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FOLLOW-UP OF A CHILD WITH KEARNS-SAYRE SYNDROME AND IMPLANTED PACEMAKER: A CASE REPORT

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A clinical case of a child with a rare mitochondrial disease, Kearns-Sayre syndrome, who had a pacemaker implanted due to the development of complete atrioventricular block, is presented for the first time in the Republic of Kazakhstan. The issues of complex diagnostics and management tactics are discussed.

Key words: mitochondrial myopathy; severe neurological deficit; atrioventricular block of the third degree in children; children; implantation of a pacemaker in children

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Kearns-Sayre Syndrome (KSS) is a rare mitochondrial disorder, first described in 1958 by Thomas Kearns and George Pomeroy Sayre in their publication “Retinitis pigmentosa, external ophthalmoplegia, and complete heart block” [1]. The disease is characterised by the classical triad of symptoms: onset before the age of 20 years, chronic progressive external ophthalmoplegia, and pigmentary retinopathy [2]. A distinctive feature of KSS is the high prevalence of cardiac conduction disturbances, which significantly influence the prognosis of the disease.

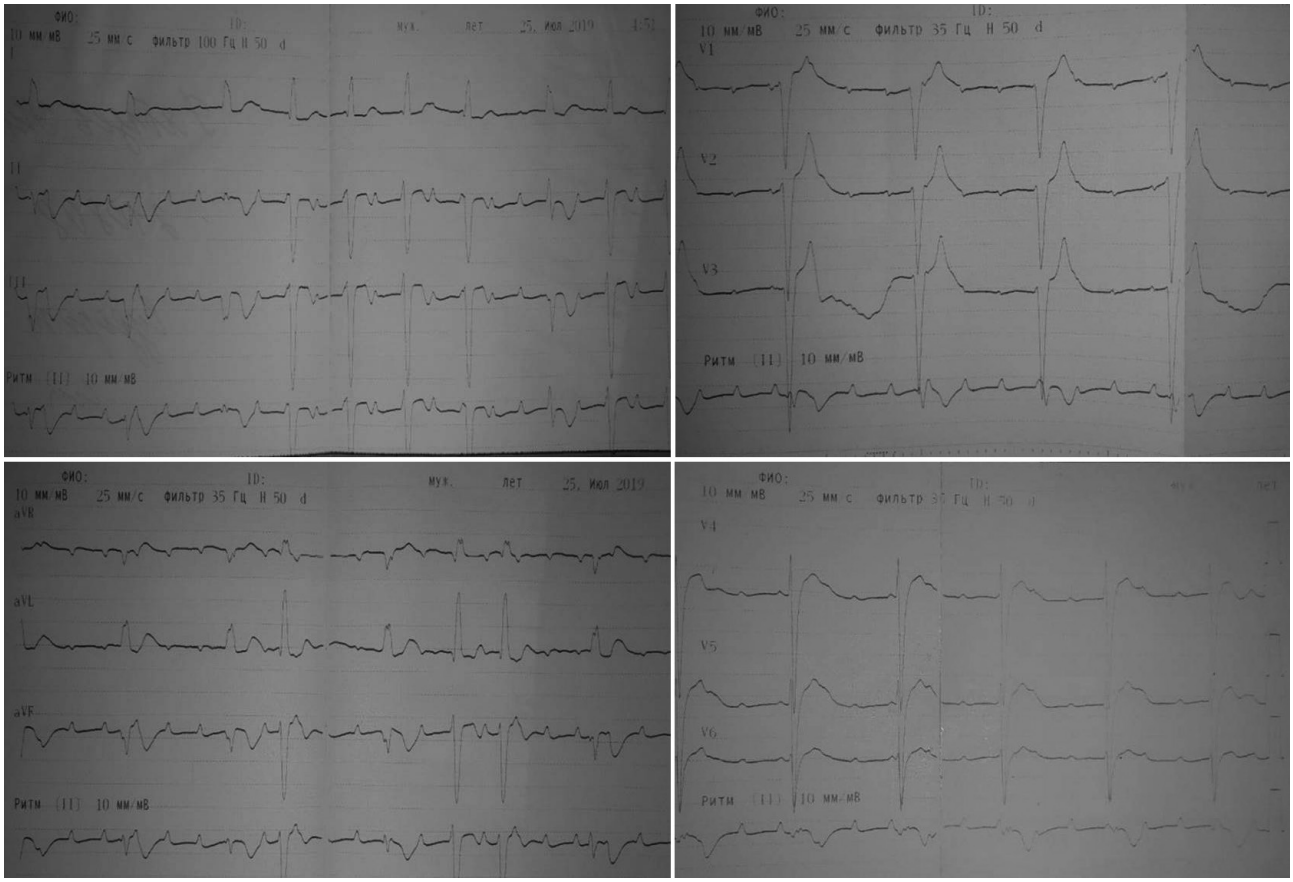

Fig. 1. Electrocardiogram of a patient with third-degree atrioventricular block.

Epidemiological data indicate a prevalence of 1-3 cases per 100,000-125,000 population [3-5]. Approximately 90% of KSS cases are sporadic and are caused by large deletions of mitochondrial DNA (mtDNA) ranging from 1.1 to 10 kilobases. The most common is the so-called “standard deletion” - a loss of 4,977 base pairs, accounting for more than one-third of all cases [6,7]. The aetiological factors responsible for these deletions remain unclear.

Patients with KSS frequently present with conduction abnormalities, ranging from PR-interval prolongation to complete atrioventricular (AV) block. These disturbances are associated with a high risk of stroke and sudden cardiac death [4], which underscores the need for timely implantation of a pacemaker (PM). This article presents a clinical case of PM implantation in a 10-year-old patient with KSS. According to the literature, fewer than 10 cases of this syndrome have been reported in the post-Soviet space since the 20th century. The described case is the first documented in Kazakhstan.

The patient was a 10-year-old boy, born from the second pregnancy. The first pregnancy ended with the death of the child on the first day of life due to sepsis. The second pregnancy occurred 6 months later and was complicated by pre-eclampsia with a threat of miscarriage during most of the gestational period. He was delivered at 40 weeks, weighing 3550 g and measuring 53 cm in length. Family history on the paternal side included systemic lupus erythematosus in the grandmother, hand tremor in an aunt and her daughter; the maternal family history was unremarkable.

From the age of 3 years, the patient presented with eyelid ptosis, visual impairment, headaches, unsteady gait, and developmental delay (both mental and physical). From the age of 8 years, muscle weakness and tremor of the limbs developed. At 10 years and 11 months, complete AV block occurred (Fig. 1). A dual-chamber PM with active-fixation endocardial leads was implanted; the generator was positioned in the left subclavian region (Figs. 2, 3). Laboratory tests revealed hypokalaemia, hyperglycaemia, and elevated transaminases; creatine phosphokinase levels were within the normal range. Echocardiography showed left ventricular (LV) ejection fraction (EF) of 50-54% without other abnormalities.

At the age of 14 years, molecular genetic testing using long-fragment PCR identified a deletion of approximately 7000 base pairs (positions 1650-16,565) in a heteroplasmic state (~70% mutant copies), confirming the diagnosis of Kearns-Sayre syndrome.

Later that year, the patient was urgently hospitalised in the intensive care unit with multiple episodes of vomiting with mucus, marked weakness, lethargy, dyspnoea, and fever of 38.7 °C. On admission, his condition was assessed as coma grade I-II. Laboratory results: lactate 6.1 mmol/L; marked leukocytosis with neutrophilia and lymphopenia; D-dimer 4164.4 ng/mL; C-reactive protein 12.75 mg/L; NT-proBNP 17,499.8 pg/mL; procalcitonin 1.56 ng/mL; glucose 16.2 mmol/L. Blood cultures showed no microbial growth. On physical examination, there was pharyngeal hyperaemia and purulent follicular tonsillitis.

ECG revealed atrial fibrillation with paroxysms of non-sustained ventricular tachycardia. An elevated pacing threshold of the right ventricle was noted, with an episode of pacing failure and a minimal heart rate of 46 bpm; after increasing the pacing amplitude, effective capture was restored. Echocardiography demonstrated severe diffuse LV systolic dysfunction (EF 20-25%), without chamber dilation or valvular abnormalities.

In the intensive care setting, vasopressor, antibiotic, detoxification, and hypoglycaemic therapy was initiated. Infectious-toxic myocarditis was suspected. Despite treatment, the patient’s condition continued to deteriorate, culminating in cardiac arrest. Resuscitation was performed for 35 minutes without success. The patient died at the age of 14 years and 11 months from progressive cardiovascular failure. The parents declined autopsy.

DISCUSSION

Patients with KSS are characterised by increased susceptibility to infectious diseases, attributable to multi-

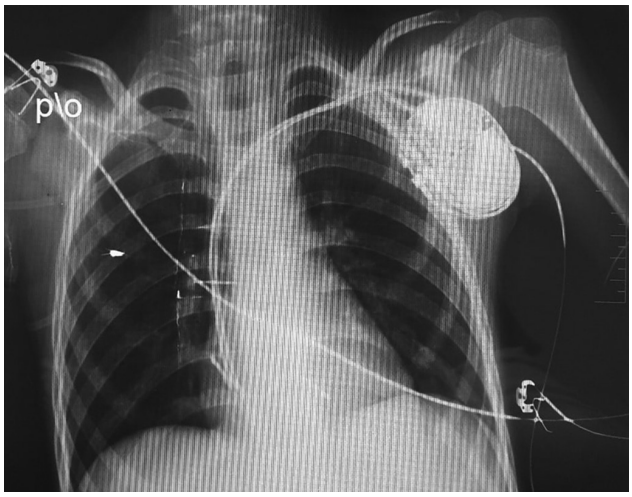

Fig. 2. Chest radiograph of a patient after pacemaker implantation.

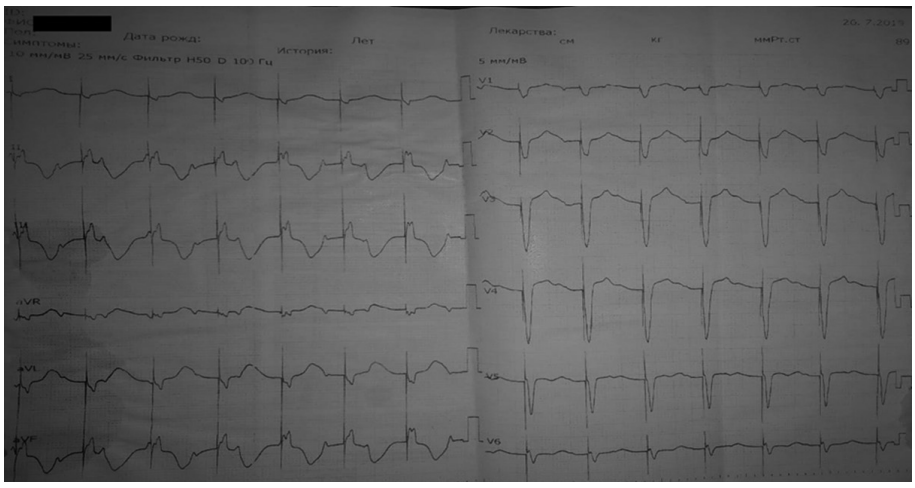

Fig. 3. Electrocardiogram of a patient after pacemaker implantation.

system mitochondrial dysfunction and impaired immune responses. In the present case, acute tonsillitis likely triggered an infectious-toxic myocarditis, which subsequently led to acute heart failure and death.

Currently, there are no pharmacological treatments for mitochondrial diseases supported by high-level evidence. The main therapeutic strategies focus on reducing excessive free radical production and enhancing adenosine triphosphate synthesis, both of which are critical for improving mitochondrial metabolism and the cellular energy balance.

Monitoring of patients with mitochondrial disorders should include regular electrocardiography, echocardiography, Holter monitoring, audiometry, and endocrine assessment [8], given the unpredictable disease course and the potential for progression to AV block [9].

Considering the high risk of complete AV block, ventricular arrhythmias, and sudden cardiac death in patients with KSS, implantation of an implantable cardioverter-defibrillator (ICD) should be considered [10]. In the case described, pacemaker implantation was performed before genetic confirmation of the diagnosis. An ICD was not implanted initially due to the lack of clear recommendations for primary prevention of sudden cardiac death in this patient category [11]. Pacemaker telemetry did not reveal life-threatening arrhythmias, LV ejection fraction remained above 40%, and no LV hypertrophy was present, all of which supported the choice of pacemaker over ICD [12].

According to the literature, among 15 children with KSS followed between 2007 and 2019, 11 underwent pacemaker implantation, and one with non-sustained ventricular tachycardia received an ICD. The mean age of patients with conduction disturbances was 13.7 years. Four patients died at a mean age of 14.7±2.6 years; however, no cases of sudden death were documented. Two deaths were due to heart failure, in one case combined with septic shock; in these patients, LV dysfunction had developed before pacemaker implantation. Other reported causes of death included pancreatitis and unidentified factors [13]. Details of these fatal outcomes were not specified.

Modern approaches to the management of patients with KSS emphasise the need for multidisciplinary care involving cardiologists, geneticists, endocrinologists, and neurologists. Early diagnosis and close monitoring allow timely detection of progressive conduction disturbances and help prevent severe complications, including sudden cardiac death. The question of prophylactic ICD implantation or cardiac resynchronisation therapy devices with defibrillator function remains an area of ongoing research and requires further clinical validation.

The patient's parent provided written informed consent for publication of these data.

CONCLUSION

Patients with Kearns-Sayre syndrome (are prone to the development and progression of conduction system abnormalities, which necessitates regular and thorough cardiological monitoring. Early diagnosis enables frequent electrocardiography and Holter monitoring to ensure timely decisions regarding implantation of pacemakers, ICDs, or cardiac resynchronisation therapy devices with a defibrillator function. At present, cases of prophylactic implantation of such devices immediately following the diagnosis of KSS have not been described, highlighting an important area for further investigation.

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