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Short report

Hereditary progressive chorea without dementia

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SUMMARY A family with hereditary non-Huntington's chorea is presented. Transmission was autosomal dominant with variable penetrance. Chorea commenced in childhood and affected predominantly the head, face and upper limbs. Dysarthria appeared later, followed in two family members by elements of an axial dystonia. There was no intellectual impairment. Unlike previously described families, symptoms progressed steadily up to the eighth decade, causing considerable physical disability.

Famial non-paroxysmal chorea without dementia is now a well-recognised clinical entity.[1–4] It presents in infancy or early childhood with choreiform movements which are absent only during sleep. Intellectual development is normal, although a recent report suggests there may be some impairment of verbal skills.[5] It is further distinguished from juvenile-onset Huntington's disease by the absence of rigidity, seizures or cerebellar features, but it shares with this disorder an autosomal dominant inheritance pattern. Beyond childhood, affected family members are said to progress no further, and, indeed, there may be an improvement in the severity of the chorea in adult life, thus prompting the label of "benign" familial chorea.

We report here a family in which the disease has shown undoubted progression throughout adult life, although it has not shortened the life-span of affected members.

Case reports

Case 1 JB, a 75 year old right-handed Caucasian male, presented with a severe movement disorder. As far as is known, his birth and neonatal period were normal. There was no history of jaundice, rheumatic fever or febrile convulsions in infancy. Early development was normal, until at the age of 7 or 8 years he developed jerky involuntary movements of his limbs. They interfered with his handwriting at school and stopped him from playing football except in goal. In his teens he started noticing a tendency for his head to be pulled down and to the left. His involuntary limb movements became gradually more pronounced in adult life and prevented him from training for any job beyond part-time gardening. He was, however, able to ride a bicycle up to the age of 60 years. In his twenties he first noticed problems with his speech, which worsened with time and became virtually unintelligible in the last 10 years. Abnormal brief jerky movements of his face and tongue had also recently started to interfere with swallowing solids. His referral was prompted by the presence of a severe flexion deformity of his neck which, together with continuous involuntary jerking of the head, had led to abrasions of the jaw and anterior chest wall.

He was on no drugs other than diazepam at night and had not been on psychoactive medication in the past. He was childless. There was no parental consanguinity and no family history of dementia or of psychiatric illness. However, at least three other family members were afflicted with the same movement disorder (fig). His sister MW is described below. Another sister died at the age of 1 year of unknown causes. An older brother also had had jerky involuntary limb movements and a tendency to hold his neck flexed since early childhood. Unlike JB, he was able to write and successfully completed an apprenticeship in engineering, but had to give up full-time work in his twenties. In later years his head and neck movements became very pronounced. He died at the age of 75 years from carcinoma of the throat. A younger brother was alive and well, as were his two children. He was approached but declined to be examined. JB's parents were apparently unaffected, but a paternal aunt suffered from severe involuntary movements of her limbs and head. She died childless at the age of 100 years. JB's paternal grand-

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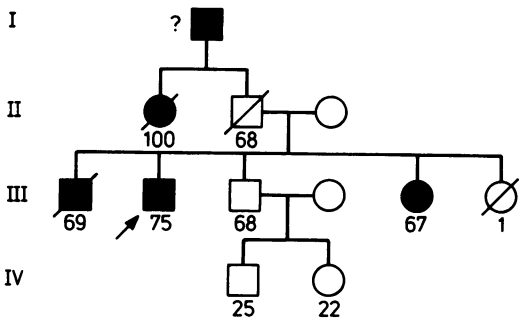

Fig *Family pedigree. The propositus (JB) is marked with an arrow.*

father is said to have been "nervous", although it is uncertain whether he, too, had abnormal movements.

Clinical examination revealed a stooped posture with marked cervical kyphosis and thoracolumbar lordosis. There was a deep abrasion on his chest wall at the point where the jaw rubbed against it, and a smaller one on the jaw itself. He had constant random involuntary jerky movements of the distal parts of his limbs which were choreiform in nature. Handwriting was impossible and he could feed and dress himself only with great difficulty. His gait was grossly disturbed by jerking of his legs. Prominent orofacial dyskinesia, with spontaneous protrusion of the tongue and continuous grimacing, resulted in sialorrhoea and severe dysarthria. There were no Kayser-Fleischer rings. His shoulder muscles were mildly wasted and bilaterally weak. The left lower limb was hypertonic, but there was no tendon reflex change. Plantar responses were flexor. Examination of his abdomen and cardiovascular system was unremarkable.

Formal assessment of his speech patterns revealed a hyperkinetic dysarthria with imprecise consonants, bursts of speech and poor breath control. Nevertheless, detailed neuropsychological testing showed no evidence of cognitive impairment. On similarities testing (sub-group of WAIS) he achieved a scale score for his age-group of 17, suggesting a high degree of abstraction skills. He had a forward digit spread of 8 and a reverse span of 5, both surprisingly good for a man of his age. He scored 25/30 correct on the mini mental state, the only errors occurring in the two test items that required manual dexterity (writing and drawing). Memory and perceptuo-spatial abilities were above average for his age-group.

Full blood count, blood film, sedimentation rate, serum urea and creatinine, electrolytes, liver function tests, creatine kinase, blood glucose, lipid profile and serum and urinary copper studies were normal. There were no acanthocytes in the blood film. An ECG showed no evidence of a cardiomyopathy or cardiac dysrhythmia. A chest radiograph was normal. Blood WR and VDRL were negative. Nerve conduction studies were normal except for slowing of motor conduction in the right ulnar nerve across the elbow to 38 m/s. EEG, CT brain scan and evoked potential studies were technically impossible because of the severity of his movement disorder. Genetic analysis of both JB and his sister MW by means of the G8 probe proved to be uninformative, both being identical at the G8 allele.

He failed to respond to treatment with either pimozide or tetrabenazine. Since discharge he has continued to look after himself at home, but relies heavily on support from relatives and the social services.

Case 2 MW is JB's 67 year old sister. Her birth was normal and apparently she did well at school and showed normal proficiency at games. In her early teens she started becoming "nervous" when in crowds, and attendance at school concerts caused odd twitching movements of her hands. By the age of 18 her handwriting had deteriorated and she had developed brief jerky movements of her head. She first noticed dysarthria in her late twenties. Both the dysarthria and the abnormal movements of limbs and head progressed slowly over the years. They became more noticeable in situations of stress or anxiety. Although less severely affected than JB, she has become moderately incapacitated in her ability to perform household chores and can walk at most one mile without stopping. She had no children.

Examination showed a right-handed female of normal build. There was no spinal deformity. Severe jerky involuntary movements affected her head and face, causing repeated grimacing with platysmal contraction. She was markedly dysarthric. Similar choreiform movements were present in her upper limbs, especially on arm elevation, but were less severe in the legs. There was moderate weakness of the shoulder girdles, with depressed biceps and supinator jerks. Hip flexors were mildly weak, lower limb reflexes were brisk and the left plantar response was extensor. There was no dystonia and sensation was intact. Kayser-Fleischer rings were absent. There was no evidence of intellectual impairment or of a behavioural disturbance.

Full blood count, blood film, sedimentation rate and a biochemical screen similar to JB's were normal. The blood WR was negative. Thyroid function tests and copper studies were normal. A CT brain scan was marred by movement artefact but showed only symmetrical fullness of the lateral ventricles.

Discussion

The clinical features of the family under study correspond to those of previously described patients with hereditary chorea without dementia. Choreiform movements beginning in childhood, facial grimacing, dysarthria and the absence of cognitive impairment are all characteristic of this condition. Inheritance is nearly always autosomal dominant, as in our family, and cases described in the literature as recessively transmitted could be due to incomplete penetrance.[5] Such variability in penetrance is obvious from the fact that our propositus' father must have been an obligate asymptomatic carrier. Male to male transmission in our family also helps to rule out an X-linked dominant gene. As in previous cases, investigation in our patients failed to disclose an underlying metabolic disorder.

Despite similarities with previous reports, certain distinctive features in our patients are worth noting. Firstly, the onset of symptoms appears to have been later than in previous cases, most of which presented in the first 3 years of life.[1 3 6] However, considering

the age of our patients, it would not be surprising if their recollection of events in childhood were somewhat blurred. In the second place, there was an additional element of an axial dystonia to the overall movement disorder in JB and probably also in his brother. Dystonic posturing was not observed in patient MW. Axial dystonia has not been described in connection with familial chorea before but may have contributed, unrecognised, to the gait disturbance which is often present. It should be emphasised that the dominant feature of the movement disorder in both cases examined was that of a true chorea. Autosomal dominant dystonia with rapid jerky movements is recognised in the literature but such movements are repetitive and not choreiform in nature.

The most remarkable discrepancy with previous reports is the clear progression of the disease with time. It has been repeatedly stated that affected individuals either remain static or improve after the third decade.[1 2 5] This was not the case in the third generation members of our family. Their involuntary movements became gradually more pronounced, although they remained most severe in face and hands, and the dysarthria increased. In every case, the disorder caused not only severe social embarrassment but also inability to hold down a job beyond the fourth decade of life. Dysphagia appeared late in life in the most severely affected family member and his speech became almost unintelligible. It is possible that loss of striatal neurons with age caused an acceleration of the movement disorder in late life, as has been reported in Sydenham's chorea.[7]

It is therefore incorrect, in our view, to term this form of chorea "benign", since it obviously severely affected our patients' lives. We do not know whether our cases are at the extreme end of the spectrum of severity or whether, given their advanced age, they represent the "normal" endstage of the disease. Most reports in the literature are of children and young adults, whose clinical state in later life is not known. We would agree with Behan and Bone[8] that the most accurate terminology is "hereditary chorea without dementia", omitting the label "benign".

This disorder remains a far less devastating disease than Huntington's Chorea, as evidenced by our patients' longevity and preserved intellect. The propositus' aunt reached the age of 100 years and, as a group, our family contains the oldest described sufferers of the disease. Despite the great length of the history, there were no signs of intellectual impairment in our patients and no evidence of frontal cortical atrophy on CT scanning of the brain. Arguably, the deficit in verbal skills and abstract concept formation reported by Leli *et al*[4] in a large kindred with hereditary non-Huntington's chorea may have resulted from disrupted education. If it were a primary feature of the disease one would have expected it to progress concurrently with other symptoms and signs, and should thus have been striking in our patients.

Our attempts at controlling the involuntary movements pharmacologically met with failure. The role of the physician in these cases is limited to advice regarding prognosis, genetic counselling, speech therapy and the provision of physical aids when required to allow continued independence.

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