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Letter to the Editor

LETTER TO THE EDITOR

Diagnose Kearns–Sayre syndrome genetically and investigate the phenotype comprehensively

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We read the article by Leal *et al.* with interest about a 17-year-old male with Kearns–Sayre syndrome (KSS), diagnosed upon the clinical presentation, instrumental findings and the muscle biopsy findings [1]. Despite some peculiarities of the phenotype, the presentation at onset was mild and the further course uneventful. We have the following comments and concerns.

The main disadvantage of this case report is that the diagnosis was not genetically confirmed. Since phenotypic features of mitochondrial disorders (MIDs) may overlap in various syndromic MIDs, it is not reliable to diagnose KSS only upon the clinical manifestations and muscle biopsy findings. This is of particular importance since a few cases of KSS were reported which did not carry a single mtDNA deletion but a mtDNA point mutation such as the mutation m.3243A>G [2] or m.3249G>A [3]. There are also KSS patients due to a single mtDNA duplication.

Rarely, KSS patients may present with epilepsy. Did the presented patient ever undergo EEG recordings? Was paroxysmal activity recorded indicative of mitochondrial epilepsy? Was ever any type of seizure observed in the presented patient?

Rarely, KSS patients may develop embolic stroke, resulting from intracardiac thrombi. Even more rarely, stroke-like episodes, the phenotypic hallmark of mitochondrial encephalopathy, lactic acidosis, and stroke-like episode syndrome, have been reported in KSS. Was cerebral MRI indicative of a previous ischemic stroke or a metabolic stroke manifesting with a stroke-like lesion?

It would also be helpful to know more about the neurological findings in the presented patient. Were tendon reflexed preserved or diminished; was there wasting or muscle weakness; were there fasciculations, fatigue or exercise intolerance; and was the gag reflex preserved or abolished? Was there any indication for dystonia as has been described in some KSS patients?

We should also be informed about the findings on cerebral imaging since KSS patients may manifest with cerebral involvement including intellectual decline, dystonia, epilepsy or encephalopathy.

Rarely, KSS patients may develop dilated cardiomyopathy. Thus, it is important that KSS patients undergo regular echocardiographic investigations and regular clinical cardiologic examination. Cardiomyopathy is usually accessibly to cardiac therapy, why adequate treatment may improve a patient's condition significantly.

Repeatedly, sudden cardiac death has been reported in KSS. Concerning the indication for implanting an implantable cardioverter defibrillator (ICD), KSS patients should undergo regular Holter monitoring not to overlook ventricular arrhythmias. The indication for implantation of an ICD should follow the current guidelines.

Some KSS patients with corneal endothelial dysfunction have been reported. Did the patient ever complain about corneal problems? Did ophthalmologic investigations ever detect corneal involvement in the underlying metabolic defect?

KSS may also go along with hypogonadism. Were hormone levels determined and was pituitary insufficiency excluded?

Finally, there is some confusion concerning the course of symptoms [1]. The authors mention that the patient was first seen by them at a 'regular ophthalmic and general health check' [1]. At the same time, they mention that the patient was not seen by a physician since the last 5 years [1]. When were ptosis, ophthalmoplegia, and double vision first recognized? In the discussion, they mention that the patient was diagnosed with chronic porgressive external ophthalmoplegia at the age of 21 years, but in the case description, KSS was diagnosed at the age of 17 years. These contradictory statements require clarification.

Overall, this interesting case presentation could be improved by genetic studies, more extensive work-up for potential multisystem disease and by regular follow-up investigations, particularly

cardiologic investigations. Additionally, some inconsistencies require clarification.

CONFLICT OF INTEREST STATEMENT

None declared.

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