

Defibrillators in Jervell-Lange Nielsen Syndrome

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Introduction

The Jervell and Lange-Nielsen syndrome (JLNS) is a genetically determined disease characterized by congenital deafness, long QT interval and high lethality due to episodes of polymorphic ventricular tachycardia of *torsade de pointes* (TDP) type that occur in early childhood^{1,2}. As with other forms of congenital long QT syndrome (there are more than eight variants), the automatic defibrillator implantation is indicated in patients who have undergone cardiac arrest or those with recurrent syncope despite beta-blocker therapy. However, clinical experience with children with JLNS submitted to an ICD (implantable cardioverter defibrillator) is limited.

The objective of this report is to describe the clinical evolution of two patients, a boy of 3 and a girl of 17 years with a diagnosis of JLNS, submitted to ICD implantation.

Case 1

Patient MAT, 3 years old, male sex, with congenital deafness, history of recurrent syncope since the first year of life, many of them with cyanosis and seizures. The parents associated the crises with physical stress, fear, anger and emotion. The child showed behavioral disorder, restlessness and aggression. Neurological evaluation, EEG and cranial CT scan were normal, and he was initially misdiagnosed as having "psychological disorder and breath holding spells". After referral to cardiology service, JLNS was diagnosed based on the clinical history and ECG, which showed sinus rhythm and prolonged QTc interval (630 ms). The 24-hour Holter did not detect ventricular arrhythmias and confirmed long QT interval. The two-dimensional echocardiography was normal.

Treatment was started with metoprolol up to a dose of 50 mg/day. He had no bradycardia at the examinations, even after medication. Family counseling was provided, with psychological and educational support. The patient had severe bronchospasms due to bronchial asthma, at which time the

medication was suspended. Due to recurrent syncope, a left cervicothoracic sympathectomy was performed. The initial evolution was satisfactory, with evidence of sympathetic denervation by anisocoria (left miosis), mild ptosis of the left lid and left upper limb heating (compared to the right). However, during a psychological stress test (the arrival of a group of doctors in the room to simulate blood collection), performed three days after the sympathectomy, the child had an episode of ventricular fibrillation, requiring cardiopulmonary resuscitation and electric defibrillation. After this event, he underwent internal automatic defibrillator implantation, which was performed uneventfully via epicardial route with unicameral generator positioned in the lower abdomen and maintaining treatment with metoprolol.

During the following 13 months, 105 appropriate shocks occurred; the last event occurred after 4 months without shocks, when the patient had bronchospasm and respiratory infection, which led to the abrupt discontinuation of metoprolol. Two days later, he had an "arrhythmic storm" with sequence of 48 appropriate shocks on the same day. He was taken to the emergency room, where he had cardiac arrest that required resuscitation and external defibrillation due to a dead battery. The patient was intubated and sedated, but died on the same day, eight hours after the onset.

Case 2

FMS, 17 years, with congenital deafness, history of syncope since the age of 3 and some seizure episodes. She was hypertensive and had chronic renal failure since childhood and had recent initiated dialysis. ECG showed sinus rhythm, QTcB (Bazette) 633 ms and QTcH (Hodges) 571 ms, ECGs with alternating T-waves and periods of very aberrant QT. Echocardiogram showed moderate left ventricular dysfunction. She underwent automatic internal cardiodefibrillator implantation in July 2010 due to beta-blocker drug refractoriness. She had an arrhythmic storm in January 2011, with 122 episodes of polymorphic ventricular tachycardia and ventricular fibrillation, reversed with appropriate shocks. She received carvedilol and Lasix. A new arrhythmic storm occurred after 6 months, even at high doses of carvedilol in the presence of mild hypokalemia and she was hospitalized again and carvedilol was replaced by metoprolol, with good evolution to date (6 months later).

Keywords

Defibrillators, implantable; Jervell-Lange Nielsen syndrome / mortality; syncope.

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Manuscript received May 13, 2012; manuscript revised August 21, 2012; accepted October 18, 2012.

DOI: 10.5935/abc.20130039

Discussion

Jervell and Lange-Nielsen syndrome is a subgroup of extreme severity of the genetic variants of long-QT syndrome. It derives from a mutation in *KCNQ1* or *KCNE1*

genes, which encode the potassium-ion channel (Iks), being autosomal recessive. Its treatment is usually widely debated due to the severe and numerous episodes of ventricular tachycardia, which are generally insufficiently treated with beta blockers and sympathectomy, showing high mortality^{3,4}. Risk stratification can be accomplished with genetic testing (expensive and less accessible), age of onset of syncope (the earlier, the worse), sex (males have more unfavorable evolution), symptoms at onset (cardiac arrest) and degree of QT prolongation (> 500 ms). Therapy with internal defibrillators is used as additional therapy, but little is known about the evolution of these patients when an ICD is implanted^{5,6}. We report on two cases, both with refractory and prolonged arrhythmic storms.

In the first case, the fatal one, the patient was asthmatic, but still received selective beta-blockers as the left sympathectomy was unsuccessful. He had an arrhythmic storm during a bronchospasm episode, when the use of beta-blockers was interrupted. This child had already had several other episodes of effective shocks, non-syncopal, even with effective doses of beta-blockers, and had spontaneously changed his behavior, as he attributed the shocks to exertion and misbehavior.

In the second, nonfatal case, the patient also had hypertensive dilated cardiomyopathy, renal disease that required dialysis and the ICD was implanted for secondary prevention, as the patient had prolonged episode of arrhythmic storm by VT and VF, effectively treated by the device, at the first justified the use of low doses of beta blockers and the second due to hypokalemia. This patient will be submitted to a sympathectomy.

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Conclusion

The internal automatic defibrillators represent therapeutic options in congenital long QT syndrome, particularly in high-risk subgroups after therapeutic failure with beta-blockers. In JLNS, it seems to be a life-saving association due to the extreme severity, albeit complicated by the high incidence of arrhythmic storms, requiring multiple shocks. As it is a very rare disease, the evaluation of therapeutic strategies is difficult to achieve, including the impact on survival, considering that many episodes of *torsades* are self-limited.

Author contributions

Conception and design of the research: Rocha EA; Acquisition of data: Rocha EA, Pereira FTM, Monteiro MPM; Analysis and interpretation of the data: Rocha EA, Pereira FTM, Monteiro MPM, Rocha Neto AC; Writing of the manuscript: Rocha EA, Rocha Neto AC, Scanavacca M; Critical revision of the manuscript for intellectual content: Rocha EA, Pereira FTM, Monteiro MPM, Rodrigues Sobrinho CRM, Scanavacca M.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Sources of Funding

There were no external funding sources for this study.

Study Association

This study is not associated with any post-graduation program.