A CASE OF JAKOB'S DISEASE.

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IT is generally agreed that the occurrence of marked clinical dementia and accompanying cortical pathological lesions is rare in cases of idiopathic paralysis agitans. Cases which show this association have been described by Jakob (1923), and by Critchley and Greenfield (1937). The name "Jakob's disease" has been assigned to this clinico-anatomical syndrome by the latter authors. Our case is clinically a typical one of this syndrome, and possesses some unusual pathological features which make it worthy of record.

History.—A widow, aged 65 on admission to Tooting Bec Hospital in 1932. Died 1936.

Her mental disability was said to be of one year's duration. No satisfactory previous history could be obtained. One son was interviewed, and he suffered from parkinsonism.

Examination.—There was nothing of note except for the findings in the nervous system.

She had a typical paralysis agitans tremor of the right arm and leg. She showed to a moderate degree the set, expressionless facies, but no tremor of the face. There was marked rigidity on the right side, and to a lesser extent on the left. Both knee-jerks were much exaggerated. Plantar reflexes were equivocal, the left definitely abnormal. The pupils appeared normal. She could walk without assistance and use her upper limbs. All voluntary movements were very slow. She had the typical dull monotonous voice of parkinsonism.

Blood Wassermann and cerebro-spinal fluid examination showed nothing abnormal.

Mentally she was extremely lost and confused, and showed a complete inability to answer even the simplest questions, and when pressed gave irrelevant replies, with a tendency to perseveration. She could not understand written words, could give no information about herself, and failed to realize what sort of a place she was in. She said her age was 26 and that she was married to her son. She was quiet and apathetic and at that time was clean in her habits.

Progress.—She became steadily worse, both in her tremor and rigidity and in her dementia. Only very occasionally would she leave her chair in the ward. She made no effort to go to bed with the others and had to be taken there and undressed. Judging by the faint smile on her face she recognized her son on his visits. Her speech ultimately became completely anarthric, and she exhibited marked logoclonia. When spoken to she often repeated a single word, e.g., "Harry, Harry"

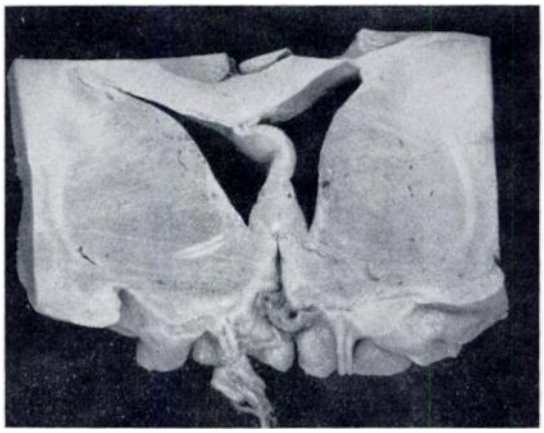
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—becoming faster and softer, till it died away. She sometimes laughed to herself.

Finally she sustained a fall, fracturing her femur, and died some weeks afterwards.

Pathological findings: Post-mortem.—Hypostatic pneumonia. Heart, aorta and coronary arteries healthy. Kidneys mildly fibrosed. Fracture of the neck of the right femur.

The brain: Here and there at the base the arteries show atheromatous lesions. The frontal lobe appears mildly wasted. Coronal sections of the formalin-hardened brain show *état criblé* in the left caudate nucleus (see Fig. 1), the latter being somewhat smaller than the right. The mid-brain is symmetrical and there is some diminution of pigment in the substantia nigra on either side. Both lateral ventricles are slightly enlarged.



Left. Right.

FIG. 1.—*État criblé* in the left caudate nucleus.

Microscopic examination of the brain.—Cortex: All parts show typical senile plaques and Alzheimer's neuro-fibrillary changes. The distribution of this is general with the exception that the occipital lobes are more affected. These specific changes are only found in the cortex. There is some dropping out of ganglion-cells in patches corresponding in size and amount to the plaques, but the architectonics are fairly well preserved. The ganglion-cells show a great increase in lipofuscin pigment, which stains red with Scharlach R, and green in the Nissl preparations, and shows in the typical position as large inclusions near the nuclei. There is an increase in oligodendroglia, astroglia and fibrous glia everywhere in the cortex. The subependymal fibrous glia is accentuated around the plaques (Holzer stain). The walls of the vessels are somewhat thickened and show some capillary fibrosis.

Caudate nucleus and putamen: There is an increase in microglia on both sides. The small cells contain much lipoid. There is a marked difference between the two caudate nuclei; the right is very little affected, while there is an *état criblé* and *lacunaire* on the left side. The lacunæ are seen sometimes as holes, often surrounding a blood-vessel, and others appear to be filled with a poorly staining substance. There are some Elzholz bodies on either side.

Globus pallidus: A mild degree of diffuse demyelinization is seen on both sides, most pronounced on the left. The cells are loaded with fat, unequal in size, and some show pyknosis. Marked increase of fibrous glia is visible to the naked eye

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on the slide. Microscopically there is a diffuse proliferation of astrocytes, with beginning formation of a glial felt. The gliosis is particularly marked around the blood-vessels. Both sides are approximately equal in this respect.

Substantia innominata: There is a definite decrease in cells and a fine gliosis.

Ansa lenticularis: Demyelinization is more accentuated on the left side.

Substantia nigra: There is a reduction of the number of cells, more marked on the left. The cells vary in size and shape, and most show "chronic cell change". Intra-cellular pigment is poor, and in places there are extra-cellular deposits of melanin.

The Luys body is normal in appearance.

The left paraventricular nucleus appears more rich in glia-cells than the right, but the other hypothalamic nuclei show no pathological changes.

The red nuclei, pons, medulla and cerebellum are unaffected.

The anterior horn-cells of the spinal cord show a great increase in lipoid, but no diminution of their number.

COMMENT.

It is not intended to present here an exhaustive discussion of this syndrome nor of the pathology of paralysis agitans, which latter subject is dealt with fully in its historical aspects in a recent paper by Juba and Szàtmari (1937). In this case it is of interest that the cortical process—Alzheimer's cell change and plaques—was observed only in the cortex, whereas the changes in the basal ganglia are those which have been generally regarded as the substrate of paralysis agitans. The case of Critchley and Greenfield showed this distinction, but differed from ours in that no neurofibrillary changes were observed in the cortical cells. There is some doubt here also as to whether we are dealing with a case of Alzheimer's disease or of senile dementia, as the onset was certainly before the age of 64 years. The pronounced speech defect, and particularly the tendency to perseveration of syllables, show a similarity to the logoclonic speech disturbances in Alzheimer's disease.

It has been suggested by some (Lewy, 1923; Jakob, 1923) that paralysis agitans is actually a senile process, but this is contested on the one hand by Foix and Nicolesco (1925), Bielschowsky (1922) and others, who believe an underlying vascular disease to be the primary factor in the *état criblé* and hence in the whole pathological picture, and on the other hand by Juba and Szátmari, who contend that heredity studies show paralysis agitans to be a specific entity. This case suggests, from the histological examination, that there are two distinct processes at work, and the incidence of the parkinsonian syndrome in the son is in favour of a genetic factor.

With regard to the localization, it is remarkable that the symptoms were generally more severe on the right side, and a difference in intensity of the changes in each pair of basal ganglia was found, with the worst lesions in the left-sided nuclei. Tremor was observed only on the right side, and an intense *criblé* process was found in the left caudate nucleus, with that on the right practically undamaged. If one follows the views of C. and O. Vogt (1920), that lesions of the caudate nuclei are responsible for the tremor, and lesions

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of the pallidum are responsible for the rigidity, then the observations here are in accord with this. However, the severity of the lesions was generally greater on the left side, and one cannot say which of the affected nuclei is of the greatest importance for any of the symptoms.

Summary.

A case of Jakob's disease possessing some unusual features is reported and its nosological position briefly discussed.

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