International Journal of Contemporary Pediatrics
Agarwal K et al. Int J Contemp Pediatr. 2021 Jul;8(7):1307-1309
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: https://dx.doi.org/10.18203/2349-3291.ijcp20212495

Case Report

Compound heterozygote KCNQ1 mutation causing Jervell Lange Neilson syndrome: a case report of genotype-phenotype correlation

Khushboo Agarwal, Guruprasad H. Shankar, Bhakti Sarangi*, Ajay Walimbe

Department of Pediatrics, Bharati Vidyapeeth Medical College and Hospital, Pune, Maharashtra, India

Received: 17 May 2021
Accepted: 10 June 2021

***Correspondence:**
Dr. Bhakti Sarangi,
E-mail: dr.bhaktisarangi@gmail.com

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Congenital sensorineural hearing loss (SNHL) is a common phenomenon with several genetic and non-genetic associations that require early diagnosis and work-up to prompt appropriate interventions. Of the genetic associations, Jervell and Lange-Nielsen syndrome (JLNS) remains a rare monogenic disease that is characterized by SNHL, prolongation of QT interval, syncopal attacks due to ventricular arrhythmias and sudden cardiac death from very early in life. We hereby report a 5 years old girl with SNHL and recurrent blackout episodes in early childhood with significant family history, admitted for cochlear implant who developed ventricular arrhythmias requiring multiple interventions with further investigations revealing a prolonged QT interval on electrocardiography (ECG) with metabolic abnormalities (hypomagnesemia and hypokalemia). Her clinical exome study showed a compound heterozygous KCNQ1 mutation, a more sporadic form of JLNS managed using oral beta-blocker. This experience illustrates the relevance of a detailed systemic evaluation with an elaborate cardiac assessment in children with SNHL, more so in the presence of frequent unexplained acute life-threatening episodes.

Keywords: Sensorineural hearing loss, Long QT, Arrhythmia, Syncope, Beta blockers

INTRODUCTION

The prevalence of sensorineural hearing loss (SNHL) is 2-3 per 1000 live births in India.[1] The aetiologies for the same have been attributed to genetic and non-genetic associations and hence, a meticulous questioning about prenatal, perinatal, postnatal and family history and comprehensive review of systems may identify risk factors as well as possibility of genetic associations. Jervell and Lange-Nielsen syndrome (JLNS), is a rare inherited autosomal recessive disorder characterized by congenital bilateral SNHL, prolongation of QT interval, syncopal attacks due to ventricular arrhythmias and sudden cardiac death from very early in life affecting 3 to 5 in 1 million children.[2] We hereby discuss a case of SNHL with history of frequent acute life threatening episodes admitted for cochlear implant surgery who developed ventricular arrhythmias post-operatively and was diagnosed as JLNS with a compound heterozygote KCNQ1 mutation on clinical exome study.

CASE REPORT

A 5-year-old girl, the second child born following an uneventful pregnancy to parents with no history of consanguinity or any heart disease was diagnosed with SNHL at the age of 3 years. Parents also mentioned repeated blackout episodes preceded by an aura and lasting for a few seconds occurring every few months starting from 4 years of age. Her evaluation for the same had revealed a normal EEG and normal MRI brain, but with the consideration of possible seizures, she had been put on an anti-epileptic (oral levetiracetam at 30 mg/kg/day) by the treating paediatrician. There was significant family history of an older male sibling having SNHL and undergoing cochlear implantation at the age of

3 years. His procedure was uneventful and he remained well until 4 years of age when he also developed similar blackout episodes occurring every few months. His evaluation showed no underlying neurologic abnormalities. His growth and development remained unhampered and was treated with oral carbamazepine as treatment for possibility of seizures. However, he had a sudden cardiac arrest at the age of 11 years which in retrospect has been attributed to a possible ventricular arrhythmia. Neither child had complaints of palpitations and exercise / emotion induced symptoms.

The girl was admitted to our centre for cochlear implantation. Her pre-anaesthetic assessment was otherwise normal. A routine electrocardiographic evaluation was not part of hospital policy at that time. Though the surgery was uneventful, prior to extubation she developed ventricular fibrillation requiring cardiopulmonary resuscitation (CPR), intravenous (IV) adrenaline (0.1 ml/kg of 1:10000 dilution) and defibrillation with return of spontaneous circulation achieved after 3 minutes. She was put on a continuous IV adrenaline infusion and shifted to PICU with endotracheal tube in situ where she was continued on sedation and continuous ECG monitoring. Her 12-lead ECG showed prolongation of QT interval (560 ms as seen in Figure 1) with lab evaluation showing presence of hypokalaemia and hypomagnesemia both of which were corrected. She was started on oral propranolol in consultation with cardiology. Over the next 24 hours, she was weaned off adrenaline and extubated successfully. Subsequent 24-hour ECG monitoring showing no further arrhythmias. She was discharged from the hospital after another 48 hours on oral propranolol and remained well on follow-up with no further blackout episodes. Her clinical exome study revealed a compound heterozygous KCNQ1+ mutation which corresponded with the clinical picture of Jervell and Lange-Neilsen syndrome.

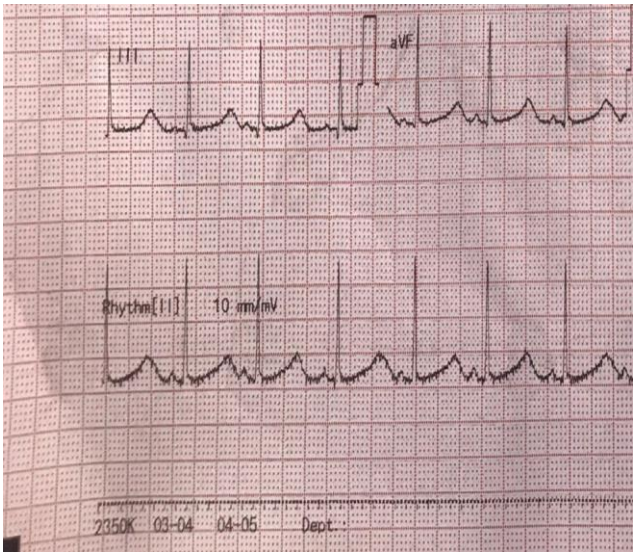

Figure 1: Prolonged QT interval with a corrected QT interval of 560 ms.

DISCUSSION

The long QT syndrome is a congenital or acquired disorder of ventricular myocardial repolarization, and is one of the more common causes of sudden cardiac death in the young. In the congenital form, at least 17 mutations have been identified. A homozygous (with autosomal recessive inheritance) or a compound heterozygous (rare, sporadic as in our case) mutation of KCNQ1 gene causes Jervell and Lange Nielsen (JLN) syndrome (Type 1 long QT syndrome), which accounts for 1-7% of congenital long QT syndromes.[3] This disease represents one of the best studied genotype-phenotype correlations. KCNQ1 gene encodes α-subunit of the K+ channel Kv7.1, generating IKs which, when defective, QT interval fails to shorten appropriately during tachycardia leading to arrhythmogenicity. Reduced IKs in the inner ear causes deafness.

Frequently, children with LQTS may present with generalised seizures and may be misdiagnosed and treated as epilepsy. A careful history may distinguish syncope from seizure, or a hypoxic seizure following a syncope, association of sensorineural deafness and a family history of premature sudden deaths, unexplained motor accidents or drowning may alert the need for a cardiac evaluation. Diagnostic criteria as proposed by Schwartz may be used prior to performing genetic testing or while waiting for the results.[4] Lack of awareness in the treating physician, of these associations and long QT in JLNS may prove to be costly, with a mortality of 21% in the first year after the initial syncope.[5]

Beta blocker prophylaxis is effective in reducing syncope and sudden cardiac death in LQTS especially in LQT1. Despite this benefit, 32% of previously symptomatic patients had another cardiac event during the five-year period while on a beta blocker. Nearly one-half of these events occurred within the first six months of therapy.[6] An implantable cardioverter defibrillator (ICD) may be considered as an alternative to beta blocker therapy. However, ICD activation in infants and young children may lead to significant pain and anxiety, and maybe counterproductive resulting in activation and a 'storm' of shocks. Hence, ICDs may be reserved for cases where cardiac arrest has occurred, or those refractory to beta-blocker therapy.[7] It is acknowledged that ICDs are safe to use with a cochlear implant, and unlikely to cause any problems.

All children who are posted for a cochlear implant must undergo an ECG and a thorough clinical history must be taken. If indicated, a cardiac evaluation must be then performed. Anesthetic precautions during surgery including avoidance of excessive noise or stress at the time of induction, not using halothane and preventing hypoxia, hypo/hypercapnia and brady/tachycardia are important.[2] Continuous cardiorespiratory monitoring and presence of a bedside defibrillator with personnel experienced in handling arrhythmias is imperative.

CONCLUSION

Due to the proven mortality benefit of close to 1% with appropriate treatment, it is very important to spread awareness of this disease and the clinical scenarios in which long QT syndromes should be evaluated.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES

1. Reddy MVV. Perinatal risk factors for congenital sensorineural hearing loss. Indian J Otol. 2006;12:7-12.
2. Broomfield SJ, Bruce IA, Henderson L, Ramsden RT, Green KM. Cochlear implantation in children with Jervell and Lange-Nielsen syndrome - a cautionary tale. Cochlear Implants Int. 2012;13(3):168-72.
3. Schwartz PJ, Crotti L, Insolia R. Long-QT syndrome: from genetics to management. Circ Arrhythm Electrophysiol. 2012;5(4):868-77.
4. Schwartz PJ, Crotti L. QTc behaviour during exercise and genetic testing for the long-QT syndrome. Circulation. 2011;124:2181-4.
5. Schwartz PJ. Idiopathic long QT syndrome: progress and questions. Am Heart J. 1985;109:399-411.
6. Moss AJ, Zareba W, Hall WJ, Schwartz PJ, Crampton RS, Benhorin J et al. Effectiveness and limitations of beta-blocker therapy in congenital long-QT syndrome. Circulation. 2000;101(6):616-23.
7. Crotti L, Celano G, Dagradi F, Schwartz PJ. Congenital long QT syndrome. Orphanet J Rare Dise. 2008;3(18):1-16.
8. Schwartz PJ, Crotti L. Long QT and short QT syndromes. In: Zipes DP, Jalife J, eds. Cardiac Electrophysiology: From Cell to Bedside. Philadelphia, PA: Elsevier/Saunders. 2009:731-44.

Cite this article as: Agarwal K, Shankar GH, Sarangi B, Walimbe A. Compound heterozygote KCNQ1 mutation causing Jervell Lange Neilson syndrome: a case report of genotype-phenotype correlation. Int J Contemp Pediatr 2021;8:1307-9.