MITOCHONDRIAL MULTIORGAN DISORDER SYNDROME (MIMODS) DUE TO MUTATIONS IN THE SLC25A46 GENE

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Introduction

In a recent article, Braunisch et al. reported about 4 patients (VI-5, VI-4, II-3, II-4) with pontocerebellar hypoplasia (PCH) due to mutations in the SLC25A46 gene¹. We have the following comments and concerns.

We do not agree with the notion that patient II-3 with absent motor responses had axonal neuropathy. Autopsy clearly showed that there was loss of motor neurons in the anterior horns of the spinal cord and the remaining motor neurons had a “ballooned” appearance¹. Thus, it is much more likely that this patient had neuronopathy with secondary degeneration of the axons than polyneuropathy why motor responses were absent on electrical stimulation. Were F-wave studies carried out in any of the four patients to confirm absence of a proximal response upon retrograde stimulation?

PCH is not confined to the brainstem and the cerebellum. Most of the patients diagnosed with PCH present with involvement of organs or tissues other than the brain and also present with cerebral lesions other than PCH²-⁴. This was also the case with the four current patients. They manifested in the central nervous system (hypotonia, cerebellar atrophy, global brain atrophy, optic atrophy, paroxysmal activity on EEG, degeneration of anterior horn cells), the heart (bradycardia), the lungs (diffuse pulmonary capillary hemangiomatosis), and the bones (talipes equinovarus). Due to the short life span of these four patients (1-18 days) only few investigations for multiple organ involvement could be carried out. Was there involvement of the eyes, ears, endocrine organs, heart, intestines, kidneys, skin, or bones on autopsy?

Overall, this interesting case series confirms that mitochondrial disorders (MIDs) may manifest as motor neuron disease and that MIDs are usually multisystem diseases (mitochondrial multiorgan disorder syndromes (MIMODS)). Anterior horn cell degeneration with axonal loss has to be classified as neuronopathy and not polyneuropathy.

References


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