Mitochondrial myopathy with chronic progressive external ophthalmoplegia

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(Index words: Electron microscopy, EMG, ECG, clinical features)

Introduction

Mitochondrial diseases are a diverse group with multisystem involvement caused by structural, biochemical or genetic derangement of mitochondria. Cerebral neurones and myocytes which require a high yield of energy are particularly vulnerable to mitochondrial dysfunction and neuromuscular manifestations are common in mitochodrial disorders. We report two cases of mitochondrial myopathy presenting as chronic progressive external ophthalmoplegia.

Case 1

A 37-year old man had slowly progressive drooping of both eyelids for five years. There was no diplopia, pain or weakness of muscles after exercise, seizures, or a family history of similar illness. Examination revealed bilateral symmetrical partial ptosis without fatiguability, complete ophthalmoplegia without diplopia, and mild palatal weakness. Other neurological and systemic examinations were unremarkable.

Routine haematological and biochemical screening was normal. Serum creatine kinase (CK) level was normal. ECG revealed a first degree heart block. The echocardiogram, CSF analysis and the EEG were also nomal.

The edrophonium test was negative. Electromyography (EMG) was consistent with a myopathy. Electron microscopic studies of the right deltoid muscle biopsy revealed antiphagic vacuoles and abundant mitochondrial inclusions confirming a diagnosis of mitochondrial myopathy (Figure).

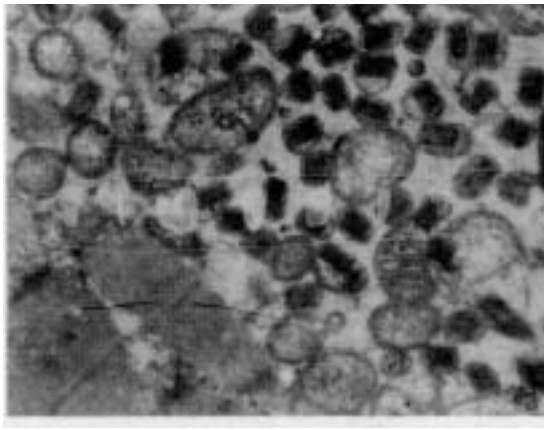

Figure. *The electron microphotograph of muscle biopsy of patient 1 showing numerous abnormal mitochondria with inclusions (×12 000).*

Case 2

A 49-year old woman had progressive drooping of eyelids and weakness of proximal muscles for 3 years. There was no diplopia, pain or weakness of muscles, seizures, or a family history of a similar illness.

Examination showed bilateral symmetrical partial ptosis without fatiguability, complete external ophthalmoplegia without diplopia, and mild proximal weakness of all four limbs. Other neurological and systemic examinations were unremarkable.

Routine biochemical and haematological tests were normal. Serum CK, CSF analysis, serum lactate, thyroid axis hormones, ECG and echocardiogram were normal. The edrophonium test was negative. EMG showed features typical of a myopathy. Electron microscopic studies of the left deltoid muscle biopsy showed several antiphagic vacuoles with "para-crystalline" inclusions in mitochondria suggestive of mitochondrial myopathy.

Discussion

Chronic progressive external ophthalmoplegia (CPEO) is the classical phenotype of mitochodrial myopathy (1). It is characterised by ptosis, external ophthalmoplegia and limb myopathy. Additional clinical and laboratory features typical of mitochondrial disorders may also be present (2), including seizures, encephalopathy, neuropathy, cardiomyopathy and conduction defects, and lactic acidaemia. Diplopia and strabismus are uncommon in CPEO owing to the symmetrical nature of the extraocular muscle involvement (3).

Based on the age of onset and clinical severity, CPEO can be divided into 3 groups. The most severe variant is Kearns-Sayre syndrome, characterised by early onset, pigmentary retinopathy, deafness, ataxia, diabetes mellitus, elevated CSF proteins and heart block. The second variant known as "CPEO plus" has an intermediate severity and an adolescent onset. In the mildest variant, there is isolated CPEO with an adult onset. Both patients described above probably belonged to the last group.

Diagnosis requires a high degree of clinical suspicion, and is confirmed by histology and electron microscopic studies of biopsy from affected muscles (4). Typical features include ragged red fibers on Gomori trichrome stained sections and abnormal mitochondria with perinuclear antiphagic vacuolation and "paracrystalline inclusions".

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Fasting lactate level in the blood and CSF may be increased. EMG usually shows evidence of a myopathy, and nerve conduction studies a peripheral neuropathy. EEG may show subclinical seizures. All patients need ECG and echocardiography evaluation for conduction defects and cardiomyopathy. Most patients with CPEO have mitochondrial DNA deletions, although some may be associated with point mutations (5,6). In these instances the disease is maternally inherited. Supportive care with physiotherapy and maintenance of a moderate level of exercise are beneficial. Precautions are required before general anaesthesia as these patients are more susceptible to anaesthetic complications (7).

Mitochondrial disease should be considered in any patient with unexplained progressive myopathy or other neurological disorder, particularly when there is a multisystem involvement and a relevant family history.

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Child soldiers: understanding the context

Tiger casualties show that most of the children are aged 14-18, while the younger ones are usually kept in reserve. But in large scale, mass attacks children may be used in greater numbers. In specialised units such as the leopards children form an effective fighting force in difficult battles.

Because of their age, immaturity, curiosity, and love for adventure children are susceptible to “Pied Piper” enticement through a variety of psychological methods.

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