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Case Report

ICD implant in 6-year-old with Jervell and Lange-Nielsen (JLN) syndrome

T. Joseph Theodore[1,*], Ponnagiri GKM. Dhilipan[2], S. Ajay[3]

[1]Department of Cardiology, Kauvery Hospital - Heart City, Trichy
*Correspondence: josephtheodore84@gmail.com

Abstract: Jervell and Lange-Nielsen syndrome (JLNS), a rare autosomal recessive subtype of long QT syndrome (LQTS) caused by potassium channel gene mutations, is characterized by congenital bilateral sensorineural hearing loss and prolonged QT interval, predisposing patients to life-threatening cardiac arrhythmias. A 6-year-old girl with congenital bilateral sensorineural hearing loss (right cochlear implant at age 3 years) experienced six emotion- and exercise-triggered syncope episodes since the age of 3 years. Her electrocardiogram (ECG) revealed a corrected QT interval (QTc) of 600 ms and T-wave alternans, indicative of JLNS, which was confirmed by genetic testing. Despite beta-blocker treatment, her symptoms persisted, necessitating the successful placement of a subpectoral transvenous implantable cardioverter-defibrillator (ICD) to prevent sudden cardiac death, despite the challenges posed by her thin chest wall and age. ICD pacing has been employed to reduce QTc, and left cardiac sympathetic denervation is planned if the symptoms recur.

Keywords: Pediatric cardiology; cardiac management; cardiac arrhythmia; genetic disorders; congenital heart disease

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1. Introduction

Jervell and Lange-Nielsen syndrome (JLNS) is a rare autosomal recessive disorder affecting both auditory and cardiovascular systems. It features congenital bilateral sensorineural hearing loss and a prolonged QT interval on ECG, leading to potentially life-threatening cardiac arrhythmias if undiagnosed or untreated. JLNS is a subtype of long QT syndrome (LQTS), distinguished by profound hearing loss [1]. It results from mutations in genes encoding potassium channels critical for inner ear and heart function.

JLNS typically manifests in early childhood, often before age three, with profound bilateral sensorineural hearing loss from birth, affecting all frequencies and impacting language development if untreated. Cardiac symptoms include syncope or seizure-like episodes caused by a prolonged QT interval, increasing the risk of torsades de pointes—a dangerous ventricular tachycardia [2]. This arrhythmia can cause syncope or progress to ventricular fibrillation, potentially leading to sudden cardiac death if untreated.

JLNS stems from mutations in the KCNQ1 or KCNE1 genes, which encode subunits of the slow delayed rectifier potassium channel (IKs), essential for heart rhythm and inner ear function. In JLNS, both gene copies are mutated, leading to complete loss of channel function, unlike Romano-Ward syndrome, another LQTS form where only one gene copy is affected [1-3].

Diagnosis of JLNS involves clinical evaluation, family history, electrocardiography, and genetic testing. Congenital deafness and a prolonged QT interval on ECG strongly indicate JLNS, which can be confirmed by identifying mutations in the KCNQ1 or KCNE1 genes. Genetic confirmation is crucial for family screening, as parents and siblings may be carriers.

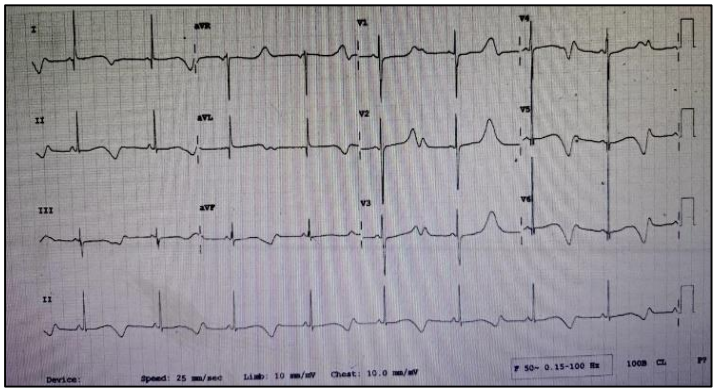
Early diagnosis and management are vital to preventing sudden cardiac death in JLNS patients. A multidisciplinary approach is required, addressing both cardiac and auditory issues. Beta-blockers are typically the first-line treatment to shorten the QT interval and reduce arrhythmia risk. If beta-blockers are insufficient, other antiarrhythmic medications are considered [4]. High-risk patients or those with cardiac events despite medical therapy may need an implantable cardioverter-defibrillator (ICD) to detect dangerous arrhythmias and restore normal heart rhythm [5].

Hearing loss management is equally important. Cochlear implants effectively restore hearing function, and early implantation is crucial for language development and quality of life. Some studies suggest cochlear implants may also reduce cardiac event risk by alleviating profound deafness-related stress [6].

Lifestyle modifications are critical in managing JLNS. Patients should avoid QT-prolonging medications, maintain proper electrolyte balance, and be cautious with activities that could trigger syncope, such as competitive sports or unsupervised swimming. Genetic counseling is essential for families affected by JLNS [7]. As an autosomal recessive disorder, both parents must be carriers for a child to be affected. This information is crucial for family planning and identifying at-risk family members. Research into JLNS continues, focusing on improving genetic testing, developing new therapies, and understanding the cardiac and auditory function interplay. Gene therapy and targeted molecular interventions are promising areas for future treatments [8,9].

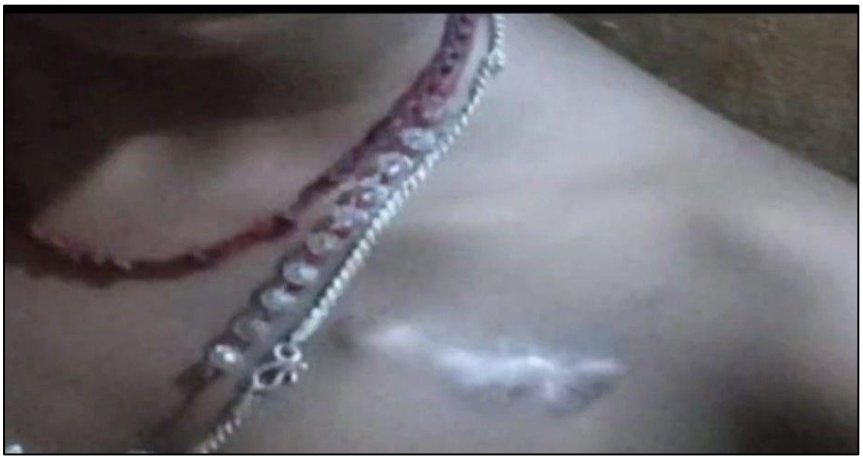
2. Case Presentation

A 6-year-old girl presented with a history of six episodes of syncope precipitated by emotions and exercise since the age of 3. She had congenital bilateral sensorineural hearing loss, for which a right cochlear implant was performed at the age of 3. The patient's electrocardiogram (ECG) revealed a corrected QT interval (QTc) of 600 milliseconds and T wave alternans, raising suspicion for JLNS. Genetic testing was done which confirmed the diagnosis.

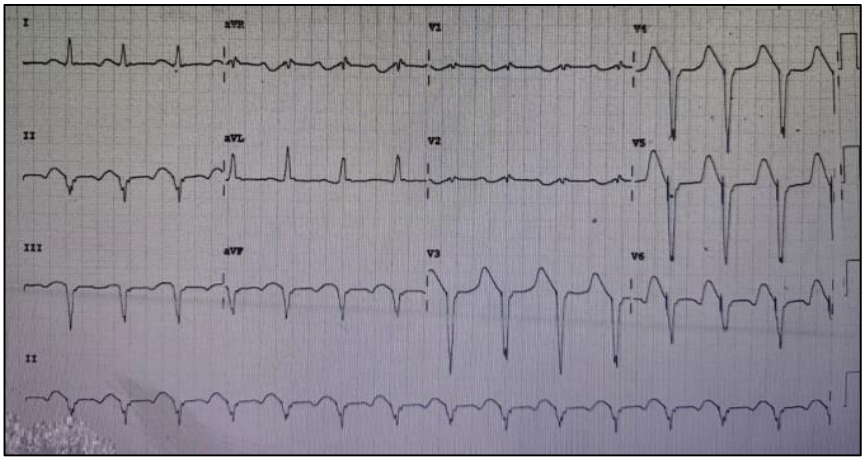


2.1. ECG (Pre ICD)

Despite medical management with beta-blockers, the patient continued to experience symptomatic episodes. Given the severity of her condition and the risk of sudden cardiac death, a subpectoral transvenous implantable cardioverter-defibrillator (ICD) was successfully implanted. The procedure was challenging due to her thin chest wall and young age, but it was performed without complications. ICD pacing has been done to decrease the QTc. If the patient presents again with symptoms, it has been planned to perform Left cardiac sympathetic denervation



ICD Implant scar



ECG (Post ICD)

3. Discussion

JLNS is caused by mutations in the KCNQ1 or KCNE1 genes, which encode subunits of the potassium channels involved in cardiac repolarization. These mutations result in a dysfunctional potassium channel, leading to a prolonged repolarization phase of the cardiac cycle (QT interval prolongation). This prolonged QT interval predisposes patients to ventricular arrhythmias, including torsades de pointes, which can result in syncope, seizures, or sudden cardiac death.

The majority of JLNS cases are linked to mutations in the KCNQ1 gene, with a smaller proportion involving mutations in the KCNE1 gene. These mutations are inherited in an autosomal recessive manner, meaning that two copies of the defective gene (one from each parent) are necessary for the syndrome to manifest. Carriers of a single defective gene may exhibit a milder form of LQTS without the hearing loss.

The diagnosis of JLNS is based on a combination of clinical findings, ECG characteristics, and genetic testing. Key diagnostic criteria include:

1) Congenital bilateral sensorineural hearing loss.
2) Prolonged QT interval on ECG, typically greater than 500 milliseconds.
3) T wave alternans on ECG.
4) Family history of JLNS or sudden cardiac death.
5) Confirmation through genetic testing identifying mutations in KCNQ1 or KCNE1 genes.

Management of JLNS involves both pharmacological and non-pharmacological strategies aimed at reducing the risk of arrhythmias and sudden cardiac death. Beta-blockers are the first line of treatment and work by reducing sympathetic stimulation to the heart, thereby lowering the risk of arrhythmias. However, beta-blockers may not be completely effective in all patients. In patients who remain symptomatic despite medical therapy or those at high risk of sudden cardiac death, an ICD is recommended.

ICD is indicated in patients with h/o cardiac arrest, QTc>550ms, syncope before the age of 5, males>20 years with KCNQ1 pathogenic variant.

The device monitors heart rhythms and delivers shocks to terminate life-threatening arrhythmias, in this case ventricular tachycardia. Patients are advised to avoid triggers that can provoke arrhythmias, such as intense physical activity, emotional stress, and certain medications that prolong the QT interval. Genetic counseling is important for affected families to understand the inheritance pattern and the risks for other family members.

4. Conclusion

Jervell and Lange-Nielsen syndrome is a rare but serious condition that requires prompt diagnosis and management to prevent life-threatening cardiac events. This case underscores the importance of recognizing the characteristic signs and symptoms of JLNS, including congenital hearing loss and prolonged QT interval, and highlights the challenges in managing young patients with this syndrome. The successful implantation of an ICD in this patient, despite anatomical and age-related challenges, emphasizes the role of advanced therapeutic interventions in improving patient outcomes. Regular follow-up and comprehensive care are essential for managing this complex condition.

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