

# Kearns-Sayre syndrome

## Case report

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### Summary

The Kearns-Sayre syndrome (KSS) is a mitochondriopathies characterized by multiorgan dysfunction that typically develops before the age of twenty. The diagnostic criteria most widely accepted in the literature are a triad: progressive external ophthalmoplegia, pigmentary retinopathy and disorders of cardiac conduction. KSS prognosis is related to the number of tissues affected and the severity of the alterations. In this article we report on a patient who presented 18 clinical features consistent with the Kearns-Sayre syndrome.

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### Introduction

In 1958, Thomas P. Kearns and George P. Sayre described through a report of a case a syndrome that presents with external ophthalmoplegia, pigmentary retinopathy and cardiac conduction block (CCB), which was later named: Kearns-Sayre syndrome (KSS)<sup>1-3</sup>. The KSS is a mitochondriopathies characterized by multiorgan dysfunction, which typically takes place before twenty years old. Cerebellar ataxia, hipoproteinorraquia, proximal myopathy, endocrinopathies, small stature and acid-base equilibrium disorders are other manifestations often associadas<sup>1,3-5</sup>. The KSS is a rare syndrome that belongs to a heterogeneous group of neuromuscular diseases caused by mutations in mitochondrial DNA. The phenotypic expression depends directly on the number of mutations in alleles and systems affected, directly interfering directly in the phenotype and severity of the syndrome. The cardiac conduction disturbance is responsible for high mortality syndrome. It is estimated that the ratio is 1.6 cases per

100,000 population<sup>6</sup>.

The objective of this study is to describe a case of a patient with KSS and discuss the clinical and laboratory criteria, promoting the review of the literature on this topic.

### Case report

Male patient of 18 years, student, native of Niterói (RJ, Brazil), sought outpatient service complaining of progressive loss of visual acuity with the acceleration process in the last two years, associated with bilateral ptosis (Figure 1),



**Figure 1.** Patients with Kearns-Sayre syndrome. Bilateral ptosis.

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Informed consent was obtained from the patient in question during the presentation of images in this article.

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**Figure 2.** Patients with Kearns-Sayre syndrome. Short stature. Chronological age of 18 years old. Height: 1.43 meters. Deficit in relation to bone age: 15 years.

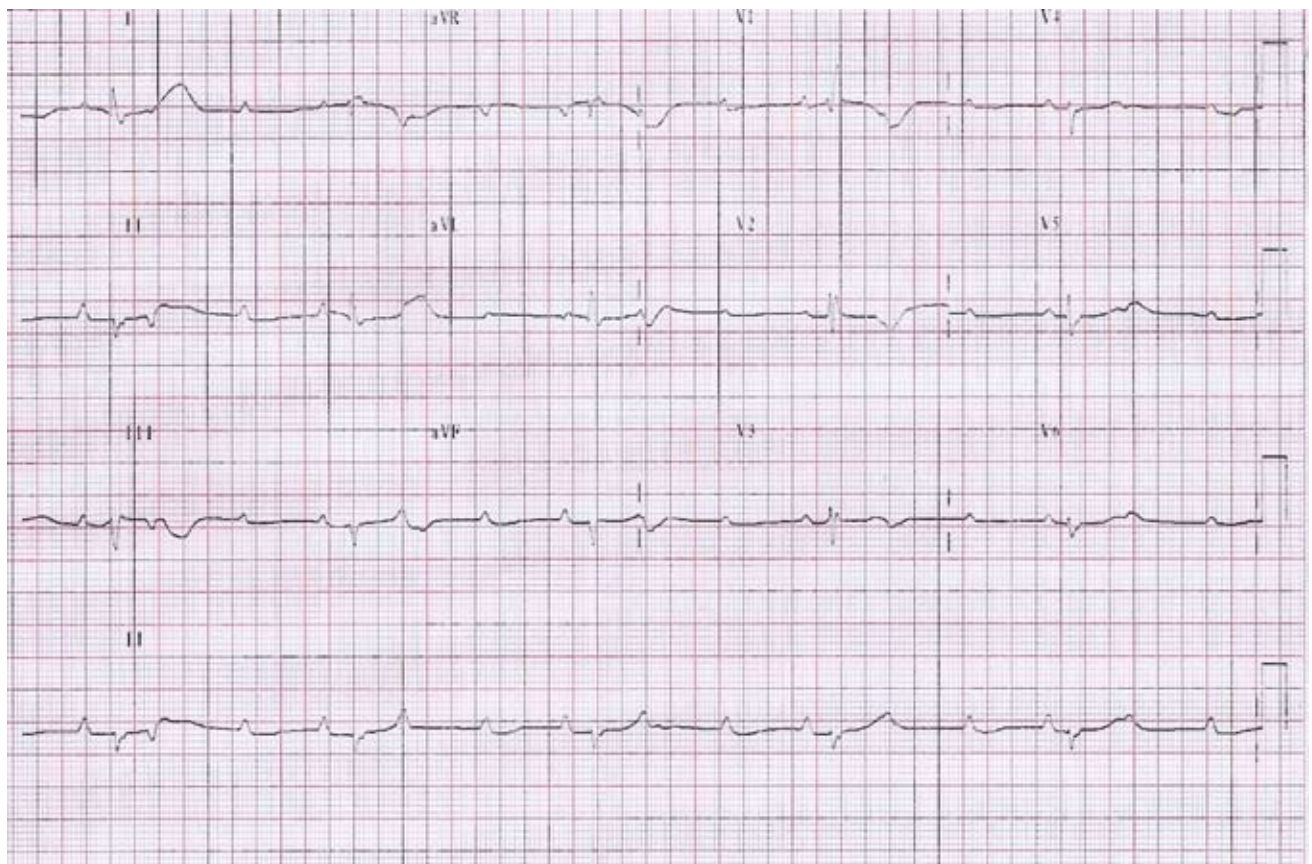
small stature (Figure 2), delayed pubertal development and dyspnea on moderate effort with a history of clinical investigations inconclusive.

Until then remained undiagnosed for two years, he developed the same symptoms and electrocardiogram (ECG) with complete right bundle branch block and left anterior hemiblock and growth hormone test positive with no indication of any therapy. Two months ago reported recurrent episodes of dyspnea with minimal exertion followed by syncope. In the final episode of syncope was admitted to the intensive care unit and received a diagnosis of heart failure secondary to bradyarrhythmias and showed complete right bundle branch block, left anterior hemiblock and complete atrioventricular block (Figure3).

Physical examination in ectoscopia highlighted: a marked reduction in visual acuity, muscle atrophy diffuse and bilateral ptosis. The cardiovascular examination, jugular venous pulse showed a cannon "a" wave and an irregular heart rhythm with breath systolic tricuspid focus more audible.

Laboratory tests and chest radiographs were normal. A transthoracic echocardiogram showed cavitations size and normal wall thicknesses, as well as systolic and diastolic function of the ventricles.

The adolescent remained hospitalized in intensive care unit with continuous cardiac monitoring, opting initially for transcutaneous pacing and subsequent permanent



**Figure 3.** Patients with Kearns-Sayre syndrome. Electrocardiogram with complete right bundle branch block, left anterior hemiblock and complete atrioventricular block.

pacemaker implantation of a bicameral type. He moved to the floor on the third day of hospitalization and was discharged the next day. We were given guidelines to return to the consultation with your doctor and follow-up investigation of the underlying disease.

After the clinical follow-up by specialists, based on clinical findings the patient was diagnosed as having a KSS and currently he is treated with coenzyme Q10, eye drops, calcium and expects a muscle biopsy. Maintains outpatient follow.

## Discussion

The onset of clinical manifestations of this patient, even in childhood, coincides with the literature, since the KSS is characterized by ophthalmoplegia and pigmentary retinopathy, usually manifests before the age of twenty; however other changes are associated in several published case reports such as protein concentration, proximal myopathy, thyroid disorders, hypoparathyroidism, Addison's disease, dysphasia in achalasia and renal tubular acidosis, short stature, cerebellar ataxia and cardiac conduction disturbance were also identified in the case reported<sup>3,6,8</sup>.

The KSS is a genetic disorder caused by mutations in mitochondrial DNA. The inheritance of the mitochondrial genome is maternally, because during fertilization, the sperm tail, which contains the mitochondria, is displaced during the penetration of the ovule. Thus, it is not made part of the mitochondrial DNA of the zygote. Mitochondria are cytoplasm structures responsible for the production of intracellular adenosine triphosphate, which is necessary to supply energy for various metabolic functions. Tissues with high energy demand such as muscle and nervous system are particularly vulnerable to mitochondrial dysfunction, a consequence of deletions, rearrangements or other mutations in mitochondrial DNA. These mutations in most cases are random and are not usually inherited from the maternal DNA; the case example above the patient's mother was phenotypic normal<sup>8</sup>.

Due to the large spectrum of clinical manifestations, the KSS has several differential diagnoses, among these other syndromes mitochondria encephalomyopathies, CCB and oftalmopatias<sup>4,9</sup>. The most widely accepted diagnostic criteria in the literature are the triad: progressive external ophthalmoplegia, pigmentary retinopathy and CCB. This patient had all the classic manifestations of the syndrome, the muscle biopsy confirm the genotypic diagnosis, but would not add information for treatment and outcome<sup>6,9,10</sup>. The biopsy of skeletal muscle identifies the *ragged-red cells* (red fibers torn), and is specific for diagnosis of mitochondrial myopathies, plus the phenotype, the classic triad concludes the diagnosis of KSS. The technique for amplification of mitochondrial DNA by polymerase chain reaction, allows the diagnosis without performing the biopsy<sup>11</sup>.

Several cardiac abnormalities are reported in the literature, such as disturbance of the conduction system, arrhythmia or syncope requiring pacemaker implantation, cardiomyopathy (hypertrophic, restrictive, non-compaction of left ventricle and peripartum)<sup>10,11</sup>. The CCB are described since the first case report of the syndrome in 1958<sup>1,5</sup>. The most common is the left anterior hemiblock, isolated or associated with right bundle branch block are also found atrioventricular block 2° and 3° degrees. At the beginning of cardiac symptoms the patient presented in the case, we identified all these ECG changes and, as here, the majority of patients have indications for the implantation of permanent pacemaker or as a form of prophylactic treatment<sup>8,12</sup>. When a patient develops the KSS with heart failure and progresses to stage D, suggests that the mutation in mitochondrial DNA is not limited only to the conduction system, but also to the myocardium. The echocardiographic study to assess the systolic and diastolic functions of left ventricle by tissue Doppler allows the diagnosis of myocardial dysfunction and early-stage preclinical<sup>6,9</sup>.

No specific treatment is effective for the KSS mainly for myopathy and retinopathy. The treatment is palliative and supportive for the clinical conditions. Some patients with myopathy benefit from the use of coenzyme Q10, especially those with mutations that produce reduced synthesis of this protein. The identification of these patients is important, since there are literature reports of clinical improvement and favorable prognosis<sup>8,13</sup>. These patients should be referred for detailed cardiac evaluation, investigating the need for permanent pacemaker or other cardiac-specific treatment. It is important to monitor multidisciplinary regular, given the systemic nature of the disease. Regular physical activity improves muscle strength, self-esteem and functional capacity<sup>4</sup>.

## Conclusions

We know that the KSS is rare in our environment and resources for diagnosis are not widely available, so that the doctor should have significant clinical suspicion for the diagnosis of the disease, indicating the cases selected for muscle biopsy and genetic research. KSS prognosis is related to the number of tissues affected and the severity of the alterations. The disturbances in the cardiac conduction system are responsible for high morbidity and mortality of the disease<sup>3,11</sup>.

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## Conflict of interest

The authors have no conflicts of interest to declare.

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