Mitochondrial neuropathy in pediatric patients carrying mtDNA, POLG1, SURF1, and PDHA1 mutations

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In a recent article, Menezes et al. reported about nerve-conduction studies in 27 pediatric patients (age 3 days to 17 years, 19 males, 8 females) carrying mtDNA, POLG1, SURF1, or PDHA1 mutations1. The design was retrospective in 20 and prospective in 7 patients1. Mitochondrial neuropathy was not length-dependent1. We have the following comments and concerns.

The first shortcoming of the study is the mixture of a retrospective and prospective design, suggesting that systematic nerve-conduction studies had been carried out in only 7 patients1.

Second, follow-up investigations were carried out only in a single patient1. Thus, it cannot be assessed if neuropathy generally progressed and with which speed.

Third, it was not differentiated between primary and secondary mitochondrial neuropathy2. Mitochondrial disorders (MIDs) are usually multisystem disorders, also known as mitochondrial multiorgan disorder syndromes (MIMODS)3, manifesting as diabetes, thyroid dysfunction, parathyroid dysfunction, renal insufficiency, or malignancy4. Secondary causes of neuropathy need to be excluded before primary mitochondrial neuropathy can be diagnosed, also with regard to their different treatment.

Fourth, mitochondrial neuropathy may not only affect spinal but also cranial nerves2. In how many patients was there involvement of cranial nerves, which cranial nerves were affected, and was cranial nerve involvement bilaterally symmetric or asymmetric?

Fifth, MIDs may also manifest as neuronopathy5. Patients carrying POLG1 mutations may even present with sensory ganglionopathy6. Did the authors also investigate the proximal segments of the peripheral nerves? Were F-wave or H-reflex investigations carried out? Was there myelon atrophy on spinal MRIs?

Sixth, were first-degree relatives of index cases investigated for the presence or absence of neuropathy? In how many patients was the family history positive for a MID?

Seventh, which type of treatment did the patients receive? In how many did mitochondrial neuropathy manifest with neuropathic pain? How many required gabapentin or pregabalin or other agents known to be effective for neuropathic pain? How many received cocktails of vitamins, co-factors, or antioxidants? How many were under a ketogenic diet? How many profited from physiotherapy?

How do the authors explain recovery from neuropathy in one MELAS patient? Was neuropathy in this patient primary or secondary? Was it attributable to lactacidosis? Was neuropathy in fact a neuronopathy due to involvement of the myelon and anterior horn cells in the stroke-like episodes? Was there a stroke-like lesion on spinal cord documented in this particular patient?

To summarise, this interesting study could profit from application of a prospective design, systematic investigations of cranial nerves, systematic follow-up investigations, investigations of first-degree family members, and from systematic treatment to see if the course of mitochondrial neuropathy can be beneficially modified.

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References
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