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CASE REPORT

Mexiletine in The Treatment of Long QT Syndrome Type 2 in Infants: A Case Report

Jessica Laureano Martins,[1] Nicole Sarmento Queiroga,[2] Fernanda Calumby Nóbrega Guimarães,[2] Guilherme Augusto Teodoro Athayde,[3] Halbiege Léa Silva Quirino da Silva,[4] Rogério Braga Andalaft[5,6]

Instituto Dante Pazzanese de Cardiologia,[1] São Paulo, SP – Brazil
Centro Universitário de João Pessoa,[2] João Pessoa, PB – Brazil
Universidade de São Paulo, Instituto do Coração,[3] São Paulo, SP – Brazil
UFPB,[4] João Pessoa, PB – Brazil
Instituto Dante Pazzanese de Cardiologia,[5] São Paulo, SP – Brazil
Hospital Israelita Albert Einstein,[6] São Paulo, SP – Brazil

Introduction

Congenital Long QT Syndrome (LQTS) is one of the main causes of sudden cardiac death (SCD) in the pediatric age group, with a prevalence of approximately one case for every 2,000 newborns. The most prevalent inheritance is dominant, with the typical phenotype associated with cardiac manifestations.[1]

The genetic alteration of LQTS is multigenic, with 17 main genes, and in 80% of the cases, it identifies: KCNQ1 (LQTL1), KCNH2 (LQTL2), and SCN5A (LQTL3).[2] The LQTS type 2 (LQTS2) subtype alters the expression of potassium channels in myocytes, causing electrical instability and ventricular arrhythmias.[3] The most common arrhythmia is *Torsades de Pointes* (TdP), a type of polymorphic ventricular tachycardia, which can lead to syncope, seizures, and sudden death.[1]

The therapeutic objectives are to reduce the QT interval and maintain the sinus rhythm. Beta blockers are the most commonly used medication to treat this condition. In cases of refractoriness, other drugs or left cardiac sympathetic denervation (LCSD) can be considered.[1]

This article reports on the case of an infant with LQTS2 who shows early manifestations, discussing relevant aspects about diagnosis and treatment, in addition to our experience of using mexiletine associated with beta-blocker therapy to control arrhythmias.

Keywords

Long QT Syndrome; Cardiac Arrhythmias; Torsades de Pointes.

Case report

A 23-day-old female newborn, with no family history of congenital heart disease, presented a history of choking and seizures and was hospitalized for investigation of hypoactivity and bradycardia.

She developed tachyarrhythmias with a heart rate of 300 bpm and serial electrocardiograms (ECG) with a maximum QTc interval of 690 ms, TdP, and macroalternating T waves (Figure 1). Analysis of the clinical picture and electrocardiographic tracings initially led to the diagnosis of acquired alterations in the QTc interval, due to the previous use of amiodarone to control arrhythmic events.

After discontinuing all medications with the potential to prolong the QTc interval, the prolonged interval persisted, suggesting not only drug alterations, but also a phenotypic expression of LQTS, with a high probability when applying the Schwartz score. The patient scored 6.5 points when applying the score.

Clinical manifestations predominated during sleep and rest, more characteristic of LQTS type 3. Therefore, propranolol was started at the maximum tolerated dose, and spironolactone, with a gradual and slow reduction in QTc. Genetic testing confirmed LQTS2, showing alterations in the KCNH2 gene. Despite optimized therapy, the QT interval persisted above 500 ms. Mexiletine, a drug used in LQTS3, was chosen, which provided a significant reduction in QTc (Figure 2).

The patient is being monitored with optimized treatment, using propranolol at a dose of 5 mg/kg/day, magnesium 50 mg/kg/day, spironolactone 1 mg/kg/day,

Mailing Address: Fernanda Calumby Nóbrega Guimarães
Centro Universitário de João Pessoa. Rodovia BR-230, Km 22. Postal code: 58053-000. Água Fria, João Pessoa, PB – Brazil
E-mail: fefecalumby@outlook.com
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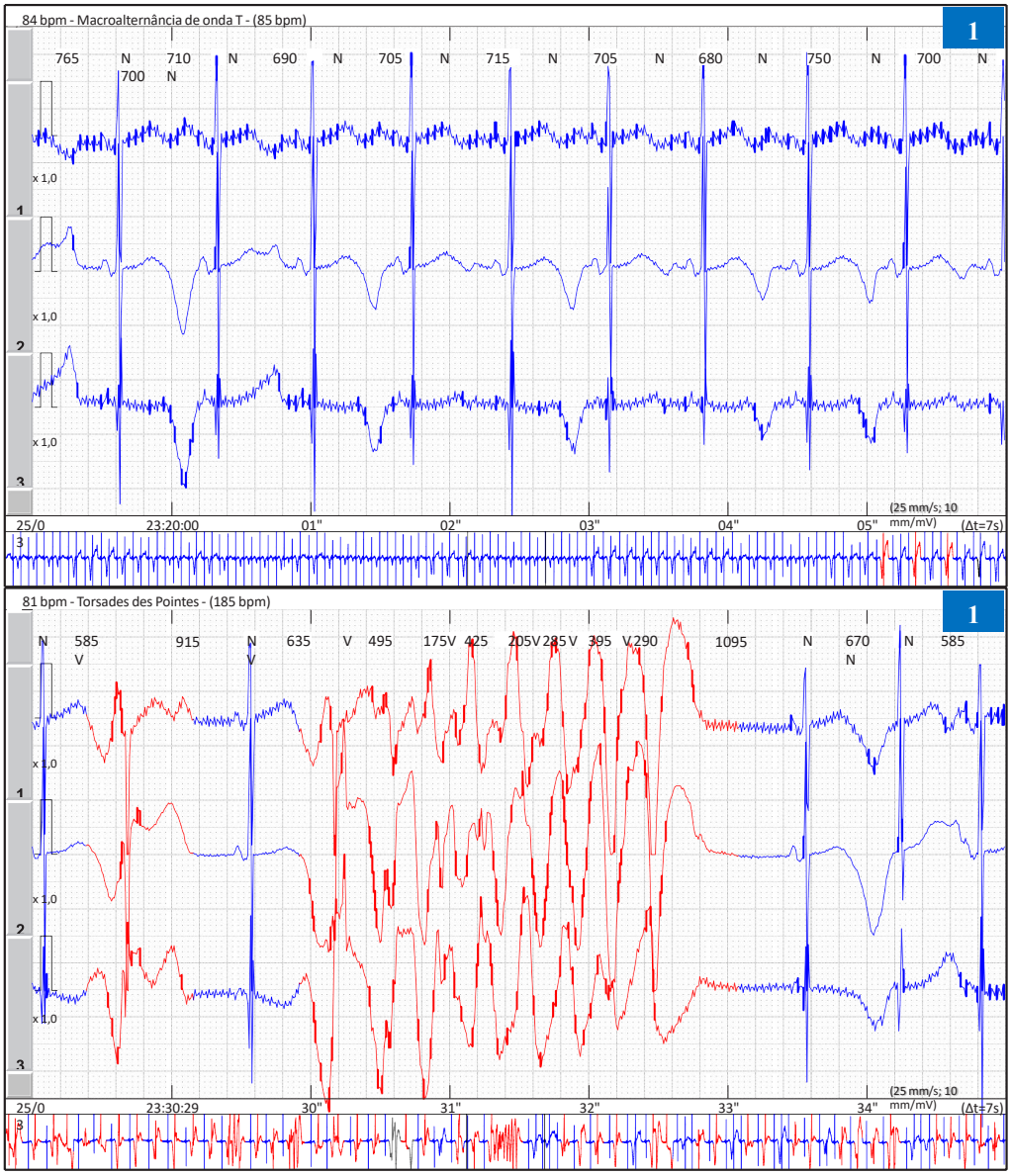

Figure 1 – 24-hour Holter tracing showing: A) Macroalternation of the T wave, B) QTc interval of 640ms and a short-long-short sequence generating an episode of polymorphic ventricular tachycardia associated with prolonged QTc interval - TdP (B).
Source: Research data, 2023.

and mexiletine 5 mg/kg/dose, 8/8h, without arrhythmias, with QTc control at values below the pro-arrhythmic threshold and adequate growth and development.

Discussion

Patients with congenital LQTS may be asymptomatic for a long period, resulting in underdiagnosis and underestimation of incidence. Symptoms of LQTS2 begin during puberty and, among symptomatic patients, one in four presents an arrhythmia that triggers the syndrome or sudden death. In the present case report, the patient presented atypical manifestations from the ECG and clinical perspectives, which began at one month of age.[4]

The clinical picture of the syndrome is triggered by specific triggers depending on the genotype. Patients with LQTS2 develop arrhythmias triggered by abrupt sound stimuli, fright, and emotional stress. In LQTS3,

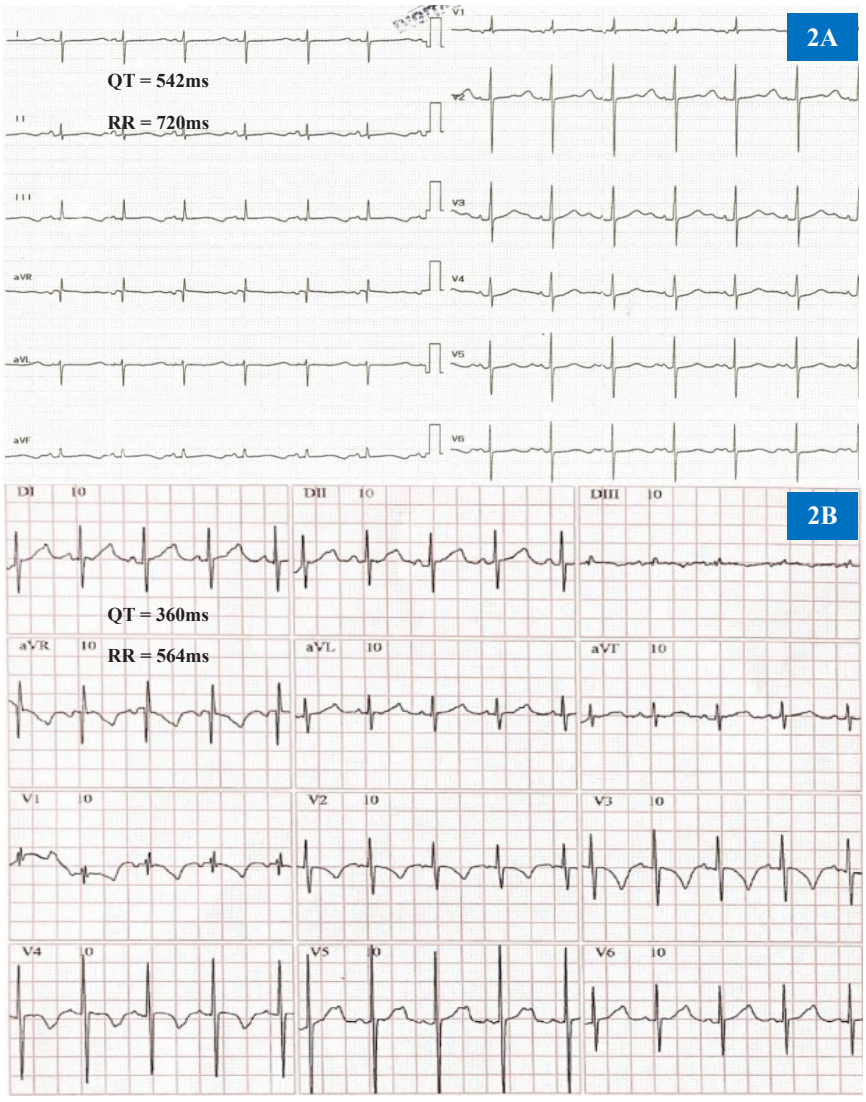

Figure 2 – Electrocardiographic tracing showing in A a QTc interval (Bazzet) of 619 ms and a significant reduction in the QTc interval to 437 ms (image B).
Source: Research data, 2023.

they are triggered during sleep and rest, as occurred in the patient in this study.[5]

The ECG findings, in addition to the long QT interval, indicate morphological alterations in the T wave. In LQTS2, the T wave is bifid or notched, asymmetrical, and of low amplitude, which was not characteristic of the patient; in LQTS3, the T wave has a later peak. Although these alterations are found, they are nonspecific and increasingly less valued.[6]

In the first moment, the investigation of secondary causes is extremely important. Next, serial ECG, clinical parameters, family history, and the Schwartz Score are assessed. The scoring of this score defines the probability of the disease; a value of ≥ 3.5 points indicates a high probability.[7]

The therapy of choice is beta-blockers, at the maximum dose tolerated by the patient.[4] In LQTS2, these drugs are less effective in monotherapy and can be optimized with magnesium and potassium-sparing diuretics.[1] Mexiletine may be an alternative in refractory cases. A case of this nature would refer to an antiarrhythmic that acts by selectively suppressing

sodium channels in myocytes, corroborating its therapeutic efficacy in LQTS3.

Bos et al.[8] developed a retrospective cohort with 12 patients with LQTS2 using beta-blockers and associated with mexiletine, to assess the control of the syndrome. The analysis was performed using serial ECG, comparing QTc values before and after medication. A 65ms reduction in QTc value was observed in 8 patients and a 90ms reduction in the others. They concluded that pharmacological targeting of the late physiological sodium current may provide additional therapeutic efficacy to beta-blocker therapy in patients with LQTS2.

A meta-analysis that evaluated six studies with 217 patients with LQTS, using mexiletine, confirmed a reduction in the QTc interval in LQTS2 by 40 ms and an absence of cardiac events, especially TdP during the study, confirming the efficacy of the drug in this genotype, with the need for further studies to understand its action.[9]

Therefore, although the therapeutic approach using mexiletine in LQTS2 is not fully described in the literature, its use showed significant efficacy in controlling the QTc interval to values below the proarrhythmic threshold in the patient. After the administration of mexiletine, the QTc remained below 500 ms, and an absence of arrhythmias was observed.

Author Contributions

Conception and design of the research: Martins JL, Silva HLSQ; acquisition of data: Martins JL, Queiroga NS, Guimarães FCN, Athayde GAT; analysis and interpretation of the data: Martins JL, Queiroga NS, Guimarães FCN, Athayde GAT, Andalaft RB; statistical analysis and writing of the manuscript: Queiroga NS, Guimarães FCN; obtaining financing: Martins JL, Andalaft RB; critical revision of the manuscript for intellectual content: Martins JL, Silva HLSQ, Athayde GAT, Andalaft RB.

Potential Conflict of Interest

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

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Study Association

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Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of the Centro Universitário de João Pessoa - UNIPÊ under the protocol number 74114823.7.0000.5176. All the procedures in this study were in accordance with the 1975 Helsinki Declaration, updated in 2013. Informed consent was obtained from all participants included in the study.

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