ENCEPHALITIS PERIAXIALIS DIFFUSA WITH SURVIVAL FOR THIRTY-SIX YEARS

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IN 1928 Symonds (1928) recorded a case of Schilder's encephalitis, the disease being remarkable for its familial incidence and the presence of a progressive double hemiplegia. Since this date other writers have fully confirmed his observations.

Familial forms of Schilder's Encephalitis have been described by Ferraro (1928) and Van Bogaert and Nyssen (1936) while Bouman (1934) has emphasized that in children quadriplegia is the usual clinical finding.

The present report deals with the clinical and pathological findings in a girl who was the second of thirteen children in the family studied by Symonds. Clinically, the case was remarkable for the very long period of survival and pathologically, by reason of the extensive degree of spinal cord degeneration with but little evidence of sclerosis in the cerebral hemispheres.

CASE REPORT

Family History

The father earned his living as a skinner and enjoyed good health. The mother died of pulmonary tuberculosis, aged 44 years.

There were 13 children in the family:

1. Male, died aged 2 weeks: cause not known.
2. N. P. the patient, died Schilder's encephalitis, aged 36 years.
3. Male, died aged 18 years, pulmonary tuberculosis.
4. Female, died aged 13 months, "meningitis".
5. Female, died aged 13 years, "meningitis".
6. Female, aged 30 years, alive and well.
7. Male, died aged 16 years, Schilder's encephalitis.
8. Sex not known, died aged 7 months, "meningitis".
9. Sex not known, died aged 9 months, convulsions.
10. Male, died aged 6 years, Schilder's encephalitis. Dr. Symond's case.
11. Male, died aged 9 months, "meningitis".
12. Male, aged 18 years, alive and well.
13. Female, aged 17 years, alive and well.

N.P. was born on 16 December, 1906. She talked early and walked at 10 months. The exact date of the attack of encephalitis is uncertain. The mother thought her daughter was about 18 months old while the medical officer who certified her to be mentally defective described her as "paralysed and helpless from the age of ten months". It seems certain, however, that the illness commenced before the second year. In March, 1918, on admission to the Fountain Hospital, she was described as being helpless, unable to sit or stand alone, with contractions of the hands and crippled lower limbs. Her mental state was one of imbecility. Later reports said she talked to the other patients and was remarkably observant.

On her admission to Leavesden Hospital in April, 1922 she was noted to be unable to read or to count beyond ten. Though her vision was impaired she was able to recognize simple objects. The paralysis progressed slowly and by February, 1925 she had become blind and almost helpless.

On 18 December, 1926 she was examined by Symonds when the following notes were made.

From nurses. She will converse in a childish way with them and with other patients. Takes food slowly out of a spoon, has no dysphagia. Knows where she is. Recognizes people by their voices. Can see a little. Has not changed much in last year or so, except that she has become more faulty in her habits. No epilepsy.

Examination. On hearing strange voices became agitated and distressed, crying and shrieking for Nurse Mabel, and saying "Go away". Articulation clear, voice strong. Can distinguish light from darkness. Told by nurse that the visitors were gone, she said "Go

away" when I flashed an electric torch in her face. Optic discs pale and clear cut, the appearance of primary optic atrophy. Pupils dilated and do not react to light. Divergent strabismus but no definite ocular paresis detected. No nystagmus. Right face weaker than left as she cries. Sensation not examined for want of co-operation.

Motor system: As she lies in bed the head is somewhat retracted, but this is less evident when she is sat up, and it is difficult to distinguish between resistance and true rigidity. The upper limbs are symmetrically fixed in the following position: Adduction at the shoulders. Extreme flexion at the elbows. Extreme pronation at the wrists. Extreme flexion at the wrists and metacarpophalangeal joints. Extension of inter-phalangeal joints. Adduction of thumbs. The rigidity appears to be of the clasp-knife type, but voluntary resistance and contracture make examination difficult. There is apparently no voluntary power, but handling the limbs produced flexor spasms. No wasting.

Trunk: Nothing abnormal noted.

Lower limbs: Both semiflexed at hips, and knees and ankles with toes flexed and curled downwards.

Reflexes: Tapping under limbs provoked some clonic spasms of biceps. Abdominals not elicited—but interfered with by crying. In the lower limbs tapping produces clonic spasm of calf muscles; no other reflexes obtained.

Sphincters: Wet and dirty.

General physique: Head and trunk normally developed. Pubic hair normal. Limbs small as in an infantile hemiplegia, with cyanosed extremities. Extreme pyorrhoea. Liver and spleen not felt. Kyphosis of lumbar spine. Chest not examined on account of struggling.

Reflexes. Abdominals present but diminished; plantars, double extensor response. Jaw jerk present. Biceps and triceps jerks exaggerated; supinator jerks normal. Knee and ankle jerks exaggerated. Adductor jerk present. Ankle clonus can be induced by tapping toes. No sphincter loss. No Magnus and de Kleyn neck reflexes.

Progress. In November, 1942 a small pressure sore appeared on the inner aspect of the right knee. It proved resistant to treatment and finally gave rise to a general septicaemia to which the patient succumbed three weeks later.

Autopsy Findings

Brain. Weight after formalin fixation 849 g. Microcephalus symmetrical and firmer than normal. No abnormality of membranes or vessels and no convolutional atrophy. Brain stem small, optic nerves and tracts atrophic, olives conspicuous and pyramids represented by narrow flattened bands.

Coronal sections of the cerebral hemispheres show a very striking diminution in the amount of white matter in the centrum ovale, the cortical grey matter being apparently intact. Both lateral ventricles are moderately dilated and close scrutiny reveals the presence in the white matter of a few faint grey bands. These are beneath the convolutions and in relation to the ventricular walls. They are more numerous in the frontal than in the occipital lobes.

In each hemisphere the claustrum appears attenuated. One small sharply defined cavity is present in the white matter of the right precentral convolution.

The spinal cord is small and sections of cervical and dorsal segments show widespread degeneration in the lateral and posterior columns.

Microscopic Examination

Cerebral Hemispheres. The changes present are all of a chronic character. The small disseminated patches of sclerosis, scanty in number, do not impinge on the subcortical U fibres; histologically, they are quite typical of the pathological findings in this form of encephalitis. In them there is an almost complete loss of myelin sheaths with uneven thickenings on those surviving at their periphery, a disappearance of many of the axis cylinders and a very vigorous proliferation of fibrous glia. Inside the patches the blood vessels have proliferated and show thickening of their walls. In the cortical grey matter the normal columnar arrangement of nerve cells is preserved. In the precentral areas no groups of giant Betz cells can be seen, while most of the smaller nerve cells show finely granular Nissl bodies.

In the area striata of the occipital lobes the densely crowded cells of lamina IV are less numerous than normal. Both here and in the frontal lobes astrocytes and oligodendroglia are increased in number. In certain areas the subcortical white matter shows a fine fibrillary gliosis. A few rod cells are present. In the optic nerves there is complete loss of myelin sheaths.

Pons. There is marked degeneration of the myelinated fibres of the posterior longitudinal bundles, of the cortico-spinal tracts and of the transverse fibres of the formatio reticularis. Holzer preparations show a coarse marginal gliosis, greatest on the floor of the fourth ventricle and in the pyramidal bundles; in other areas of the pons there is a very fine gliosis.

Cerebellum. A single area of sharply defined sclerosis is present in the central white matter of the right hemisphere. There are no noteworthy cellular changes. Purkinje cells are normal in number and appearance.

Medulla Oblongata. The medulla is small, the inferior olives being relatively large and the pyramids rudimentary. Occupying roughly its dorsal third there is a large sharply defined area of demyelination. It reaches almost to the floor of the fourth ventricle and involves the restiform bodies and the formatio reticularis. In it one notes the complete absence of the

normally conspicuous fibres of the fasciculus solitarius. The fibres of the medial lemniscus and of the posterior longitudinal bundle stain well, but there is a loss of some of the olivo-cerebellar fibres. Many olivary cells present a degenerate appearance but elsewhere the larger nerve cells show no loss, even in areas where sclerosis is most pronounced.

The whole of the medulla is permeated by a fibrillary gliosis which assumes a marked density in the dorsal sclerotic area, in the olives and in the two pyramids.

Spinal Cord. The cord is small and shows wide-spread degeneration in the lateral and posterior columns. The areas of demyelination are present throughout the cervical and dorsal segments of the cord. Except in the postero-external columns the myelin sheaths stain badly.

Cervical Cord. In the cervical cord a conspicuous patch of complete demyelination is present in the column of Goll. Its borders are sharply circumscribed and are separated from the margin of the cord and its central grey commissure by partially degenerated areas in which some nerve fibres survive. In each lateral column there is a symmetrically placed band of sclerosis and there is also some degeneration of the direct pyramidal tracts. In the grey matter the nerve fibres stain well. Those of the anterior nerve roots are partially degenerated while in the posterior nerve roots the myelin loss is total. Holzer preparations show a wide-spread fibrillary gliosis, for the most part fine but with coarse fibres in the grey matter and in the columns of Goll. In the sclerosed areas there are many thick walled capillaries.

The cells of the anterior horn exhibit degenerative changes of a chronic nature—loss of tigroid substance and displacement of the nucleus to the periphery. There is no increase of intracellular pigment.

Dorsal Cord. The upper dorsal cord is misshapen, the posterior columns projecting beyond the general contour with the anterior horns of unequal size, the right being abnormally narrow. In this region the process of demyelination is much more widespread. Centrally placed, there is a very large area of sclerosis which involves the greater part of the posterior columns and all the grey matter except its anterior horns. Except for a zone immediately surrounding the grey matter, the anterior and lateral columns are spared. As in the cervical cord, the blood vessels in the degenerated area show numerous thick-walled vessels.

Conspicuous in the upper dorsal segments is a zone surrounding the area of demyelination in which owing to the disappearance of both myelin sheaths and axis cylinders, the white matter presents a cribriform or vacuolated appearance. Only a few nerve cells have survived in the anterior horns. These changes become progressively less marked in the lower segments, demyelination being finally represented by an isolated area in the posterior columns. Below the twelfth dorsal segment no degeneration can be found.

Discussion

Clinically, this case affords confirmation for the view that familial cases of Schilder's encephalitis can pursue an extremely chronic course. One may, perhaps, go further and say that the history indicates that the disease is capable of arrest for in the last few years of the patient's life her symptoms underwent no change, death being due to an intercurrent infection.

From the pathological aspect the case is of interest in that the incidence of the disease seems to have been exercised as much, if not more, on the brain stem and spinal cord as on the cerebral hemispheres.

In the majority of cases previously recorded stress has been laid on the cerebral lesions, possibly because opportunity is seldom afforded for histological study of the spinal cord. No examination was made of the cord of the two siblings of this patient nor in any of the six cases described in Bouman's (1934) monograph. Flatau (1925) noted in the spinal cord small celled infiltration of vessels, principally in the neighbourhood of the pyramidal tracts. In the grey matter there was an increase in the number of glial cells. In their third case of Schilder's encephalitis, Grainger Stewart and his co-workers (1927) observed swelling of the cervical region of the spinal cord in its right half. Some cervical segments were completely involved while at a lower level the white matter bordering on the grey horns was acutely congested, the horns themselves appearing healthy. Microscopically, the myelin sheaths in the damaged areas were swollen and broken up, there being many compound granular corpuscles laden with fatty material and scattered throughout the tissue or collected round vessels.

In an example of diffuse sclerosis reported by Bielschowsky and Maas (1932) patches closely resembling those of disseminated sclerosis were found

throughout the cord and very similar appearances were reported by Wertham (1932) in two adult cases of diffuse sclerosis.

In the case under consideration the degenerative changes in the cerebrum were on the whole typical of Schilder's encephalitis, though in view of the patient's loss of vision, the comparatively slight involvement of the occipital lobes was an unexpected finding. The total blindness was doubtless due to demyelination of the optic nerves. In the cerebellum, medulla oblongata and spinal cord the areas of demyelination bore a considerable resemblance to those of disseminated sclerosis. They lacked, however, the sharply defined margins which characterize the lesions in that disease and the loss of axis cylinders was another distinguishing feature. In the cord the maximum intensity of the disease was in the mid-thoracic region where the cribriform appearance—*Lückenfelder*—of some segments was perhaps more in harmony with the findings in subacute combined degeneration than those of disseminated sclerosis.

Another noteworthy feature was the paucity of white matter in the centrum ovale. Clearly, the microscopic smallness of the brain was attributable not to the intensity of the sclerosis but to an arrest of development occurring at the end of the first year when symptoms became manifest. It may be recalled that the largest contribution to the rapid increase in the weight and size of the brain during the first years of childhood is determined principally by formation of the medullary substance which according to Donaldson (1895) in the mature brain constitutes 47 per cent. of its total weight.

In a chronic case, such as this, it cannot be expected that the pathological findings will throw any light on the predisposing or precipitating causes of Schilder's encephalitis and related conditions, nor on the vexed question of whether the demyelination is one of disintegration of a myelin defectively formed or a primary change in normal myelin which has suffered nutritional deficiency. And on the clinical side the history fails to indicate any factors in the home which were operative in causing the death from nervous disease of no less than five siblings in the first few months of life in addition to the three afflicted by Schilder's encephalitis. In particular, nothing is known of the state of nutrition in the home or of such questions as whether the children were breast or bottle fed. It is known, however, that the family were slum dwellers and the somewhat lowly occupation of the father suggests that the children may have been the victims of a dietary deficiency. In this connection it is of interest to note that Meyer and Tennent (1936) have suggested avitaminosis as a causative factor in Schilder's encephalitis.

Summary

A familial case of Schilder's encephalitis is described in which the patient survived the acute phase of the illness for thirty-six years. The microcephalic brain showed not only diffuse demyelination but also a very marked poverty of white matter. In the cerebellum, medulla oblongata, cervical and dorsal segments of the cord there were numerous circumscribed lesions bearing a superficial resemblance to those of disseminated sclerosis.

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