INTRODUCTION

"AS THE DISEASE progresses some jerky irregularity develops in the movement of the neck and head so that the head presents slight movements, sometimes like an irregular tremor, sometimes simulating chorea". This is how Gowers in 1899 described the occurrence of titubation in hereditary ataxy in his book on the diseases of the nervous system. But this feature of hereditary ataxia seems to have received scant attention in recent textbooks. Two siblings of a family are reported here to stress the fact that titubation may be a predominant feature of this condition. One had also a persistent tachycardia, a normal glucose tolerance test (g.t.t.) and normal peripheral nerve conduction whereas her brother (Case 1) had an abnormal g.t.t. and impaired nerve conduction.

CASE REPORTS

Case 1

J.E., a single man first went to hospital at the age of 24 years with symptoms of duodenal ulcer. He was observed then to be unsteady while walking. At the age of 35 years he developed pulmonary tuberculosis for which he received a course of treatment. He was first seen in the neurological unit, aged 38 years, with the complaints of pain in the back and was then noted to have titubation and ataxic gait. Ten years later when he was admitted to Claremont Street Hospital, Belfast, his main symptoms were "shake in the head and in the hand and unsteadiness". His walking had deteriorated considerably over the years. An examination revealed titubation - slow (4 per sec) head tremor which was a rotatory movement of the head with a range of about 30° and which was present on sitting and standing but disappeared on lying down; he had intention tremor and inco-ordination in the upper limbs, the tendon reflexes were depressed and plantar responses flexor. He had an ataxic gait. A routine full blood count, E.S.R., E.C.G. and C.S.F. examination was normal; a g.t.t. was abnormal (106, 140, 200, 180, 130 mg./100 ml.). Nerve conduction studies were abnormal; the motor velocity of the ulnar and the median nerves was slow (40 and 28 metres/second respectively), with prolonged distal latency (5.8 and 6.3 milliseconds respectively); the sensory potentials from 5th digit to wrist and from ankle to knee were absent. He developed jaundice eight months later and was admitted to a surgical unit where he was found to have carcinoma of the pancreas at operation. His general condition gradually deteriorated and he died three months after the operation. No autopsy was performed.

Case 2

M.J.E., an unmarried sister of J.E., aged 39, was first seen in hospital at the age of 24 years with complaints of nervousness in the preceding 18 months. She was then noted to have titubation and tremor and inco-ordination in the upper limbs. She was also found to have tachycardia (100/minute) and was treated with Carbimazole with no improvement. Gradually the head shake got worse and more persistent and inco-ordination in the hands became more obvious. She attended the neurological unit two years later with the main complaint of head shaking and unsteadiness of
the upper limbs. She had markedly depressed tendon reflexes and flexor plantar responses. The abdominal reflexes and gait were normal. There was no dysarthria nor any nystagmus. She was again found to have tachycardia (108/minute). A C.S.F. examination was normal. A radiograph of the skull and chest was normal. Urine chromatography revealed generalised aminoaciduria. A recent examination revealed the further deterioration with progress signs and, in addition, a markedly ataxic gait. The titubation although like that of her brother was much more marked. A g.t.t. and the peripheral nerve conduction were found to be normal.

There was no family history of similar disease or pes cavus and two members of the same generation were examined personally and were found to be normal.

COMMENTS

The main features of the two siblings described here are titubation and ataxic gait with mild inco-ordination of the limbs. There were neither any pyramidal signs nor any suggestion of posterior column involvement. These features perhaps fall into the predominantly cerebellar form of hereditary ataxia in Greenfield's classification (1954). Although titubation has been noted in nearly all types of spinocerebellar degeneration including Friedreich's ataxia, it has been observed mostly in the type with mainly cerebellar and/or brainstem degeneration (Fickler, 1911; Thorpe, 1935; Aring, 1940; Rosenhagan, 1943; Hall, Noad and Latham, 1941). Generalised aminoaciduria noted in one of the siblings raised the possibility of Hartnup's disease but many of the features of the latter including photosensitive skin rash were absent (Baron et al 1956). Aminoaciduria has also been noted in a number of other neurological disorders including paraplegia (Banerji and Millar, 1971). Disseminated sclerosis can also affect several siblings in a family but many of its features and the pattern of involvement of the nervous system (Millar, 1971) makes it unlikely in the present cases.

Russell in 1946 reported histological findings in the hearts of four cases of Friedreich's ataxia. Since then there have been many reports of heart disease in this condition (Novic, Adams and Anderson, 1955; Hewer, 1969). An electrocardiographic study (Thorén, 1964) showed an abnormality in 92 per cent of 49 patients, and also a changing E.C.G. pattern. In case 2 there was a persistent tachycardia but no other abnormality in E.C.G. Perhaps this indicated that the heart was involved.

Electrophysiological studies in Friedreich's ataxia have demonstrated the absence or marked reduction in amplitude of the median and ulnar sensory nerve action potential and also some slowing of motor conduction (Bauer, Meyer and McMorrow, 1963; McLeod, 1971). The involvement of the peripheral nerves has been further supported by histological examination (McLeod, 1971) but the causative factor has not been identified so far. The other association of note with Friedreich's disease is that of diabetes mellitus (Ashby and Tweedy, 1953). Recently Hewer and Robinson (1968) found that out of a series of 113 cases of Friedreich's ataxia, 9 were diabetic and a further 12 had abnormalities of the glucose tolerance test.

Peripheral nerve conduction studies have supported the suggestion that peripheral neuropathy in diabetes is due to a disturbance of carbohydrate metabolism
(Chopra and Hurwitz, 1969). The electrophysiological study in synalbumin positive and negative subjects, however, turned out to be inconclusive (Chopra, Connon and Banerji, 1969). However, no one has so far attempted to show whether there is any relationship between impaired peripheral nerve conduction in Friedreich's ataxia and the associated diabetes mellitus. It is of interest to note that one of the siblings, reported here, who had an abnormal g.t.t. also showed an abnormal peripheral nerve conduction whereas the other with normal g.t.t. had a normal nerve conduction. It is possible that the impaired nerve conduction in the former and perhaps in hereditary ataxia is due to a disturbance of carbohydrate metabolism, as in patients with diabetes mellitus.

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