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# Kearns-Sayre Syndrome Requires Clinical and Genetic Diagnosis

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## Letter to the Editor

In a recent article Ortiz et al. reported about a 55yo female with presumed Kearns-Sayre syndrome (KSS) associated with retinitis pigmentosa and abnormalities on high definition spectral domain optical coherence tomography (HD SD OCT) and on OCT angiography [1]. We have the following comments and concerns.

We do not agree with the diagnosis KSS. Diagnosing KSS requires not only the presence of clinical manifestations but also genetic confirmation of a single, large-scale deletion on muscle biopsy. Despite the presence of chronic progressive external ophthalmoplegia (CPEO), retinitis pigmentosa, and a left bundle branch block (LBBB), the clinical manifestations are somewhat atypical. Heart block in KSS usually manifests as AV-block III and only rarely as LBBB [2]. In addition to the classical triade, KSS may manifest as encephalopathy with short stature, elevated cerebrospinal fluid (CSF) protein elevation, cerebellar ataxia, intellectual decline, dystonia, epilepsy, stroke-like episodes, ischemic stroke, optic atrophy [3], corneal epithelial dysfunction, hypoacusis, dilated cardiomyopathy with severe arrhythmias, including sudden cardiac death (SCD), arterial hypertension, chronic fatigue, hypothyroidism, and hypogonadism [4]. Except for arterial hypertension, none of these additional phenotypic manifestations were described in the presented patient. Did the authors not prospectively look for these abnormalities or were they truly absent? Furthermore, CPEO and retinitis pigmentosa have been reported in other MIDs.

Since CPEO, retinitis pigmentosa, and LBBB may also occur in patients with non-specific mitochondrial multiorgan disorder syndrome (MIMODS), it is inevitable to confirm the diagnosis of KSS by demonstrating a single large-scale deletion on muscle biopsy. Single, large-scale mtDNA deletions usually occur *de novo* which is why the family history is usually negative for mitochondrial disorders (MIDs). However, in four percent of the cases, KSS may be maternally transmitted [5], suggesting that the mother also presented with clinical manifestations. Did the mother show any typical features of KSS or features of MIMODS? Since *de novo* and inherited mtDNA deletions are usually heteroplasmic, we should be informed about the heteroplasmy rates in different tissues to see if it correlated with the severity of organ affection.

Since LBBB is a risk factor for SCD, it is advisable that the index patient undergoes long-term ECG recordings. In case pauses or ventricular arrhythmias were recorded, implantation of a pacemaker or an implantable cardioverter defibrillator may be indicated. Was the family history positive for SCD?

The authors reported right ventricular hypertrophy in the presented patient. Did this diagnosis derive from ECG findings or did the patient undergo echocardiography? Did the patient suffer from pulmonary hypertension, pulmonary valve stenosis, or chronic lung disease?

We should be extensively informed about the family history. Were other first-degree relatives affected by a MID or MIMODS? Did any of the typical clinical manifestations of a MID segregate with the generations?

Overall, this interesting case could be more meaningful if the diagnosis of a MID would be genetically

confirmed. Furthermore, we should be informed about the family history and clinical findings in first-degree relatives.

## Author Contribution

Both authors contributed equally

JF: design, literature search, discussion, first draft

SZ-M: literature search, discussion, critical comments

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