FAMILIAL PRESENILE DEMENTIA WITH SPASTIC PARALYSIS *

By

C. WORSTER-DROUGHT, T. R. HILL and W. H. McMENEMEY
LONDON

THE recognized forms of primary presenile dementia preceded or accompanied by motor disturbances are (1) Pick's disease; (2) Alzheimer's disease; (3) arteriosclerotic presenile dementia; (4) Jakob's spastic pseudosclerosis; and (5) Huntington's chorea.

The chief characteristics of Pick's presenile dementia have been described by Grünthal¹ and Urechia² as follows: The condition is most commonly met with in women; the average age is between 50 and 60 years, but it may occur as early as the third decade; the duration of the course is between three and four years, more rarely from two to 10 years; acute and chronic forms have been distinguished; occasionally a family history has been described but no constant etiological factors have yet been discovered. The pathological basis appears to be a primary degeneration of the ganglion-cells of the cerebral cortex, most commonly affecting the frontal lobes and next in order the parietal and temporosphenoidal lobes and less frequently the occipital lobes. The outstanding clinical manifestation of this type is the progressive and eventually profound dementia with considerable disturbance of personality from the outset. Following the earliest stage there is usually no insight displayed by the patient. Most cases are characterized by inertia and lack of initiative together with a progressive global aphasia and in many instances apraxia and agnosia. It differs clinically from the majority of cases of Alzheimer's disease in the frequent absence of restlessness and the extreme rarity of hallucinations and delusions.

In both these conditions there is usually negligible degeneration below the level of the cerebral cortex, whereas in cerebral arteriosclerosis focal symptoms are earlier and more frequent. In the latter condition, further, there is good insight and preservation of the personality until a relatively late stage. Bleuler³ has said that the main feature of an arteriosclerotic dementia is its lacunar character and that the symptoms have a disturbing effect on the patient, causing considerable anxiety.

The rare condition described by Creutzfeld⁴ and Jakob⁵ in 1920 and known as Jakob's 'spastic pseudosclerosis' begins at middle age or later

* From the West End Hospital for Nervous Diseases, London.

and consists of slowly developing disturbances of motor and sensory functions; frequently a tremor of the hands and head is the earliest sign. Gradually the motor symptoms become more pronounced; slow spontaneous movements, rigidity and tremor are outstanding features. The speech may be slow, monotonous and indistinct. At first the mental symptoms are slight, consisting of anxiety, irritability and depression; later, confusion, confabulation, hallucinations and finally dementia may appear. A Kayser-Fleischer corneal ring is sometimes observed.

The pathological changes include atrophy of the cerebral cortex and the corpus striatum, especially of the putamen. Histologically, degenerative changes are found in the corpus striatum, thalamus, red nucleus and the dentate nucleus. There is also a diffuse loss in the ganglion-cells with slight increase of glia. The liver may be small, firm and nodular. Jakob, Davison⁶ and others have expressed the view that this form of pseudosclerosis, as well as that of Westphal and Strumpell, is closely allied both clinically and anatomically to Wilson's hepatolenticular degeneration.

Huntington's chorea is a definitely inherited malady that usually begins in the fourth decade and is characterized by the development of involuntary jerky movements of wide excursion. Mental changes leading to dementia may accompany or follow after some years the appearance of the choreic movements. In a few instances dementia precedes the motor disturbances.

DESCRIPTION OF PERSONAL CASE

C. G., age 47, was first seen on June 14, 1929. He then complained of defective memory, general lack of interest and that people had difficulty in understanding his speech.

History.—His speech began to be affected about a year ago and more recently he has appeared less interested and become less efficient at his work, that of engine-driver. He has had no previous illnesses of importance.

Physical Examination.—Pupils, optic discs and all cranial nerves are normal. Speech is indistinct and somewhat slurred. Sensation: All forms normal. Upper limbs: Tone of right arm slightly increased; motor power and all arm-jerks moderate and equal. Lower limbs: Tone generally increased; knee- and ankle-jerks brisk, right slightly greater than left. Plantar reflexes flexor. Abdominal reflexes moderately brisk and equal; gait normal. No tremors; coordination normal. Sphincters intact. Heart not enlarged; pulse-rate 80, regular; blood-pressure 155 systolic, 90 diastolic.

By June, 1930, there was no material change in the above condition excepting that the gait had become more deliberate.

Present Condition: 1. *Mental State.*—He remains inert all day, sits for hours looking into space and makes no attempt to occupy himself beyond smoking. His mood is complacent and he confabulates very readily. He states that he reads the *Daily Herald* when in fact he never reads at all. He has no idea how long he has been in hospital, stating when asked that he came in last night when indeed he has been in several weeks. He does not know the date or even the month. His remote memory is excellent, e.g., states correctly that he entered the S.E. & C. Railway Service at the age of 13; he gives correctly the date of the beginning of the War and also that of the Armistice. He also knows the name of his school and the age at which he left. He

understands all questions readily but has no memory of recent events, e.g., does not know when his wife last came to see him. His speech is scanty, somewhat slurred and indistinct. His attention is fairly good, but there is some delay in answering any question and on some occasions no answer can be obtained. His answers are invariably brief and there is complete absence of spontaneous speech. He is able to repeat a question after one or two minutes and when asked the cause of the delay will say 'I was dreaming.' When up, he goes regularly to the lavatory, but when in bed he is incontinent. He is quite devoid of insight, and retention tests show great impairment. There are no delusions or hallucinations.

2. *Physical Examination*.—Pupils equal, central, circular, react a trifle sluggishly to light but normally on accommodation. Optic discs normal beyond a slight degree of arteriosclerosis. Speech hesitant and somewhat slurred. Overaction of facial muscles and slight tremor of tongue. Sensation normal to all forms of stimuli. Upper limbs: Motor power good but tone definitely increased in both arms. All reflexes, including supinator, biceps, triceps and ulnar jerks, are exaggerated. Lower limbs: Gait slow, deliberate and somewhat spastic on a widened base. Muscular tone of legs much increased, the right more so than the left. Knee- and ankle-jerks exaggerated but equal. No ankle clonus; plantar reflexes flexor; abdominal reflexes not elicited. No tremor of limbs. Coordination of arms good but slight swaying in Romberg position. Arteries only slightly thickened, e.g., radial and dorsalis pedis just palpable. Pulse-rate 76, regular; blood-pressure 140/90. Liver impalpable. Blood Wassermann reaction negative (on three occasions in the last three years). Cerebrospinal fluid: two small lymphocytes per centimetre; total protein 0.05 per cent.; globulin, faint detectable trace: Wassermann and Lange reactions negative.

FAMILY HISTORY

The accompanying diagram shows the family history as far as it can be ascertained. For the sake of convenience each member is numbered. Our patient, C. G., is no. 29.

His maternal grandmother (4) was born in 1830 and at the age of 40 became afflicted with 'paralysis.' She died at the age of 53. Her sister (5) was affected in exactly the same way at about the same age. Nothing is known of their parents (1) and (2), or of their aunts and uncles. There is said to have been other brothers and sisters but no trace of them can be found.

Our patient's maternal grandmother married into a healthy family, her husband (3) being born in 1829 and dying in 1903 at the age of 74. Until a last short illness he had been perfectly well. They had 10 children. The eldest, Jane (7), was born in 1851 and died at the age of 52. Her husband (6) was a healthy man. The extent of their family is not known but one daughter (24) is known to have died in a mental hospital.

The second son, Charles (8), was born in 1853. He was a coachman by occupation and developed the 'paralysis' at the age of 57; he died at the age of 60. His wife and two children were healthy. The third, Sophie (11), the mother of our patient, was born in 1855. In her case, the 'paralysis' came on at the age of 44, somewhat rapidly, and was followed by insanity. She died in a mental hospital at the age of 54. The records unfortunately

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cannot be traced. Her husband (10), the father of our patient, came of a healthy family and he himself was well until his terminal illness at the age of 76. Their children numbered six, of whom our patient was the second. They will be referred to later. The fourth, Julia (12), was born in 1857. Insanity began at the age of 48 and she was sent to an asylum. Whilst there she slowly developed 'paralysis' and died at the age of 53. Inquiry has been made but the asylum notes cannot be traced. The fifth was Alice (14), born in 1861. 'Paralysis' started at the age of 48 and she died at the age of 66. It was noted that whereas the 'paralysis' was the same as in the other members of the family, the mental disturbance was less obvious; at no time did she require certification. Her husband (13) was a healthy man and their children (39-44) are all alive and well, with the exception of a daughter who is said to be 'very nervy'; their ages vary from 48 to 29. The sixth was Lorris (16). She was born in 1865, was afflicted with the 'paralysis' at the age of 48 and died at the age of 50. She was not certified. Her husband (15) and children (45-53) were all healthy. The ages of the children are from 47 to 25. The seventh, Henry (17), was born in 1870. He is now alive and well at the age of 63. His wife (18) and two sons (54-55) are also well; the latter are 10 and nine years old respectively. The eighth was Rose (19), born in 1872. She was mentally deficient, could not walk until she was five years old and died of scarlet fever at 14. The ninth, Ada (21), born 1874, is alive and well. Her children (56-58) are all well, the eldest being aged 36. The youngest of the family, Edith (23), was born in 1875. She had 12 children, six of whom (65-70) died in infancy. The other six (59-64) are alive and well, the eldest being aged 28.

We will now refer to the family of Sophie (11), the mother of our patient. The eldest of her children was Esther (28), born in 1879. She developed 'paralysis' at the age of 44 and died at 54. We are greatly indebted to Dr. J. W. Wayte of Croydon for a lucid account of the clinical features of this case. He writes that when he first saw her, some two or three years before her death, she presented many features of resemblance to paralysis agitans. Her limbs were held stiffly and she would progress 'by chasing her centre of gravity,' but the facies was never at any time suggestive of Parkinson's disease. After two years her gait changed in character and she seemed to lose her sense of position in space. She now moved stiffly and awkwardly, in so uncertain a manner that it was fascinating to watch where she would finish up her stride. She began to lose flesh and became slowly demented. She seemed to understand much of what was said and tried to answer in a slow scanning manner suggestive of the speech of disseminated sclerosis. She was bedridden in her last year and incontinent of urine and faeces. She became progressively more spastic, lying in bed with knees rigidly drawn up in flexion, but during sleep the rigidities would relax somewhat. She became emaciated towards the end. For many months before her death she would emit spontaneous and apparently quite purposeless cries.

She would scream for a long time without stopping, but if roused would grin in an understanding manner. She never admitted to having pain. At no time did she suffer from hallucinations or delusions. Her husband (27) was an epileptic and died a few years ago of 'bad health following exposure whilst in war service.' Their only child (71) is 24 years old; she is of neuro-pathic disposition and worries unduly about the 'family paralysis.'

Our patient (29) was born in 1882. His wife (30) is a healthy woman and they have one child, a healthy lad of 18.

The third of Sophie's family is Mabel (32), born in 1889. She is now, at the age of 44, under close observation and is believed to be an early case (March, 1933). She herself makes no complaint beyond that for the last two years she has felt continually cold even in warm weather. It is said that all the other affected members of the family had the same symptom a year or two before the appearance of 'paralysis.' Her husband, however, states that she has recently become very irritable and quick-tempered; 'quite unlike herself,' as he puts it. Also her memory has become faulty; she will tell her husband or children the same thing at comparatively short intervals. She is neither restless nor emotional but rather apathetic, and has no insight regarding her irritability or her obviously faulty memory. Physical examination shows no abnormality beyond general exaggeration of the deep reflexes.

Her husband (31) is a healthy man and their four children (73-76) are all alive and well, the eldest being 28.

The fourth of Sophie's family is Fred (33), born in 1892. He is quite well, also his wife (34) and two children (77-78), the eldest being 30 years old. The fifth is Violet (36), born in 1895. She is under treatment for anæmia but is otherwise well. Her husband (35) is a healthy man and so are her three children (79-81); the eldest is 33. The youngest of Sophie's family is Ernest (37), born in 1897. He is quite well except for astigmatism, and his wife (38) is a healthy woman; they have a normal son (82), age three years.

It is interesting to note that our patient's maternal grandmother first showed signs of the disease when she was pregnant with her seventh child (17). The eighth child (19) was mentally defective but the ninth and tenth (21 and 22) together with the seventh were considered to be the healthiest of her children in their youth and early adult life. None of them or their families have been affected.

Our patient's mother (11) developed the disease when she was pregnant with her youngest child (37). Thus there are nine cases of the disease spread over three generations (4, 5, 8, 11, 12, 14, 16, 28, and 29) and two possible ones (24 and 32). It is open to objection that many of these cases were in reality not examples of the disease under consideration but more common cases of paralysis such as ordinary hemiplegia. It is, of course, difficult to answer so obvious a criticism, but it is a most significant fact, and one to which much importance may be attached, that the family are fully aware of their 'family paralysis' and have learnt to recognize its early features.

They are certain that all of the nine members of the family have suffered from the same complaint and they have themselves made the observation that the disease is apparently transmitted through the female side.

Of the members of the family who have died of the disease, the ages of onset were : two at 40, two at 44, three at 48 and one at 57. The longest course was 13 years, the shortest two years and the average eight years. It will also be seen that the tendency is to affect only the elder members of the generation.

COMMENTARY

The mental changes in the cases we have described resemble those of Pick's disease and of Jakob's pseudosclerosis more closely than those of the other types of presenile dementia. As far as we have been able to trace, however, no such pronounced family history has been described in connection with Pick's disease. A few familial examples have been recorded by Grünthal,¹ e.g., two brothers with the disease ; also in two sisters one of whom had a child similarly affected. Urechia² states that heredity plays only a minor part in Pick's disease and that familial cases are very rare. He mentions other types of mental disturbance occurring in close relatives, such as epilepsy, alcoholism and psychoses. Braünmuhl⁷ also describes a case of Pick's disease with one brother a general paralytic, one sister psychotic and another sister defective.

Clinically the cases we have described appear to differ from Pick's disease in the early development of spasticity of the limbs and the degree of dysarthria. In our patient there is muscular rigidity of an extrapyramidal type, and, from descriptions, the 'paralysis' affecting other members of the family involves all four limbs and appears to be of a similar gradually progressive extrapyramidal form. Further, in the majority of cases affected, the development of the 'paralysis' has preceded that of the mental changes (4, 5, 8, 11, 14, 16 and 28), and in our own patient (29) the first symptom appears to have been dysarthria. In only one case (24) is the mental disturbance known to have preceded the 'paralysis.'

Paresis of both a pyramidal and extrapyramidal type has been described in a few cases of Pick's disease but in all examples it appears to have developed only at a late period. Pathological examination of the brain in Pick's disease, in addition to the degeneration of cortical ganglion-cells, has occasionally shown the cells of the basal ganglia to be affected by the degeneration.

The condition we have described resembles Jakob's pseudosclerosis in the muscular rigidity, dysarthria and mental changes, but it appears to differ from this latter disorder in the absence of tremor and spontaneous movements. In most of the recorded cases of Jakob's pseudosclerosis tremor has been an early and pronounced feature. Also, the inherited factor has not been very striking and there appears nothing in the literature of the condition to compare with the family history we record.

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