Cardiology in the Young

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Propranolol syrup to tablets change triggers electrical storm in Jervell-Lange-Nielsen syndrome

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Brief Report

Cite this article: Ramos-Jiménez J, Sánchez-Perez I, Moreno-Mata N, and Moreno-Planas J (2021) Propranolol syrup to tablets change triggers electrical storm in Jervell-Lange-Nielsen syndrome. *Cardiology in the Young* **31**: 141–143. doi: 10.1017/S1047951120003285

Received: 15 June 2020
Revised: 8 September 2020
Accepted: 12 September 2020
First published online: 13 October 2020

Keywords:
Jervell-Lange-Nielsen syndrome; long QT interval; electrical storm; bioavailability; thoracic sympathectomy

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Abstract

A 10-year-old girl with genetically confirmed Jervell-Lange-Nielsen syndrome treated with beta-blocker and developed electrical storm after changing propranolol syrup to tablets. Jervell-Lange-Nielsen is characterised by long QT and congenital sensorineural deafness, with high risk of malignant arrhythmias at early ages. Gastric involvement and achlorhydria may be present, with subsequent alteration of medication bioavailability which can trigger severe arrhythmic complications.

Case report

A 10-year-old girl with confirmed Jervell-Lange-Nielsen syndrome was admitted to our Paediatric Intensive Care Unit because of multiple episodes of Torsade de Pointes correctly treated by her implantable cardiac defibrillator. She was diagnosed with Jervell-Lange-Nielsen syndrome diagnosis at 3 years of age (homozygous mutation KCNQ1) and had previously received an implantable cardiac defibrillator for secondary prevention, with subsequently administered appropriate shocks. Previous history included bilateral sensorineural deafness, iron deficiency anemia, and hypochlorhydia with hypergastrinemia. Seven days prior to admission, the patient treatment had been changed from propranolol oral solution 30 mg/8 hours (1.2 mg/kg/8 hours) to propranolol tablets 30 mg/8 hours (1.2 mg/kg/8 hours). The baseline electrocardiogram (Fig 1) at admission showed sinus rhythm at 78 beats per minute, left anterior fascicular block, and corrected QT interval of 604 milliseconds. Biochemical analysis showed no metabolic alterations. During the first 4 hours in ICU, she presented 17 new episodes of Torsade de Pointes that were treated with sedation, orotracheal intubation, rapid overdrive pacing, and perfusion of esmolol, with an initial dose of 50 mcg/kg/minute titrated to 200 mcg/kg/minute, achieving control of the electrical storm. Because of previous appropriate device therapies despite beta-blockade and the ongoing episode, a T1–T5 sympathectomy and partial ablation of the stellate ganglion were successfully performed on day +3 of admission. Esmolol was replaced by propranolol 0.3 mg/kg/day with favourable evolution, extubation on the 6th day, and hospital discharge after 21 days. Since then, she receives propranolol 60 mg/8 hours in oral solution without new arrhythmic events after 17 months of follow-up.

Discussion

Jervell-Lange-Nielsen syndrome is a rare disease included within congenital long QT syndromes. It is an inherited disease with an autosomal recessive pattern (family pedigree in Fig. 2) caused by homozygous or compound heterozygous mutations in the KCNQ1 or KCNE1 genes, which encode components of the IKs channel. It presents an aggressive course, with approximately 50% death rate before the age of 15 years in untreated patients.[1] Along with the prolongation of the QT interval, affected individuals present with bilateral sensorineural deafness due to dysfunction of the IKs channels, which maintain the endocochlear potential in the endolymph. IKs are also found in gastric parietal cells where they participate in the secretion of hydrochloric acid. IKs channels impairment produces achlorhydria, secondary hypergastrinemia, and iron deficiency anemia, since an acidic pH is required for the correct absorption of iron.[2]

Treatment of Jervell-Lange-Nielsen syndrome consists of beta-blockers, with preference for propranolol or nadolol. Propranolol plasma levels vary greatly among individuals and gastric pH is an important factor for absorption. It is known that propranolol is more stable at acidic pH being the drug decomposed in alkaline solutions.[3] Oral propranolol solution is formulated with 25% citric acid, which likely resulted in better stability and greater bioavailability in our patient with achlorhydria. The authors presume that conversion from oral solution to tablets may have

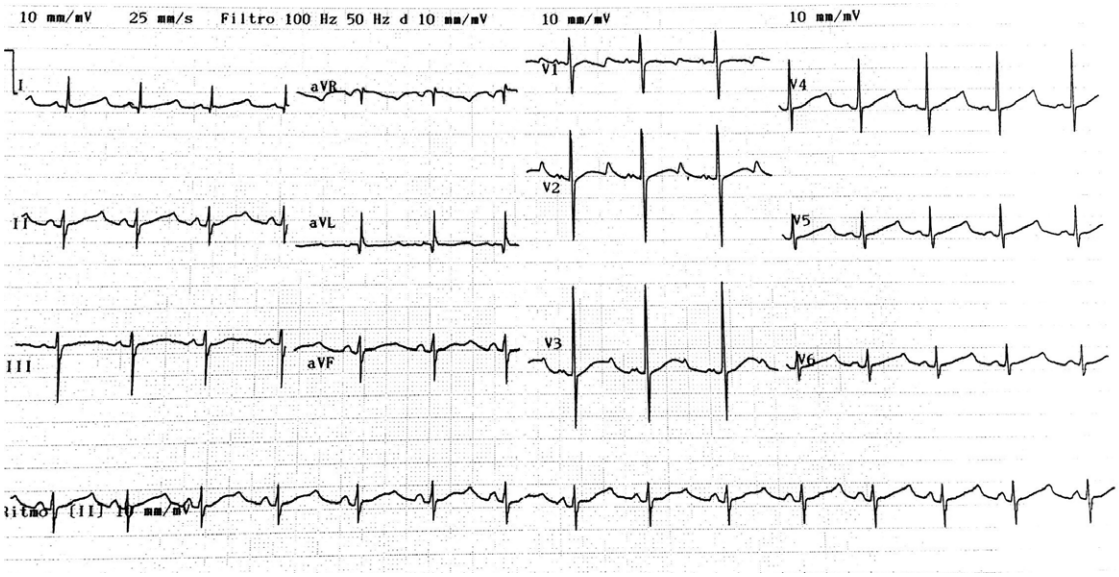

Figure 1. Baseline electrocardiogram.

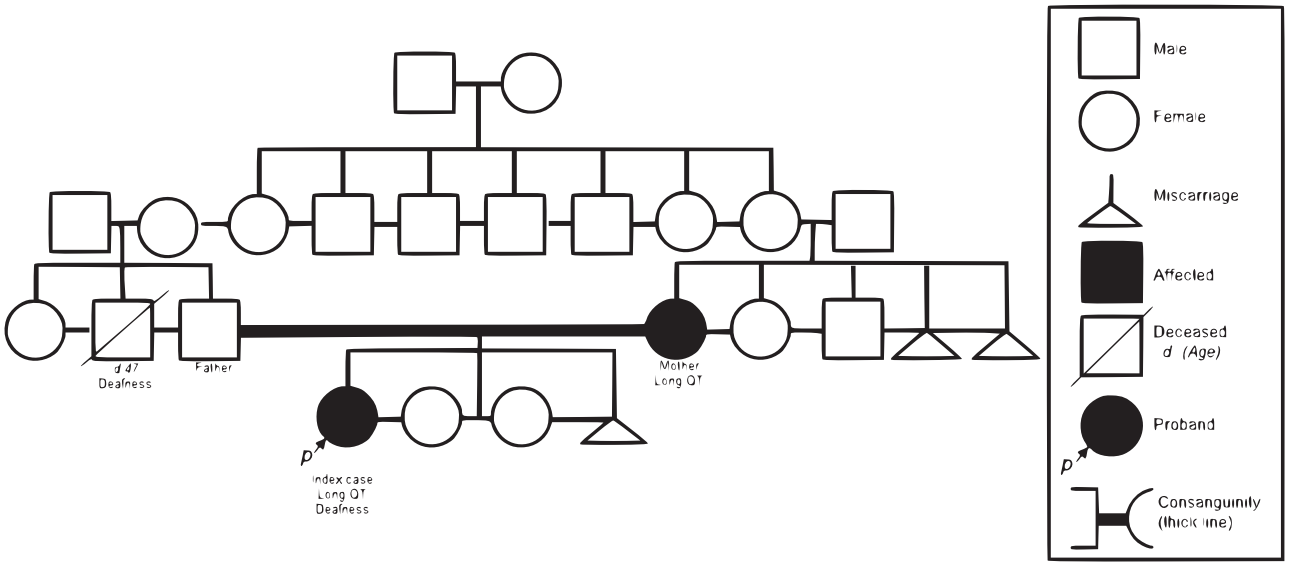

Figure 2. Family pedigree of the index case.

comprised propranolol stability, leading to a reduced bioavailability which likely contributed to the genesis of the arrhythmic storm.

In the case of beta-blocker refractory arrhythmias, thoracic sympathectomy and partial ablation of the stellate ganglion has been shown as an option with promising results in the prevention of arrhythmic recurrences in patients with long QT syndrome.[4] In our patient, although we were concerned that the conversion from propranolol solution to tablets may have contributed to the electrical storm, given the life-threatening nature of the patient's presentation, in addition to converting back to treatment with propranolol solution, we elected to proceed with surgical sympathectomy. While this combined approach was clinically effective, we were unable to determine whether the transition back to propranolol solution or the sympathectomy were most causal in obtaining arrhythmia control.

In conclusion, this case illustrates the complexity of Jervell-Lange-Nielsen syndrome with regard to how changes in drug formulations that can modify bioavailability must be performed with extreme caution. For such patients, given the risk of life-threatening arrhythmias, clinicians should consider hospitalising patients for continuous heart rhythm monitoring when changes in drug formulation are planned.

Acknowledgements. None.

Financial Support. This research received no specific grant from any funding agency, commercial or not-for-profit sectors.

https://doi.org/10.1017/S1047951120003285 Published online by Cambridge University Press

Conflicts of Interest. None.

Ethical Standards. This report does not involve any human subjects research or animal experimentation.

References

1. Schwartz Peter J, Carla S, Lia C, et al. The Jervell and Lange-Nielsen syndrome. Circulation 2006; 113: 783–790.
2. Rice KS, Dickson G, Lane M, et al. Elevated serum gastrin levels in Jervell and Lange-Nielsen syndrome: a marker of severe KCNQ1 dysfunction? Heart Rhythm 2011; 8: 551–554.
3. Sweetman SC. Martindale: The Complete Drug Reference. London, Chicago: Pharmaceutical Press, 2009: 1381–1382.
4. Al-Khatib Sana M, Stevenson William G, Ackerman Michael J, Bryant William J, et al. 2017 AHA/ACC/HRS guideline for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death. Circulation. 2018; 138: e272–391.

https://doi.org/10.1017/S1047951120003285 Published online by Cambridge University Press