CASE REPORT

The first case report of McLeod syndrome in a Chinese patient

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SUMMARY

We report the first case of McLeod syndrome (MLS) in a 47-year-old Chinese man who presented with progressive limb weakness, chorea of feet, red blood cell acanthocytosis, absence of Kx red blood cell antigen and weak expression of Kell antigens. The diagnosis of MLS was confirmed by genetic testing showing a hemizygous mutation of XK gene. We review literature on neuroacanthocytosis in the Chinese population.

BACKGROUND

Neuroacanthocytosis (NA) is a heterogeneous group of hereditary syndromes characterised by the association of neurological abnormalities with acanthocytosis. The most common ones are autosomal recessive chorea-acanthocytosis (ChAc), X linked McLeod syndrome (MLS) and neurodegeneration with brain iron accumulation.¹ Despite its recognition in the medical literature, the syndrome is rarely described in the Chinese population due to a low index of suspicion by clinicians and lack of confirmatory tests. We report the first case of MLS in a Chinese patient and review literature on neuroacanthocytosis in the Chinese population.

CASE PRESENTATION

A 47-year-old Chinese man presented with progressive wasting of limb muscles for a few years. He also had bilateral genu varus, hypoesthesia of fingers and toes to pain and involuntary movement of his legs. His gait was waddling and he had had multiple falls in the past few years. One older brother had some cognitive problems but details were not available. The examination revealed wasting of bilateral temporal, left shoulder, left thigh and bilateral hand muscles. The jerk was hyporeflexia and there was choreoathetosis of his feet.

INVESTIGATIONS

Laboratory testing was significant for an elevation in a serum creatine kinase (CK) level of 2148 U/L (normal 62–279). Serum ceruloplasmin, copper, iron, ferritin, liver function test and lipoprotein were normal. An MRI of the brain showed atrophy of basal ganglion and generalised brain atrophy. A nerve conduction study showed sensorimotor axonal polyneuropathy. An electromyography revealed combined neurogenic and myopathic changes. Muscle biopsy confirmed myopathy changes. The ECG and echocardiography were normal. Blood smear with a wet mount of red cells in 1:10 heparinised saline and examined by a

Figure 1 Acanthocytosis in blood smear. Peripheral blood; Wright Stain; $\times 100$ magnification; smear showed frequent acanthocytes (approximately 10% of red cells).

phase contrast microscope revealed 16% acanthocytes as compared with 1% in normal healthy control (figures 1 and 2). Kell blood group testing showed weak expression of Kell red blood cells (RBC) antigens and absent Kx RBC antigen. Sequence analysis of the XK gene detected a hemizygous mutation c.856_860delCTCTA (reference sequence NM_021083.2).

OUTCOME AND FOLLOW-UP

The patient's condition was stable and he was able to walk with a stick.

Figure 2 Acanthocytosis under phase contrast microscope. Peripheral blood; 1 part of blood in 10 parts of normal saline (0.9%) incubated for 90 min; phase contrast microscopy $\times 100$ magnification. Smears showed 16% acanthocytes, in comparison to normal healthy control (1%).

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DISCUSSION

NA syndromes are a group of genetically defined diseases characterised by the association of RBC acanthocytosis and progressive degeneration of the basal ganglia. NA syndromes are rare with an estimated prevalence of less than 1–5/100 000 inhabitants for each disorder.¹ In China, there were 28 case reports reporting 37 NA cases.² The prevalence of NA in China is 0.28/one billion populations. The prominent symptoms include movement disorders (97.4%), dystonia (81.6%), orofacial dyskinesia (76.3%), dysarthria (68.4%), dysphagia (42.1%), epilepsy (21.1%) and psychiatric symptoms (18.4%).² NA is very likely to be underdiagnosed in China. Kell antigen testing on RBCs for MLS and chorein Western blot or VPS13A sequencing for ChAc is presently not available in China, thus further classification of NA syndromes is not possible.² Our case is the first reported case of MLS in the Chinese.

MLS is an X linked multisystem disorder with haematological, neuromuscular and central nervous system (CNS) involvement.^{3–6} MLS is characterised by the absence of Kx RBC antigen, weak expression of Kell RBC antigens, acanthocytosis and compensated haemolysis.⁷ There are a few hundred cases of MLS worldwide. MLS has been described in Europe, North and South America and Japan without obvious clustering.⁴ Asymptomatic carriers of the McLeod blood group phenotype may be accidentally recognised by blood bank testing.^{3–7} They may develop neurological signs and symptoms with a mean onset age from 30 to 40 years, and high penetrance of the disorder.³ Neuromuscular manifestations include myopathy, sensory–motor axonal neuropathy and cardiomyopathy. All McLeod carriers have elevated serum CK levels. CNS manifestations consist of a choreatic movement disorder, ‘subcortical’ neurobehavioural deficits, psychiatric abnormalities and generalised seizures.^{3–4}

MLS is caused by mutations of the XK gene encoding the XK protein, which carries the Kx RBC antigen.⁸ A hemizygous XK mutation c.856_860delCTCTA was detected in our patient. This mutation has been reported previously in patients affected by MLS.³ The 5-nucleotide deletion is predicted to create a premature stop codon at amino position 301 (p.Leu286Tyrfs*16). Although the exact function of the human XK protein is not yet

known, the available data suggest an important role for apoptosis regulation.⁴ There is no clear-cut genotype–phenotype correlation. Thus genetic testing is not useful in accurately predicting the age of onset, the severity, the type of symptoms or the rate of disease progression of MLS.

Learning points

- ▶ Neuroacanthocytosis is rarely described and very likely to be underdiagnosed in China.
- ▶ The diagnoses rely on a high index of clinical suspicion of characteristic clinical features and a standardised wet blood smear method of peripheral blood examination for acanthocytes.
- ▶ Genetic study is the gold standard in diagnosis and further classification of the syndrome.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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