Huntington's Chorea

Report of a Chinese Family in Singapore

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Most of the reports on family groups of Huntington's chorea have come from the United States, Britain, the European Continent, and Australia. Sporadic cases, however, have been described in many countries, and in many races—American Negroes (Drewry, 1895), Africans (Gordon, 1935; Klintworth, 1962), Egyptians (El Garem, 1958), Indians (Chuttani, 1957), and Japanese (Kishimoto, 1957). Familial cases in Chinese have been recorded by Singer (1962) who found 8 cases in 4 generations in one family in Hong Kong, and by Tsuang (1969) from Taiwan who reported another family with 11 cases in 4 generations.

The present study deals with a Chinese family in Singapore in which there were 5 cases over 3 generations.

Case Reports

There were 5 affected persons over 3 generations (Table and Fig.).

TABLE

Cases	Case 1	Case 2	Case 3	Case 4	Case 5
Relationship to Case 1	—	Sister	Nephew	Mother	Brother
Generation	II	II	III	I	II
Sex	M	F	M	F	M
Age of onset	32	51	31	30	30
Duration of disease	10 yr.	1 yr.	3 mth.	28 yr.	13 yr.
Choreiform movements	++	+	+	++	++
Psychosis	++	0	+	++	++
Dementia	++	0	+	++	++
Prognosis	Died age 42 yr.	Alive	Alive	Died age 58 yr.	Died age 43 yr.

Case 1. (Propositus, II.5 in Fig.). A 42-year-old Chinese man was admitted to hospital on account of a large septic ulcer over the left ankle and gross involuntary movements. It was impossible to obtain any history from him as he was grossly demented. Subsequently, his sister (Case 2) was traced and a detailed history was obtained.

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A bachelor, and for 15 years a trishaw-rider, he noted choreiform movements at the age of 34. Twitching of the fingers was followed by grimacing of the face, jerky movements of the upper and lower limbs, unsteadiness of gait, and frequent falls. His memory, reasoning power, orientation, and capacity for mental calculation deteriorated rapidly. For instance, he took his trishaw passengers to wrong destinations, exchanged wrong fares, made wrong road turnings, and often ended up in quarrels, fights, and traffic accidents. Later, increasing clumsiness of limbs due to involuntary movement and paranoid delusions cost him his job, as he could no longer control his vehicle.

Within 4 years, he had to beg for food; he wandered aimlessly and slept by the roadside. Several times he tried to commit suicide and was sent to mental hospital on 4 occasions for severe depression and suicidal tendencies.

On examination, he was found to be dirty, unkempt, and wasted from malnutrition. Dementia was gross, as judged by the severe degree of memory loss, disorientation with regard to time and space, acalculia, and lack of insight. His mood fluctuated from mute depression to violent abusiveness. Speech was slurred and staccato in nature and his face was contorted by incessant spasmodic movements. There were grinding movements of

FIG.

the jaw, writhing movements of the tongue, and sucking movements of the lips. Both upper and lower limbs showed frequent involuntary movements which were abrupt, rapid, and semi-purposive in nature. There was flexion-extension-rotation movements of the trunk, shrugging of the shoulders, and 'piano-playing' movements of the fingers and toes. He stood on a wide base with accentuated lumbar lordosis, and walked in zigzag fashion, with frequent lurching and swaying of the trunk and tendency to fall. Slow ocular movements were found to be normal but he was unable to move his eyes in a rapid saccade. The pupils, ocular fundi, and all the cranial nerves were normal. Kayser-Fleischer rings were not seen. There was no sensory or cerebellar signs, but muscle tone was increased and tendon reflexes were exaggerated. Bilateral pyramidal signs with grasp reflex were found in the upper limbs. The Rissl's reflex was positive, but plantar responses were flexor.

Haematological and biochemical investigations were essentially normal. Radiological studies of the skull and chest were non-contributory. Cerebrospinal fluid examination was normal as was plasma caeruloplasmin level. Blood Kahn test was negative.

In the ward, he became very aggressive, attacking other patients, and on one occasion attempted suicide by jumping from the verandah. As drugs failed to control him, he was transferred to the mental hospital.

Five months later, he was readmitted for purulent meningitis and bronchopneumonia. In spite of intensive chemotherapy, he died a fortnight after admission.

At necropsy, the brain weighed 1,238 g. Patches of purulent material were present over the surface of the cerebrum. The gyri showed generalized moderately advanced atrophy, with marked dilatation of the ventricles. Atrophy was also present in the region of caudate nuclei and putamen, while the corpus callosum was thinned. A small cystic discoloration was present at the base of the temporal lobe. Both lungs were congested, oedematous, and showed pneumonic changes. All the other organs were normal.

Case 2 (II.2). The 52-year-old sister of the propositus was traced. She is married with 6 adult children and 8 grandchildren. Mild involuntary movements of the limbs and face had been present for over one year, but she had not sought medical advice, thinking these were common tics. Members of her household denied any recent mental or personality changes though her memory was not as good as before. She was found to be restless and fidgety. There were periodic writhing movements of hands and feet, shrugging of the shoulders, swaying of the trunk, and twitching of the face. Speech, gait, and all the other systems were unaffected. She was rational, co-operative, but somewhat euphoric. Dementia was not present. Her IQ was 80. Positive neurological signs were jerky ocular movements, bilateral grasp reflexes, and a positive Rissl's reflex.

Most investigations, including CSF, blood Kahn tests, and radiological examinations were normal. An EEG showed diffuse slow waves with low voltages in all

tracings. Air encephalogram revealed some widening of the sulci suggesting a mild degree of cerebral atrophy. The ventricular systems were normal.

After one year's treatment with various drugs, her clinical state remained unchanged.

Case 3 (III.1). This 31-year-old male clerk was brought by his mother (Case 2) to consult us because of his depression and insomnia for 3 months. He had a recent onset of mood changes, lapses in memory, and complained of lack of concentration in his work. The positive findings were an endogenous depression, constant finger twitching, and facial grimaces. Most investigations were essentially normal.

Case 4 (I.1). The history of this patient—the mother of the propositus and of his sister—was supplied by the latter. She developed chorea at the age of 30, soon after the delivery of her third son (Case 1). Involuntary movements started on the limbs and face and became generalized. She became 'insane' and attempted suicide several times. Though she was repeatedly admitted to mental hospital for treatment, her mental and physical condition deteriorated progressively so that she was paralysed, bedridden, and had dysphagia towards the end. She died 28 years after the onset of the disease. Her family were immigrants from Fukien Province of Southern China and she was the only daughter born in Singapore.

Case 5 (II.3). The history of the elder affected brother of the propositus was also obtained from Case 2. At the age of 30, this male hawker developed jerky movements of arms and legs and twitching of the face. Later, he was noted to have mental and behaviour changes and was admitted to mental hospital for psychosis and suicidal tendencies. One night, 13 years after the onset of illness, he was found drowned in the Singapore River.

Unaffected Family Members

All the members of this family, except the father, were local-born Singaporeans.

The father of the propositus (I.2) came from Southern China at the age of 20. He was in good health and died suddenly at the age of 78 from a 'heart attack'. His family history revealed no significant mental or physical illnesses.

The normal brother of the propositus (II.4) is now 48 years old, and is sound both mentally and physically.

The children of Case 2: apart from the eldest son (Case 3), all the five other children were found, on examination, to be unaffected. All were under the age of 30. Only 2, Case 3 and his eldest sister, were married.

The grandchildren of Case 2. The 8 grandchildren (4th generation) of Case 2 were found to be normal.

Discussion

In the present family the clinical feature, course of illness, and prognosis are similar to those reported elsewhere.

The age of onset, with the exception of Case 2, was about 30 years, and the duration of illness before death was between 10 and 13 years in the 2 brothers (Case 1 and 5), and 28 years in Case 4. Choreiform movements, the commonest and early signs of this disease, were present in all cases. The degree of severity of these abnormal movements parallels the duration of illness. Speech in 2 patients was affected, and dysphagia was present in one (Case 4). Psychiatric disturbance of varying degrees was found in all cases, but in 3 cases, suicidal tendencies were strong enough to warrant admission to mental hospital. Case 5 committed suicide by drowning.

Dementia, often a late symptom, is more severe in those with a longer history of the disease. Hence, Cases 2 and 3 were spared from the mental changes for the time being, though the former had EEG and air encephalogram findings of diffuse cerebral cortical involvement. Severe cerebral atrophy was also found in the propositus at necropsy.

The transmission in this family was clearly of the autosomal dominant type. These cases probably originated from Fukien Province in Southern China about a century ago. It is possible that Huntington's chorea does exist in mainland China, though such cases have not been documented in the English literature. Singer's family in Hong Kong and Tsuang's family in Taiwan are presumably immigrants descendants from mainland China, as is our family.

A long delay in diagnosis is not uncommon. Brothers and Meadow of Australia (1955) and Heathfield of London (1967) found a delay of 5 to 10 years in some of their cases. In this series, Case 1 was not diagnosed for 8 years, while 2 other cases died without being diagnosed.

There are several reasons for the delay: (1) the reluctance of relatives to divulge the true family history because of social stigma; (2) in the absence of relatives or friends, no accurate history is available from the demented patients, e.g. Case 1; (3) absence of a positive family history may result in some cases being misdiagnosed, e.g. post-encephalitis Parkinsonism, Wilson's disease, schizophrenia, depressive psychosis, and so on; (4) the early cases may escape diagnosis because of scanty signs and symptoms, e.g. Cases 2 and 3.

Heathfield (1967) has stressed that absence of a family history does not rule out Huntington's chorea, as half the cases diagnosed at the National Hospital, Queen's Square, London, did not have one. On the other hand, a positive family history with choreiform movements could result from other causes besides Huntington's chorea, e.g.

familial paroxysmal choreathetosis (Mount and Reback, 1940), and hereditary non-progressive chorea of early onset (Haerer, Currier, and Jackson, 1966): these are benign, non-progressive forms with minimal mental changes.

So far, no reliable methods are available to detect asymptomatic cases before the overt disease manifests itself. EEGs used by Patterson, Bagchi, and Test (1948) have recently been found to be valueless in detecting these cases (Chandler, 1967). Other tests, such as adaptive abilities and motor-sensory functions (Hansotia, Cleeland, and Chum, 1968), have been advocated, but their value has yet to be assessed.

Summary

Huntington's chorea with typical findings was observed in a Chinese family in Singapore, affecting 5 members over 3 generations. The origin of the disease was traced to Fukien Province in Southern China.

Of the three cases studied, one died and the diagnosis was confirmed by necropsy.

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