

Motor Neuron Disease in Mitochondrial Disorders

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LETTER TO THE EDITOR

In a recent article, Ruggiero et al. reported about a 45 years old male with chronic progressive external ophthalmoplegia (CPEO) due to a large scale single mtDNA deletion of 9063bp who is reported to have developed features of motor neuron disease (MND).[1] We have the following comments and concerns.

We do not agree with the interpretation of the clinical and electrophysiological findings as MND. The presented case hardly presents with features of a MND. No fasciculations were reported, there was no bulbar involvement, there was no involvement of the pyramidal tract, no clinical or electrophysiological progression, and no muscle wasting was reported. Though MND has been repeatedly reported as a manifestation of a mitochondrial disorder (MID) [2] and though MID may even mimic amyotrophic lateral sclerosis [3], abnormal spontaneous activity in association with normal motor unit action potentials and normal nerve conduction studies does not comply with the diagnosis MND.

Why do the authors interpret needle electromyography findings as neurogenic? Fibrillations, positive sharp waves, and complex repetitive discharges may also occur in myogenic lesions. Normal motor units associated with abnormal spontaneous activity do not suggest a chronic neurogenic lesion. Motor units were normal even 3y after the first electromyography. Additionally, repeated nerve conduction studies were normal [1].

We do not agree with the statement that involvement of the peripheral nerves is one of the most frequent phenotypic features of MIDs [1]. In a study of 1200 MID patients, neuropathy of peripheral nerves was found in only 12% [4]. Furthermore, the frequency of neuropathy is different among pediatric and adult MID cases.

Pediatric MID patients more rarely present with neuropathy of the peripheral nerves compared with adults. Much more frequently affected in MIDs than the nerves are the cerebrum, the eyes, endocrine organs, the heart, and the muscles.

As with MND, CPEO has been occasionally reported in association with neuropathy [5,6,7]. In a study of 18 patients carrying single mtDNA deletions neuropathy was found in the majority of the cases and was mainly of the axonal type [5]. In two siblings with CPEO carrying a 4977bp deletion of the mtDNA, one of the siblings developed prominent sensorimotor neuropathy during the disease course [6]. In a patient with Kearns-Sayre syndrome, including CPEO, subclinical neuropathy was reported [7].

MND-like phenotypic features have been only described in a single patient with a single mtDNA deletion so far [8].

A small number of mtDNA deletions may be maternally transmitted [9]. The mother in such cases may manifest clinically or may be asymptomatic. Was the mother prospectively investigated for subclinical manifestations of a MID or was only the family history taken?

Overall, this interesting study could profit from revision of the interpretation of the electrophysiological results, from revision of the diagnosis MND, and from prospective investigations of the mother. Features of MND in patients carrying mtDNA deletions are rare.

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