring at regular intervals several times a minute at electroencephalography (Radermecker, 1949; Cobb and Hill, 1950) were present at some stage of the illness in all our cases. Electroencephalographic studies were made in all save two cases by Dr. G. Pampiglione, as were polyelectromyographic records in the manner he has described (Pampiglione, 1959). The relation of the EEG findings to the episodic spasms and antispasms will form the basis of another communication.

The histological picture of the inflammatory lesion ranges from that mainly (or even exclusively) involving the grey matter of the cerebral cortex, basal ganglia and brain-stem, eosinophilic inclusions being present in the cytoplasm or nucleus of some nerve cells (Dawson's subacute inclusion encephalitis), to that involving white matter extensively, glial proliferation being greater and inclusion bodies absent (Van Bogaert's subacute sclerosing leuco-encephalitis). In six of our cases brain biopsy was performed and in four cases necropsy, the inflammatory changes falling within the range of these variations outlined.

The Periodic Spasms

The occurrence of myoclonus and of repetitive stereotyped, involuntary movements are widely recognized to be a feature of this disease. We describe a particular type of spasm here because we believe it to be pathognomonic of this disease, and quite unlike the momentary, explosive jerks of

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First Symptoms	Fate	Comments
Dementia; disturbed behaviour; clumsiness	Death 2 yr. from onset	
Dementia; disturbed behaviour; headaches	Death 20 mth. from onset	Confirmed at necropsy
Dementia; disturbed behaviour; epilepsy partialis continuans	Death 5½ mth. from onset	Confirmed by brain biopsy; focal continuous left-sided myoclonus showed repetitive cessation
Dementia; disturbed behaviour; staggering episodes	Still alive 6½ yr. from onset	
Dementia; staggering episodes	Death 4 yr. from onset	Confirmed at necropsy
Dementia; hemiplegia	Unknown	No follow-up
Transient blindness; dementia	Death 18 mth. from onset	Confirmed by brain biopsy
Sudden blindness; dementia	Death 6 mth. from onset	A congenital syphilitic; confirmed at necropsy
Headaches; dementia; disturbed behaviour	Death 8 mth. from onset	
Incoordination; dysarthria; dementia	Death 3 mth. from onset	Confirmed by brain biopsy
Headaches; dementia	Death 20 mth. from onset	Confirmed by brain biopsy and at necropsy
Disturbed behaviour; dementia	Still alive	Confirmed by brain biopsy
Staggering episodes; dementia	Death 3 mth. from onset	Confirmed at necropsy
Dementia; disturbed behaviour	Still alive	
Dementia; disturbed behaviour	Still alive	Suture diastasis; CSF pressure raised at ventriculography
Drop seizures; dementia; myoclonus (left-sided)	Death 5 mth. from onset	
Hemiplegia; staggering episodes	Still alive	

myoclonus, which may reflect many different kinds of disease. These spasms had, in this series, such clear-cut features that their significance could be appreciated and correct diagnosis made with near certainty, sometimes within a matter of seconds of seeing the patient.

Tempo. One feature of these spasms is their tempo. Each spasm begins with instantaneous shock-like abruptness typical of the myoclonic jerk; but it does not end as suddenly as it begins. Unlike the myoclonic jerk it ceases gradually, taking much longer to fade than to appear, and persisting usually for at least one second. The involuntary movement produced is thus arrested, 'frozen' or 'hung-up' for several moments, before it gently melts away. This characteristic feature, which is one clue to the diagnosis, can be seen in those early and least obtrusive localized spasms which jerk but a single small limb segment (perhaps a finger or toe as in Cases 8, 9, 11, 12, and 14) through no more than a few degrees. It is more easily recognized when many joints are involved in jerks of much greater violence. Sometimes these spasms can be provoked by stimulation such as a loud noise.

Repetitiveness. Another characteristic feature of these spasms is repetitiveness. When the disease is well advanced, the spasms are likely to be repeated at fairly constant intervals of perhaps two to six times a minute, but in the early stages of the illness, rhythmic periodicity may be lacking (as in Cases 12 and 14). Prolonged watching, however, may reveal (as in Cases 8, 9, 10, and 12) the tell-tale tempo of a 'hung-up' spasm and, perhaps, the tell-tale repetitiveness revealed by a train of several spasms repeated at more or less regular intervals.

Impediments to Recognizing the Spasms

Certain events sometimes hamper the recognition of these spasms.

(1) The spasms are more easily detected in a quiet inactive patient. In an active child the spasms may declare their presence by episodic staggering or even falling (as in Cases 2, 4, 5, 11, 13, 14, 15, 16, and 17) and sometimes by episodic manual clumsiness when one or both hands are involved. These episodes may be mistaken for akinetic seizures which, indeed, may be the responsible cause in some cases. If they are due to the episodic spasms now under consideration, then failure to recognize them for what they are means missing a valuable diagnostic clue.

(2) Sometimes repetitive spasms are almost concealed by apparently voluntary movements which are themselves repetitive. Thus an affected child lying in bed may show commonplace restlessness; but this very restlessness may be repetitive, recurring at fairly regular intervals several times a minute. Careful observation may show that the repetitive spasms, described above, are embedded in this repetitive restlessness which tends to hide them. Repetitive actions are sometimes more highly organized than simple restlessness; thus repetitive yawning was seen in Case 13 and repetitive whistling in Case 11.

(3) In the later stages of the disease the spasms are likely to become restricted in range and finally to disappear as advancing spastic paralysis dominates the scene.

Periodic Antispasms

Repetitive, short-lived akinetic episodes, involving one or many limb segments are sometimes an early feature of this disease which is more prominent than the spasms described; indeed, they may precede the recognition of repetitive spasms (Cases 14 and 15). These antispasms produce postural lapses which can be seen, for example, when the arms are outspread (perhaps with a reward balanced on the dorsum of the fingers which the child receives if the posture is kept steady till 30 is counted). The limb involved may be seen to bob repetitively several times a minute. This repetitive sagging of the limb in Case 15 was shown by Dr. G. Pampiglione to coincide with the repetitive slow wave paroxysm recorded by electroencephalography: and it was his electroencephalogram and poly-electromyogram observations that led us recently to seek clinical evidence of antispasms in this disease. Repetitive cessation of 'epilepsy partialis continuans' in Cases 3 and 17 was likewise shown by Dr. G. Pampiglione to coincide with these slow-wave paroxysms.

Unusual Features

Ocular Symptoms. Papilloedema and other evidence of raised intracranial pressure was reported by Tibbles, Donohue, Kofman, and Prichard (1964) in one of their series of 14 cases and disc blurring suggestive of papilloedema in another. Such findings, particularly when associated with dementia and epilepsy, are likely to provoke the suspicion that an intracranial mass is responsible. In this series, papilloedema was present in Case 2 and in Case 15 in association with suture diastasis and raised intracranial pressure shown at ventriculography, which revealed no obstruction to cerebrospinal fluid flow.

Optic neuritis was probably an early feature in two patients. Thus in Case 7 the right eye suddenly became blind one week after it had been struck by a

tennis ball. Within another week both eyes were blind; but four weeks later the child was back at school where she was soon noted to have become rather dull and stupid. When admitted a year later bilateral primary optic atrophy was present, together with bilateral pigmentary macular degeneration. In Case 8, a congenital syphilitic boy who at 2 years had a stroke which left him hemiplegic and epileptic, blindness developed over some seven days after striking the head in a convulsion at the age of 13 years.

Horizontal nystagmus was present in 3 patients (Cases 1, 8, and 9).

Focal Symptoms. Neurological signs in this disease are not always symmetrical. Failure to appreciate this fact can hamper diagnosis. Focal neurological signs appeared in some of the 14 cases of Tibbles *et al.* (1964), and in our series they were prominent in 8 patients. In Case 8 hemiplegia was the aftermath of a stroke sustained 11 years previously; but in 7 patients hemiparesis or hemiplegia was a new and early symptom (Cases 3, 5, 6, 8, 14, 16, and 17).

Discussion

Subacute sclerosing pan-encephalitis is not as rare a disease as a recent annotation (*Lancet*, 1963) would suggest. Even in 1959, 100 cases were reported from Europe alone at the symposium on encephalitis (Antwerp) of that year. The disease should always be considered in the differential diagnosis of dementia developing in children over the age of 6 years. It should be strongly suspected when momentary episodic staggering and/or episodic manual clumsiness is an added symptom. Diagnosis can be made with near certainty if seizures producing episodic spasms of the kind described above are witnessed. Diagnosis of the disease should not be dismissed because of the occurrence of headaches, papilloedema, optic neuritis, or the development of asymmetrical neurological defects such as hemiplegia.

Confirmation of diagnosis by electroencephalography may not always be forthcoming in the early stages of the disease; but in this series a paretic Lange curve in the spinal fluid (the Wassermann reaction being negative) was always present even in the early stages.

Summary and Conclusions

Seventeen cases of subacute sclerosing pan-encephalitis are reviewed. The criteria for diagnosis in all cases were the clinical and electroencephalographic findings, together with a paretic Lange curve in the spinal fluid. Confirmation was provided by brain biopsy in 6 cases and by necropsy in 4 cases.

Seizures producing periodic spasms of a characteristic kind were present in all but 2 cases. Two features of these spasms (tempo and repetitiveness) are described in some detail because we believe them to be pathognomonic of the disease and a common and important diagnostic clue.

Seizures producing periodic antispasms are another clinical feature that was observed only in the later cases of this series after our attention had been drawn to them by Dr. G. Pampiglione.

Ocular symptoms (papilloedema, optic neuritis, and nystagmus) and asymmetrical neurological symptoms (particularly hemiplegia) were features in some cases.

Electroencephalogram and poly-electromyogram findings are not here considered. These tests, made by Dr. G. Pampiglione in all save 2 cases, will be reported by him in a separate communication.

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