CHOREOACANTHOCYTOSIS IN A CHINESE PATIENT – A CASE REPORT

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ABSTRACT

A 50-year old Chinese woman with the rare neurological disorder of Choreoacanthocytosis is described. Her illness is characterised by seizures, buccolingual dyskinesia, choreiform movements, arreflexia and mild sensorimotor polyneuropathy. Acanthocytes were present in her peripheral blood in large numbers but the serum lipid profile was normal. Her features are consistent with those so far described in Caucasian and Japanese patients. The disease differs from Huntington's chorea in that there are acanthocytes, peripheral neuropathy, and metal function remains relatively intact.

Keywords: Chorea, Acanthocytes, Chinese patient

SING MED J. 1989; NO 30: 506–508

INTRODUCTION

There have been several reports in the literature (1-12), largely in Caucasian and Japanese patients, of this rare neurological disease characterised by progressive chorea and erythrocyte acanthocytosis, not associated with deficiency of serum lipids. The present report describes a Chinese patient in Singapore with similiar features. This condition is clinically distinct from Huntington's Disease and abetalipoproteinaemia.

CASE REPORT

ML, a 50 year old Chinese lady, first presented in 1974 with thyrotoxicosis to a general practitioner. Details of treatment are unavailable but she was already noted to be clumsy then with a noticeable change in her mental state. This was described by the family as excitability in addition to attention seeking behaviour.

A year later, she was diagnosed to have depression after an attempted suicide. In 1976, she was admitted to a psychiatric hospital and given electroconvulsive therapy and phenothiazines for Schizophrenia. A neurological opinion was first sought at this time when her abnormal movements were noted and it was recorded that she was hyporeflexic with low normal nerve conduction velocities. The initial diagnosis made was that of complex motor tics and haloperidol was prescribed. Soon after, she began to have recurrent generalised tonic-clonic seizures necessitating the addition of phenytoin sodium.

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Her abnormal movements, progressively evolved from its initial involvement of the right arm to affect all her limbs resulting in gait difficulty. The movements were aggravated by emotional stress and improved with rest.

In 1980, she was seen at the Singapore General Hospital for relapsed thyrotoxicosis where the attending physician noted choreiform movements of all limbs with a peculiar high stepping gait and a tendency to fall. There was no aggravation of this unsteadiness with darkness. The patient was still troubled by recurrent seizures and her attention span was poor. A computerised tomographic scan of the brain was performed in April 1981 which showed dilated ventricles and bilateral caudate atrophy. No examination of the peripheral blood was done and she was labelled as a case of Huntington's chorea .

In November 1985, she was referred to the University Neurology Division for an opinion. At this time, the examining physician felt that her mental state was quite normal and this was confirmed by her husband as she had quite good comprehension as well as an intact memory. The patient has 3 siblings from a non consanguinous marriage with no family history of similar neurological problems.

Physical examination revealed gross choreiform movements of all limbs with a curious gait. The latter consisted of ataxia and buckling of the knees with a high steppage component and a marked tendency to fall. Prominent oro-buccal dyskinetic movements were seen with intermittent involuntary protrusion of the tongue. The deep tendon reflexes were absent, with downgoing plantar responses. However, there was no muscle wasting or fasciculations and no sensory loss was detected to light touch and pin-prick. Fundoscopic examination revealed no abnormalities.

LABORATORY INVESTIGATIONS

The peripheral blood smear revealed 50% acanthocytes with some spherocytes and target cells. The haemoglobin was 14.3 g/dl with a white count of 6600/ml and erythrocyte sedimentation rate of 2 mm/hour. The serum cholesterol was 5 mmol/1 (4-7 mmol/1) and the triglycerides 1.85 mmol/1 (0.5-2.25 mmol/1). The transaminases and bilirubin were not elevated.

Nerve conduction studies showed decreased

evoked sensory potentials with low normal conduction velocities and needle electromyography showed mild denervation. Electroencephalography revealed a prodominant beta rhythm with occasional sharp/theta waves over the left temporal leads. A repeat computed tomographic brain scan confirmed generalised cortical atrophy with bilateral caudate atrophy.

PROGRESS

Once the diagnosis of choreoacanthocytosis was confirmed, the patient was started on sodium valproate in an attempt to control both her seizures as well as abnormal movements. She did not, however, respond and the seizures required an adjusted dosage of phenytoin sodium after discontinuation of sodium valproate. Tiapridal and later, tetrabenazine were both tried with no success in amelioration of her chorea. In fact, the latter drug considerably worsened her dysphagia.

Of her 2 siblings, only the sister consented to evaluation. This sister was neurologically normal but had 5 % acanthocytes in the peripheral blood. The brother refused repeated requests to have his peripheral blood examined or to undergo clinical assessment by the authors. Both parents died of unrelated causes.

The patient is currently cared for in a private nursing home. She is only ambulant with assistance and needs help for feeding as well as toilet. Her memory remains good although her speech is severely dysarthric.

DISCUSSION

Estes, Levine et al first described this rare familial neurological disease associated with acanthocytosis but with normolipaemia in a New England family in 1967 (1). Three generations of this unusually cooperative family were available for study and, in 1968, Levine (2) was further able to characterise the features as clinically distinct from that of abetalipoproteinaemia (Bassen-Kornzweig Disease). In that same year, Critchley et al reported another family from Kentucky with similar neurological features and acanthocytosis (3).

Acanthocytes are mature red cells with multiple irregularly arranged spiney or blunt projections and they were first described in the 1950's by Bassen and Kornzweig in a young girl suffering from malabsorption, diffuse nervous system involvement and retinitis pigmentosa. This syndrome was subsequently found to result from a congenital absence of betalipoprotein. Inheritance is autosomal recessive.

The situation is different in choreoacanthocytosis or familial amyotropic chorea with acanthocytes (FACWA), although it shares with abetalipoproteinaemia the similar presence of acanthocytes in the peripheral blood. No abnormalities in plasma or red cell cholesterol or phospholipid content are present, nor does this latter condition manifest atypical retinitis pigmentosa, long tract signs or a history of malabsorption.

Although it was originally thought that the disorder is inherited in an autosomal dominant fashion (1, 4), subsequent reports appear to suggest that choreoacanthocytosis is autosomal recessive in its inheritance pattern (3, 5, 6). Another recent report, in which the family was well studied, also suggests an autosomal recessive inheritance pattern in 1 patient, with both parents having acanthocytes in the peripheral blood and raised creatine kinase despite being normal neurologically (7).

Our patient illustrates many of the typical clinical features of this disorder and is the first case reported from Singapore and, to our knowledge, in a Chinese. We were unable to trace her family history back more than one generation but the patient's parents did not suffer from any neurological disease nor were they related. We are also unable to comment on the inheritance pattern. From the literature, many patients had histories that included probable mental illness (1, 2, 8) and this is also seen in our case.

An important differential point from Huntington's disease illustrated in the case history is the relative intactness of cognitive function with retained memory and comprehension (9). Seizure is another well documented feature (1-4, 8, 10) present in this patient.

The pattern of our patient's movement disorder is also unique, with prominent oro-lingual-facial dyskinetic movements or 'tics'. Unlike some reports, there was no tongue or lip biting and no difficulty with mastication of food (3, 4, 8, 10). Choreiform movements of the limbs is a less prominent feature and developed later. In Huntington's disease, the movement disorder, although similar, tends to be more pronounced in the limbs and tongue or lip biting have not been reported. Other features of choreoacanthocytosis include diminished tendon reflexes, minimal wasting of muscles and intact clinical sensory testing.

The abnormality of gait deserves special mention as it is characteristic and very well described especially by Yamamoto (8), and by other authors (2, 4). There is a typical curious buckling of the knees as the patient attempts to walk producing a 'high-steppage' like progression.

In terms of investigations, minor impairment of largely sensory conduction velocities with a denervation pattern on needle EMG is a typical electrophysiological finding (4, 6, 8, 10, 11). The CT Scan often shows bilateral caudate atrophy (12) and, together with the finding of acanthocytes in the peripheral blood and normal lipids, allows one to make the diagnosis.

The serum creatine kinase levels have also been reported to be elevated in some patients (5, 6-10), but this investigation was not done in our case. Some authors also noted mild abnormalities in the liver function tests (2, 6) and Gross (10) reported increased free serum sialic acid concentrations in his index case.

To date, tests of acanthocyte function in affected patients have only revealed decreased red cell survival (1, 2, 4, 5,) and the underlying cause for this aberrant membrane shape is still far from evident as is the genesis of the neurological features, although Bertelson (13) recently reported a deletion in the X chromosome in 2 brothers with McLeod phenotype, an X-linked erythrocyte phenotype, which also presents with acanthocytes and elevated creatine kinase. Estes (1) and later Critchley (3) demonstrated that normal red cells incubated in affected patients' serum adopted this abnormal shape, suggesting that a still unidentified serum factor may be at fault.

There is no known treatment and even symptomatic treatment is difficult, judging from the experience of other authors. Haloperidol was tried in our index case unsuccessfully although one report claimed that it produced improvement in the oro-lingual dyskinesia (10). We tried tetrabenazine but this produced dysphagia in our patient. Both tiapridal and sodium valproate also showed no effect in our hands, but phenytoin sodium controlled the seizures.

CONCLUSION

Choreoacanthocytosis is a rare but distinct neurological entity which can be diagnosed if the peripheral blood is examined for the presence of acanthocytes in patients who present with chorea. It is clinically possible to differentiate this condition from Huntington's disease as the oro-buccal-lingual dyskinesia is more marked and mental function is retained despite a long history and marked disability from the movement disorder itself. An elevated creatine kinase is also a feature as is the presence of peripheral neuropathy.

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