Muscle Biopsy: A Boon for Diagnosis of Mitochondrial Parkinsonism in Developing Countries

Ritu Shree, Sahil Mehta, Manoj K Goyal, Balan L Gaspar[1], Vivek Lal

Departments of Neurology and [1]Histopathology, Postgraduate Institute of Medical Education and Research, Chandigarh, India

Abstract

Mitochondrial dysfunction plays an important role in the pathogenesis of Parkinson's disease. Primary genetic abnormalities in the mitochondrial DNA or nuclear DNA can cause parkinsonism. Mitochondrial parkinsonism presents with classical features of parkinsonism along with multisystem involvement. Genetic analysis is essential in reaching the diagnosis which is not always possible, especially in developing countries. Muscle biopsy can be a boon in this setting as exemplified in our report of two siblings where a diagnosis of mitochondrial parkinsonism was made on the basis of muscle biopsy.

Keywords: Dystonia, mitochondria, muscle biopsy, Parkinsonism

Introduction

Parkinsonism with onset in childhood has a wide spectrum of differential diagnosis, ranging from treatable causes like Wilson's disease to neurodegenerative disorders like juvenile-onset Huntington's disease. In addition, primary genetic abnormalities in the mitochondrial DNA (mDNA) or nuclear DNA (nDNA) can lead to Parkinson's disease. Clue to the diagnosis of mitochondrial parkinsonism rests on multisystem involvement in the form of ptosis, myopathy, and neuropathy, with classical features of parkinsonism. Dystonia has also been seen with defects in the mitochondrial oxidative phosphorylation system exemplified typically by striatal necrosis in Leigh's disease. We report two siblings who presented with a similar phenotype of parkinsonism, dystonia, and peripheral neuropathy and were found to have mitochondrial cytopathy on histopathological examination.

Case Report

A 16-year-old boy born out of a nonconsanguineous marriage with normal birth and developmental milestones presented with slowness of daily activities since 7 years of age. He would freeze while walking and gradually started using support to walk. Subsequently, over the next 2 years, he developed weakness of both lower limbs in the form of slippage of slippers followed by difficulty in getting up from ground. Past history was suggestive of seizures at 1 year of age with poor scholastic performance. His elder sister was also suffering from similar illness with more severity [Video 1]. Examination revealed mini-mental score examination of 29/30, mask-like facies with decreased blink rate. Speech was extrapyramidal with both hypophonic and dystonic quality. There was symmetrical parkinsonism with bradykinesia and cogwheel rigidity in both the upper limbs. There was also evidence of action dystonia in bilateral feet [Video 2]. Other neurological examination showed bilateral pes cavus with hammer toes, foot drop, wasting, and weakness of distal muscles in both the upper and lower limbs (power of 5/5 in bilateral shoulders, elbow, wrist, hip, and knee; 4-/5 in bilateral ankle dorsiflexion; and 4+/5 in bilateral ankle plantar flexion, weak small muscles of hands) with absent knee and ankle jerks [Figure 1]. Fundus examination and extraocular movements were normal. Gait dysfunction was multifactorial due to extrapyramidal involvement and lower motor neuron type of weakness. Magnetic resonance imaging of brain including susceptibility weighted imaging was unremarkable with no evidence of iron deposition [Figure 2a and b]. Nerve conduction studies and electromyography were suggestive of sensorimotor axonal neuropathy [Figure 3a-c]. Serum lactate (1.6), creatine kinase (234 U/L), ferritin, ceruloplasmin, and parathyroid hormone were within normal limits. Bone marrow biopsy did not reveal any abnormal cells suggestive of storage disorder. Finally, muscle biopsy was done which revealed evidence of mitochondrial cytopathy in the form of ragged red fibers in Gomori trichrome stain, confirmed on succinate dehydrogenase (SDH) and cytochrome c oxidase COX staining [Figure 4a-d]. Genomic DNA sequencing of

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Address for correspondence: Dr. Sahil Mehta, Department of Neurology, Postgraduate Institute of Medical Education and Research, Chandigarh, India.
E-mail: mehtasahilpgi@gmail.com

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