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Letter to the Editor

Prospective Evaluation and Monitoring for Multisystem Involvement may improve the outcome of Kearns-Sayre Syndrome

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We read with interest the article by Grigalioniene *et al*. reporting on a 20 years-old male with Kearns-Sayre syndrome (KSS) due to a novel mtDNA deletion of 5.9kb [1]. Phenotypically, the patient manifested with multisystem disease affecting the brain, eyes, ears, heart, endocrine organs, and muscles [1]. The causative mtDNA deletion could be confirmed only by primer walking and Sanger sequencing, as LR-PCR and multiplex ligation-dependent probe amplification (MLPA) provided conflicting results [1]. The study is appealing but raises concerns that warrant further discussion.

Because 4% of mtDNA deletions are inherited via the maternal line we should know if the mother of the index patient carried his mtDNA deletion as well. Even if the mother was clinically asymptomatic, she may carry the deletion, why it is crucial to prospectively investigate her for this variant.

Torticollis is an unreported phenotypic feature of KSS. We should know if torticollis was also due to the 5.9 kb mtDNA deletion or of another cause and if torticollis was due to denervation of the sternocleidomastoid muscle, due to myopathy, or due to central nervous system (CNS) involvement, including dystonia. There are only few reports of KSS patients that developed dystonia but rather affecting the limb muscles than the cervical muscles [2].

The patient obviously had quadruparesis with lower limb predominance and reduced respectively absent tendon reflexes [1]. We should know if quadruparesis was due to neuropathy, myopathy, or both. Of particular interest in this respect is if needle electromyography (EMG) and muscle biopsy were indicative of myopathy or neuropathy. We also should know if nerve conduction studies showed axonal or demyelinating polyneuropathy. Myopathy, not only of the extra-ocular eye muscle but also the limb muscles, is rather a rare phenotypic feature of KSS [3]. Neuropathy of peripheral nerves is even rarer.

A limitation of the study is that not much information about cardiac involvement was provided. KSS patients may not only develop atrio-ventricular block requiring pacemaker implantation, but also ventricular arrhythmias [4] and dilated or hypertrophic cardiomyopathy [5]. We should know the results of long-term ECG recordings and of echocardiography, particularly if there were malignant arrhythmias or impaired systolic function. KSS with dilated cardiomyopathy may even require heart transplantation [6].

The patient had hypocalcemia and hypokalemia [1]. It would be interesting to know if hypocalcemia was due to involvement of the parathyroid glands manifesting with hypoparathyroidism, due to pituitary involvement, renal involvement, or due to nutrition. Hypoparathyroidism had been reported even as the initial of the syndrome.

The patient deceased from respiratory insufficiency due to pneumonia [1]. We should know if the patient deceased from COVID-19 and whether he was positive for SARS-CoV-2 shortly before death.

Overall, the study carries obvious limitations that require re-evaluation and discussion. Clarifying these weaknesses would strengthen the conclusions and could improve the study. Patients with KSS require comprehensive work-up and monitoring to apply symptomatic treatment in due time and to improve their outcome.

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