DISSEMINATED SCLEROSIS IN A WHITE SOUTH AFRICAN

A CASE REPORT WITH AUTOPSY FINDINGS

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Disseminated sclerosis is rarely diagnosed in South African Whites, and as far as we know there is no record of a case proved by autopsy in a South African-born White. The case we now report is that of a South African-born White who has been all her life in this country, but had the typical clinical history and findings.

CLINICAL HISTORY

Mrs. H.J.R. was born at Moorreesburg, in the Cape Province, in 1907. She was of German stock, but had lived in the Cape Province all her life and had never been out of South Africa. She was a dressmaker.

She was first admitted to Groote Schuur Hospital in June 1941, at the age of 34, complaining of severe headache, vomiting attacks and dizziness so marked that she had to go to bed. She also complained that her tongue felt 'dead and thick', especially on the right side, and that she had a feeling as if she might fall to the right when she attempted to walk. The previous history given was not significant, apart from rheumatic fever at the age of 25.

On examination she was found to be very drowsy and irritable. There was some neck stiffness, doubtful nystagmus to the left, and very brisk knee jerks. The CSF was under normal pressure, 60 mm. of water, with no block. The cerebrospinal fluid contained 45 mg./100 ml. of protein and a trace of globulin. There was no pleocytosis. Blood and CSF Wassermann reactions were negative.

She was discharged 16 days after admission. No definite diagnosis was made and no specific treatment was given, although the final diagnostic suggestion was ? meningovascular syphilis.

She reported back to the neurology outpatient department in December 1949, complaining that for many years she had experienced a feeling of 'thickness' of the tongue and difficulty in speaking, especially when she had a cold. She also stated that her right leg had been weak for some time, that her vision had been 'blurred' for 5 - 6 years, and that she had had diplopia for some time. This latter symptom was at first intermittent, with the images above each other, but had recently become continuous. In addition, she complained of some difficulty in 'holding her water'. On examination there was a doubtful, very slight, right lower facial weakness, poor upward conjugate deviation of the eyes, an unsteady gait with a tendency to fall to the right, absent abdominal reflexes, and brisk knee and ankle reflexes with an extensor plantar response on the right. The physician who examined her suggested the diagnosis of disseminated sclerosis.

In February 1950 she was admitted to Groote Schuur Hospital as an inpatient for the second time. On this occasion she complained that 4 weeks before admission her right leg became weak and this was speedily followed by weakness of the left leg. For the first 2 weeks this weakness was intermittent, but later became persistent. She also stated that she had had a numb feeling over the right side of her face and that her 'voice had altered'. She repeated her old complaints about diplopia and blurring of vision. On examination she was found to have a doubtful right lower facial weakness, some diminution of sensation to pinprick over the right side of the face, absent abdominal reflexes, brisk knee and ankle jerks with generalized weakness in both lower limbs, ? bilateral extensor plantar responses, poor coordination in the right lower limb with ? diminished sensation to pinprick over the right leg. The cerebrospinal fluid contained 45 mg./100 ml. of protein, a trace of globulin, 3 lymphocytes and 1 polymorph. Apparently the patient improved fairly rapidly. She was seen by a member of the neuro-psychiatric department, who could not find any unequivocally abnormal neurological signs and suggested that her complaints were hysterical. She was discharged after 9 days with a diagnosis of ? hysteria.

In November 1950 she reported to neurology outpatient department that her right lower limb was weak and that she tended to fall because her right foot caught in the carpet. She was referred to the psychiatry department. In

March 1960 the psychiatric outpatient note reads: 'This woman has deteriorated considerably and is totally incapable of looking after herself. Owing to paralysis of the right leg she falls easily, there is mental deterioration and severe memory loss for recent events and compulsive laughing and crying. She has to be fed and dressed.'

Her third and final admission to hospital was on 18 September 1961. No detailed history was available, but apparently for several years the patient had been bedridden, her speech had deteriorated and she had had increasing difficulty in using her arms. In addition her memory had been getting progressively worse. During the week preceding admission she had been unable to recognize her husband, had complained of severe pain on the left side of her face and had become increasingly drowsy.

Neurological examination at this stage was incomplete because of lack of cooperation. The patient was conscious, but her responses were limited by her illness and dysarthria. There was an impression of right lower facial weakness, a total paralysis of the palate, weakness of all limbs with increased tone in the lower limbs, brisk deep reflexes and bilateral extensor plantar responses. The patient remained in this condition and had to be tube fed. The cerebrospinal fluid pressure was 230 mm. of water and the fluid contained 65 mg./100 ml. of protein and a trace of globulin. The patient deteriorated a few days after admission so that an angiogram (vertebral) was cancelled; she then rallied sufficiently to ask for her glasses, but the following day collapsed while being anaesthetized preparatory to vertebral angiography. She had several generalized convulsions and died in coma 4 days later.

PATHOLOGICAL EXAMINATION

An autopsy was performed by Dr. M. A. H. Russell on 6 October 1961. The significant findings, apart from the central nervous system, were as follows:

Lungs: Right (690 G), left (445 G). In the right upper and middle lobes were greyish foci of infiltration. At both apices were carbon-pigmented scars of healed or healing tuberculosis. In the right lower lobe there was extensive bronchopneumonia.

Heart (350 G) showed no abnormalities apart from pallor.

Liver (1,360 G) showed some fatty change.

Spleen (90 G) was soft and reacting.

Kidneys (212 G) showed a few depressed scars from old pyelonephritis. Both organs were very pale.

Microscopically the bronchopneumonia in the right lower lobe is confirmed and shows early abscess formation. The infiltrations in right upper and middle lobes are areas of extensive active tuberculosis with small foci of caseation.

Brain (1,262 G). There was no abnormality of the meninges or basal cerebral arteries which were free from atheroma. No dilatation of the 3rd and 4th ventricles or aqueduct was noted, but the lateral ventricles appeared slightly enlarged and this was particularly evident in the posterior horns. The pons and medulla were not abnormal to the naked eye. In the cerebrum were noticed variations in consistency of the white matter suggesting more a reduction, i.e. some degree of softening, particularly in relationship to the lateral ventricles.

From the central nervous system 12 paraffin blocks are available for study, from pons, medulla, cerebellum, cerebral cortex, white matter in relationship to lateral ventricles, and upper cervical spinal cord.

With the sole exception of the cerebellum, sections from these areas show frequent and marked lesions typical of disseminated sclerosis. In sections stained for myelin by Loyez's method the characteristic plaques are evident as pale areas of demyelinization, sharply demarcated from the darkly stained white matter (Fig. 1). The largest plaque is 1 cm. long and 1·2 cm. wide. Some of these plaques, mainly in relationship to the lateral ventricles, show oedematous separation of the astrocytes and their fibres which replace the white matter, the so-called areolar lesions; these are the areas which suggested softening macroscopically. All are, however, very old lesions and some are separated from the surrounding unaffected white matter by a dense peripheral zone of gliosis, whose fibres and nuclei show a parallel orientation (Fig. 2). What appears to be nerve fibres denuded of their myelin sheaths, are seen in these plaques, but are infrequent.

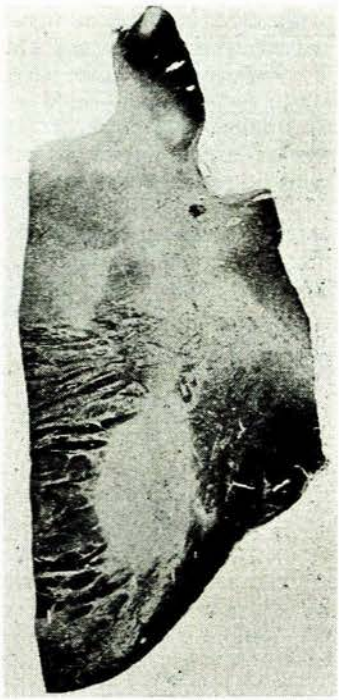

Fig. 1. Half of pons stained for myelin (black) to show multiple foci of demyelinization (lighter areas). The smaller slit-like areas on the right are artefacts due to tears in the section, the demyelinated plaques being much larger. (Loyez x 3·5.)

Acute lesions with lipoid-containing microglial cells are not identified in any of the sections, but no material is available for frozen sections. Here and there a slight perivascular cellular cuffing is noted of lymphocytes, plasma cells and histiocytes containing lipofuscin. In the larger plaques fibrosis round the blood vessels with apparent obliteration of the Virchow-Robin spaces can be seen. More striking, however, is the marked dilatation of some of the perivascular spaces which contain much granular protein material, usually free from cells, and a similar protein can occasionally be seen lying between the surface of the cerebral cortex and the pia arachnoid (Fig. 3). The separation of the granules of protein and the striking distension of the perivascular spaces indicate that a marked excess of fluid has been present, and is associated with an apparent condensation of the cerebral substance at the edges of the space. It would seem unlikely that these appearances are artefacts. In addition to the striking oedema in the plaques of areolar type, with wide separation of the astrocytes and their fibres, much of the brain adjacent to the plaques shows separation of structural elements of the unaffected white matter, suggesting that some oedema is present here also. This is especially marked in the section of the cervical cord, and results in an unusually clear delineation of the cells and fibres, even in sections stained by haematoxylin and eosin.

The amount of protein in the perivascular spaces and between cerebral cortex and pia-arachnoid seems impressive, but these lesions are very infrequent and might well be the explanation of a slight increase in the protein in the cerebrospinal fluid in these cases.

Changes in the ganglion cells are slight and unimpressive in the cerebral cortex. In the deeper grey matter the ganglion cell nuclei seem more closely approximated than usual, and this is due in some cases to disappearance of medullated fibres and the incorporation of the nuclei into a plaque. In the one section of the spinal cord available from the upper cervical segment are 2 small plaques in a posteral lateral column where demyelinization is complete, and is associated with a slight gliosis (Fig. 4).

DISCUSSION

This patient was under intermittent medical observation from the time she was 34 to her death at the age of 64. Her illness began with an 'acute encephalitic' episode

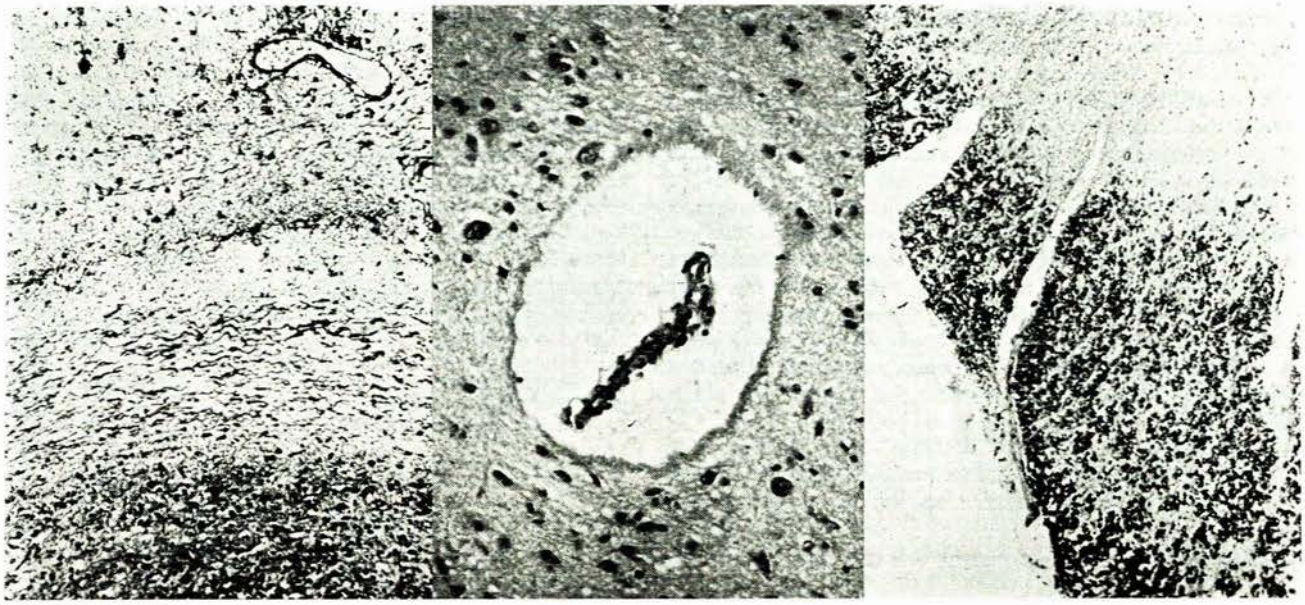

Fig. 2 *Fig. 3* *Fig. 4*

Fig. 2. Unaffected grey matter at the bottom, the edge of an oedematous plaque of areolar type at the top, and between them a zone of pilocytic gliosis, with parallel orientation of the fibres. (H. & E.—high power.)
Fig. 3. Showing the distension of the perivascular space by granular protein and fluid in the grey matter adjacent to a plaque. Note the condensation of the cerebral substance at the edges of the space. (H. & E.—high power.)
Fig. 4. Upper cervical cord, showing at the right top a pale zone of demyelinization contrasting with the black-stained myelin elsewhere. (Loyez—high power.)

which is not a particularly common mode of presentation in multiple sclerosis. However, it was followed by a remittent and relapsing neurological illness during which symptoms of brain-stem dysfunction and pyramidal involvement appeared. It was at this stage that the diagnosis of multiple sclerosis was first mooted, but during her second hospital admission her symptoms and signs disappeared and a diagnosis of hysteria was made. This is a classic error in multiple sclerosis, and is based on the fallacious belief that a patient's symptoms, if not accompanied by objective abnormal signs, must be due to hysteria. It cannot be over-emphasized that a diagnosis of hysteria should be made on positive psychological grounds. Another diagnostic error was made when the possibility of a brain stem vascular anomaly was suggested.

On clinical grounds a diagnosis of disseminated sclerosis would have been accepted in this case without comment in countries where the disease is known. To accept it as a proved case in a South African-born subject in South Africa where the existence of the disease has been denied, complete 'proof' of the diagnosis is essential, and this is fortunately available. The postmortem findings and the histological examination of the brain establish conclusively a diagnosis of disseminated sclerosis, both positively because the lesions typical of the disease are present, and in the failure to demonstrate any other basis for the neurological symptoms.

We suspect that now the existence of the disease in a native-born South African has been demonstrated for the first time, the diagnosis will be made more readily, and in a few years there will be available acceptable figures for the frequency of this disease in South Africa.

The late and greatly admired Dr. S. Berman, the senior neurologist at Groote Schuur Hospital, attended this patient during his lifetime, and we should like to acknowledge his full notes about her.

Our thanks are also due to Dr. G. Dean, of Port Elizabeth, whose enthusiastic interest in disseminated sclerosis determined the reporting of this case.