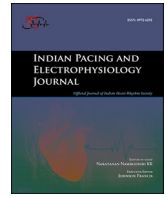


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Kearns Sayre Syndrome: Looking beyond A-V conduction



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ABSTRACT

A 15-year-old boy was diagnosed with Kearns Sayre Syndrome. He presented with pigmentary retinopathy, progressive ophthalmoplegia and complete heart block. He received a transvenous dual chamber pacemaker. Two years later he died suddenly while at home. This case highlights the importance of recognizing mechanisms other than heart block as a cause of sudden death in a patient with KSS. Copyright © 2017, Indian Heart Rhythm Society. Production and hosting by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

1. Introduction

Kearns Sayre Syndrome was first described in 1958. The key triad of features includes progressive external ophthalmoplegia, pigmentary retinal dystrophy and onset before 20 years of age. Cardiac involvement is reported in approximately 50% of cases. This involves cardiac conduction disorders with varying degrees of severity. The commonest reported tachyarrhythmia is polymorphic ventricular tachycardia attributed to a very low heart rate [1]. The insertion of a pacemaker is theoretically curative. However it is recently being recognized that a subset of patients continue to experience life threatening arrhythmias despite a functioning pacemaker [2]. We report a teenage boy who was diagnosed to have KSS with complete heart block requiring a pacemaker insertion at 14 years of age. The boy died suddenly at 16 years of age despite a functioning pacemaker possibly due to a ventricular arrhythmia.

2. Case details

A 14-year-old boy was referred to our unit with a clinical diagnosis of Kearns Sayre Syndrome. He had presented with progressive ptosis over a period of 18 months and decreased vision in dim light. His ophthalmic evaluation had confirmed external

ophthalmoplegia and a pigmentary degeneration of his retina (Fig. 1). He was also noticed to have a low heart rate. Hence KSS was suspected. His parents reported that he was not a sporty person and became fatigued earlier than his peers during physical activities. However this was not associated with breathlessness or chest pain. There were no episodes of syncope, pre-syncope or night terrors. His developmental history was normal. He had previously been evaluated at 3 years of age for recurrent episodes of vomiting. His clinical examination at that age was reported to be normal. Investigations had shown a mild elevation of lactates but tandem mass spectrometry was non-diagnostic. Hence no metabolic diagnosis was made and he was kept on follow up.

On examination he weighed 38 kg and his height was 148 cm. There were no dysmorphic features or congenital anomalies. His peripheral perfusion was good and all peripheral pulses were felt equally. His pulse rate was 47/minute with regular pulses and a normal volume. There was no clinical evidence of cardiomegaly. His first heart sound was normal, second heart sound was normally split and a grade 2/6 ejection systolic murmur was heard in the left 2nd intercostal space. His chest was clear on auscultation and his liver was not enlarged. Clinical evaluation of the neurological system was normal.

His chest x-ray showed a normal cardiac silhouette with clear lung fields. Echocardiogram conformed a structurally normal heart. The left ventricular dimensions and systolic function were within normal limits. His electrocardiogram revealed complete atrio-ventricular disassociation with an atrial rate of 100/min and a broad complex ventricular escape rhythm with a rate of 43/minute

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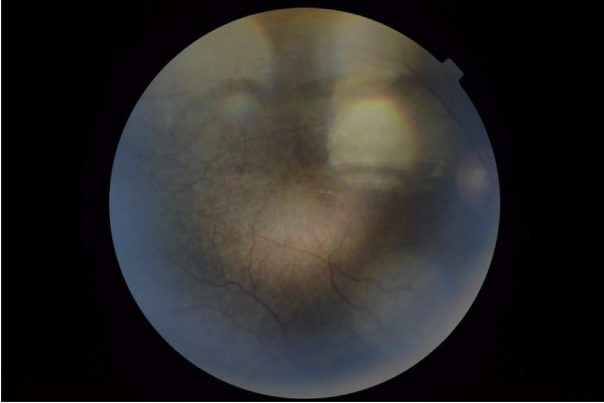


Fig. 1. Fundoscopic picture showing evidence of pigmentary degeneration of the peripheral retina.

(Fig. 2). The QRS duration was 160 milliseconds. The QT interval was 520 milliseconds and the QTc was calculated to be 474 milliseconds. Genetic testing revealed a large mitochondrial DNA deletion that on mapping proved to be a novel mutation not previously reported in literature (a 3898bp deletion m.6162_10059del that does not occur at a repeat sequence).

As KSS is associated with progressive conduction system disease and his escape rhythm appeared to be of infra-Hisian rhythm he was implanted with a dual chamber transvenous pacing system (St Jude's Accent MRI system with 52 cm (atrial) and 58 cm (ventricular) St Jude Tendril MRI leads). The pacemaker was set in DDD mode with a lower rate of 50/min, a maximum sensor rate of 110/minute and an upper tracking rate of 130/minute. The procedure was uneventful. His device was interrogated regularly with no significant concerns. On follow up, his parents reported an improvement in his effort levels as well as appetite.

Two years after his pacemaker implantation and two weeks after his last pacemaker clinic visit, his parents returned home at

12.30 PM to find him sitting on the sofa with his earphones over his ears and his computer by his side apparently asleep. He had contacted his mother approximately 45 minutes earlier. They found him to be unresponsive and started cardio-pulmonary resuscitation. An ambulance arrived twenty minutes later and continued resuscitation en route to the nearest hospital where he could not be revived and declared dead on arrival. An autopsy was not performed in honor of his parents' wishes.

3. Discussion

Cardiac involvement is important to the prognosis in KSS. It is estimated that syncope and sudden death occurs in approximately 20% if patients with KSS. Syncope is usually attributed to AV conduction disorders. Pathological studies have demonstrated increase in number and size of mitochondria in the conduction tissue with marked decrease in mitochondrial enzyme activity. The other common arrhythmia reported in KSS is bradycardia related polymorphic ventricular tachycardia [1]. The insertion of a permanent pacemaker is thought to be curative for both these arrhythmias. Recent guidelines recommend a class I indication for pacing in KSS with third degree or advanced second degree heart block irrespective of the symptom status [3].

Although the functioning status of the pacemaker was not documented by explantation and interrogation in our patient, the pacemaker was relatively new and had been found to functioning normally 2 weeks prior to his death. It is hence reasonable to presume that the pacemaker was functioning normally. In the absence of other contributing factors and given the fairly sudden nature of his death, it appears that a cardiac arrhythmia is the most likely cause of death.

Recently, a number of reports have emerged of ventricular tachyarrhythmia despite a pacemaker insertion in patients with KSS [1,2,4,5]. Most such reports are of polymorphic ventricular tachycardia and torsades de pointes in the setting of a prolonged QTc. However monomorphic ventricular arrhythmias have also been reported. The cause of the ventricular arrhythmias is a subject

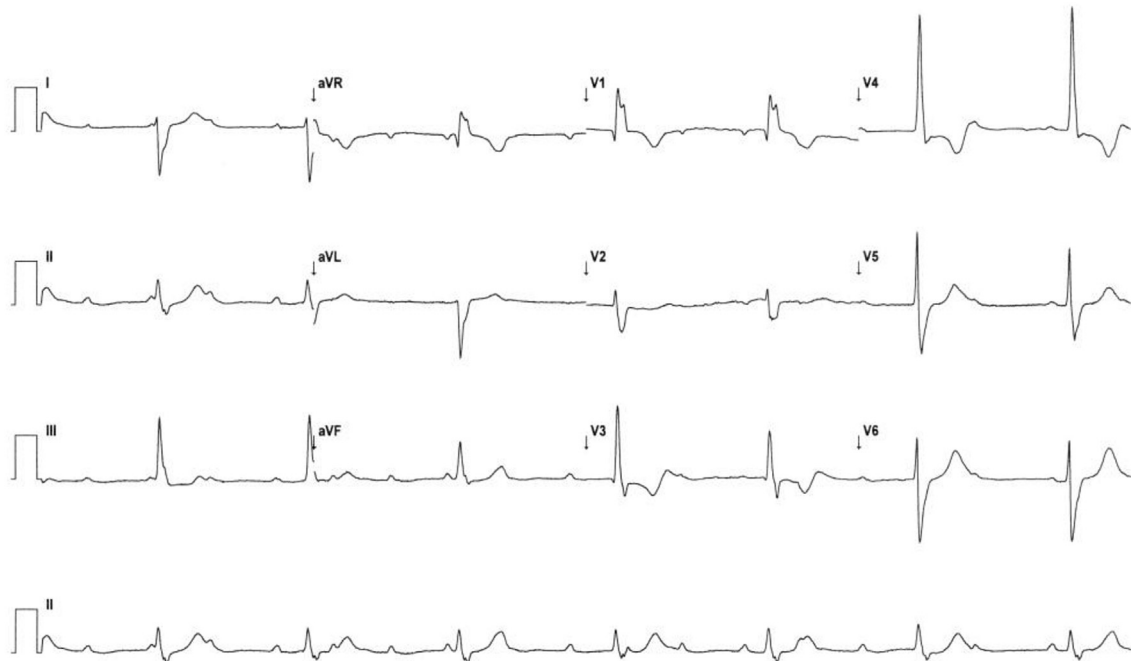


Fig. 2. Electrocardiogram showing evidence of complete heart block with an atrial rate of 100/minute and a broad complex escape rhythm with a ventricular rate of 43/minute.

of debate. Skinner and colleagues identified a novel mutation of the KCNQ1 gene that causes Long QT Syndrome (LQTS) type 1 [4]. The functional analysis of the mutation suggested a pathogenetic LQTS mutation explaining the episodes of torsades de pointes identified in their patient. However a genetic diagnosis of LQTS could not be established in all patients and hence other potential explanations could include repolarization abnormalities related to a general cardiac muscle abnormality secondary to mitochondrial mutations. Cardiac magnetic resonance (CMR) imaging of the heart in patients with KSS revealed late gadolinium enhancement in the left ventricle. Kabunga and colleagues reported evidence of left ventricular fibrosis in a patient with KSS and monomorphic ventricular tachycardia. However a causative relationship between ventricular scarring and arrhythmias has not been proven beyond doubt.

The present report support previous publications recognizing additional mechanisms and risks for sudden death in patients with KSS that are not mitigated by implantation of a pacemaker alone. The small subset of reported patients does not allow us to identify patients who are most likely to benefit from an implanted defibrillator (ICD). In the absence of obvious ventricular arrhythmias that indicate the need for an implantable defibrillator (ICD), consideration should be given to Cardiac MR imaging prior to implantation of a pacemaker. If there is evidence of myocardial scarring, an intracardiac electrophysiological test might be helpful in determining the need for an ICD as opposed to a pacemaker. It may also be prudent to avoid drugs that could prolong QTc as well as to

aggressively correct electrolyte abnormalities in these patients.

Funding

None.

Competing interests

None.

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