Long QT Syndrome Masquerading as Refractory Epilepsy in an Adolescent

ABSTRACT

INTRODUCTION: Epileptic seizures can be difficult to distinguish from other etiologies causing cerebral hypoxia, especially cardiac diseases. Long QT syndrome (LQTS) frequently masquerades as seizures due to transient cerebral hypoxia caused by decreased cardiac output secondary to ventricular arrhythmias. Early and accurate diagnosis of LQTS is crucial to prevent inappropriate treatment with anti-epileptic drugs (AEDs) and sudden death.

CASE SUMMARY: We report a rare case of Jervell and Lange-Nielsen syndrome in a 13-year-old adolescent misdiagnosed with refractory epilepsy and treated with various AEDs for nearly 10 years. The patient experienced seizure-like episodes accompanied by palpitations, typically triggered by excitement, fright, or stress. The presence of bilateral sensorineural deafness and refractoriness to multiple AEDs raised suspicion for LQTS, which was confirmed by characteristic ECG findings. The patient was treated with a beta-blocker, and over a one-year follow-up, no new episodes of syncope or seizures occurred.

CONCLUSION: This case underscores the importance of ECG in the evaluation of seizures and highlights how LQTS can mimic seizure disorders. Treatment of long QT syndrome prevents seizure like episodes and risk of sudden death.

Keywords : *Long QT syndrome, Jarvell and Lange- Nielsen syndrome, refractory seizure, sensorineural deafness, beta blocker*

INTRODUCTION

Epileptic seizures are a common neurological presentation but can sometimes be challenging to differentiate from other causes of transient cerebral dysfunction. Among these, cardiac etiologies, such as arrhythmias, are particularly significant. LQTS is a cardiac channelopathy that prolongs ventricular repolarization, predisposing to life-threatening arrhythmias such as torsades de pointes(Shwartz et al. 2012). Due to transient cerebral hypoxia during arrhythmic episodes, LQTS often mimics seizure disorders. Recognizing LQTS masquerading as epilepsy is vital to avoid unnecessary AED treatment and prevent fatal outcomes. This report presents a rare and illustrative case of congenital LQTS, Jervell and Lange-Nielsen syndrome(JLNS) presenting as refractory epilepsy.

CASE PRESENTATION

A 13-year-old adolescent presented with a history of recurrent seizure-like episodes since the age of 3years. These episodes were characterized by sudden loss of consciousness, generalized tonic posturing, and occasional cyanosis. Each episode lasted for few seconds to few minutes followed by spontaneous regain of consciousness without any neurological deficit.The events were often precipitated by emotional triggers such as excitement, fright, or stress. The patient was deaf and mute since birth. Brainstem evoked auditory response done in early childhood showed profound bilateral sensorineural hearing loss. There was no family history of similar illness.

Over the course of 10 years, the patient was evaluated by multiple physicians and treated with several AEDs, without significant clinical improvement. Electroencepahologram report done earlier was normal. On detailed re-evaluation, the seizure-like episodes were noted to be associated with palpitations and a lack of postictal confusion for which patient was referred to pediatric cardiologist. The persistence of episodes despite polytherapy raised suspicion of a non-epileptic etiology. Based on the clinical presentation and bilateral sensorineural deafness high suspicion of Jervell and Lange-Nielsen syndrome was made. Serum sodium,potassium,calcium and magnesium levels were normal. There was no history of any medication causing long QT interval.Electrocardiogram (ECG) revealed a prolonged corrected QT interval (QTc) of 550 ms with typical broad based T wave pattern consistent with JLNS variant of LQTS.(Figure 1)

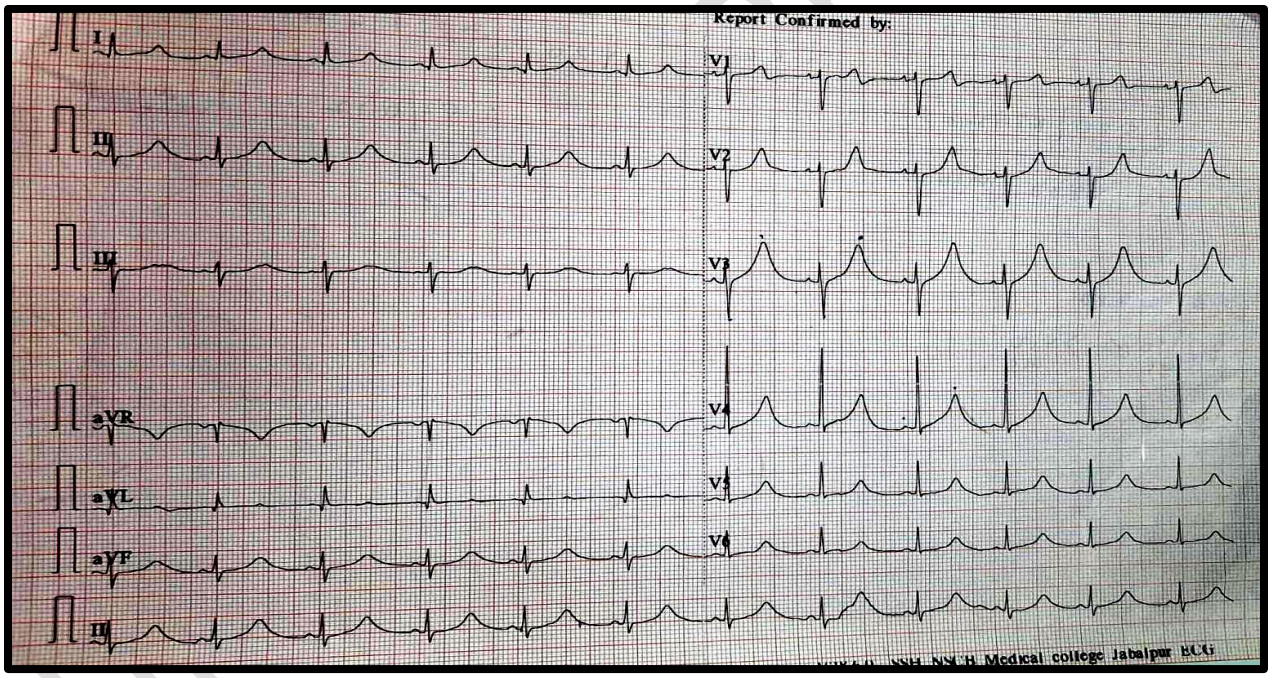

Fig. 1. ECG showing prolonged QTc with broad based T wave pattern

The patient was initiated on a beta-blocker, propranolol treatment. The family was educated about the importance of avoiding triggers, and the patient was advised to avoid medications that could further prolong the QT interval. Screening ECG of other family members were normal. Over one year of follow-up, the patient remained free of syncopal or seizure-like episodes, indicating effective management of the condition.

CASE DISCUSSION AND LITERATURE REVIEW

LQTS is a genetically heterogeneous disorder caused by mutations affecting cardiac ion channels. It is classified into congenital and acquired forms(Goldenberg et al. 2008). The congenital form commonly includes JLNS, which is associated with profound sensorineural hearing loss, and Romano-Ward syndrome, which occurs without hearing loss.

Anton Jervell and Fred Lange-Nielsen (1957) first reported a familial disorder of prlonged QT interval with congenital deafness with increased incidence of sudden cardiac death. JLNS is caused by mutations in genes encoding potassium channel subunits (KCNQ1 or KCNE1), which are critical for cardiac repolarization and inner ear function. Worldwide prevalence of JLNSis about 1/1000000 to 1/200000(Qiu et al 2020). Females and males are equally presented with females are at lower risk of cardiac arrest and sudden death (Shwartz et al, 2006). Patients typically present with syncopal episodes, which can be mistaken for seizures, as in this case.Autonomic influences and such catecholamines as in conditions of exertion, excitement, stress or fright further prolongs the QT interval and predispose to episodes of ventricular arrhythmia.(Philip &Vinay 1999)

Distinguishing LQTS from epilepsy requires a high index of suspicion, especially in patients with seizure-like episodes that are atypical or refractory to AEDs. Key clinical clues include:

- Seizures triggered by exertion, excitement, or fright
- Palpitations or chest discomfort preceding episodes
- Sensorineural hearing loss
- Absence of postictal confusion

The diagnosis of LQTS is primarily clinical and supported by ECG findings of prolonged corrected QT interval (QTc) (≥450 ms in males and ≥460 ms in females). Genetic testing can confirm the diagnosis but is often unnecessary when clinical and ECG findings are definitive(Goldenberg et al,2008).

Management includes beta-blockers as first-line therapy, which reduce the risk of arrhythmias by decreasing adrenergic stimulation. (Chockalingam et al,2012 & Wenjing et al 2024) In high-risk cases, left cardiac sympathetic nerve denervation(Schwartz et al 2004& Wenjing et al 2024) and an implantable cardioverter-defibrillator (Schwartz et al,2010) may be indicated. Lifestyle modifications, such as avoiding QT-prolonging medications and known triggers, are also essential.

CONCLUSION AND SUMMARY

This case highlights the critical role of ECG in the evaluation of refractory seizures and the importance of considering cardiac causes such as LQTS in the differential diagnosis. Misdiagnosis of LQTS as epilepsy can lead to inappropriate treatment with AEDs and increased risk of sudden cardiac death. Early recognition and appropriate management are life-saving.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that generative AI technologies such as Large Language Models, etc have not been used during writing or editing of this manuscript.

ETHICAL APPROVAL:

As per international standards or university standards written ethical approval has been collected and preserved by the author(s).

CONSENT:

As per international standards or university standards, parental written consent has been collected and preserved by the author(s).

REFERENCES

Schwartz PJ, Crotti L, Insolia R. Long-QT syndrome: from genetics to management. *Circ ArrhythmElectrophysiol*. 2012;5(4):868-877.

Goldenberg I, Moss AJ. Long QT syndrome. *J Am Coll Cardiol*. 2008;51(24):2291-2300.

Jervell A, Lange-Nielsen F. Congenital deaf-mutism, functional heart disease with prolongation of the Q-T interval and sudden death. *Am Heart J*. 1957;54:59–68

Qiu et al, Jervell and Lange-Nielsen Syndrome due to a Novel Compound Heterozygous *KCNQ1* Mutation in a Chinese Family, *Neural Plasticity*, 2020, 3569359, 8 pages, 2020. https://doi.org/10.1155/2020/3569359

Schwartz PJ, Spazzolini C, Crotti L, et al.: The Jervell and Lange-Nielsen syndrome: natural history, molecular basis, and clinical outcome. Circulation. 2006, 113:783-90. 10.1161/CIRCULATIONAHA.105.592899

Philip Salen, Vinay Nadkarni, Congenital long-QT syndrome: a case report illustrating diagnostic pitfalls,The Journal of Emergency Medicine,Volume 17, Issue 5,1999,Pages 859-864,https://doi.org/10.1016/S0736-4679(99)00096-7.

Chockalingam P, Crotti L, Girardengo G, Johnson JN, Harris KM, van der Heijden JF, Hauer RN, Beckmann BM, Spazzolini C, Rordorf R, Rydberg A, Clur SA, Fischer M, van den Heuvel F, Kääb S, Blom NA, Ackerman MJ, Schwartz PJ, Wilde AA. Not all beta-blockers are equal in the management of long QT syndrome types 1 and 2: higher recurrence of events under metoprolol. J Am Coll Cardiol. 2012 Nov 13;60(20):2092-9. doi: 10.1016/j.jacc.2012.07.046.

Schwartz PJ, Priori SG, Cerrone M, Spazzolini C, Odero A, NapolitanoC, Bloise R, De Ferrari GM, Klersy C, Moss AJ, Zareba W, RobinsonJL, Hall WJ, Brink PA, Toivonen L, Epstein AE, Li C, Hu D. Left cardiacsympathetic denervation in the management of high-risk patients affectedby the long-QT syndrome. *Circulation*. 2004;109:1826–1833.

Schwartz PJ, Spazzolini C, Priori SG, Crotti L, Vicentini A, Landolina M,Gasparini M, Wilde AA, Knops RE, Denjoy I, Toivonen L, Mönnig G, AlFayyadh M, Jordaens L, Borggrefe M, Holmgren C, Brugada P, De Roy L,Hohnloser SH, Brink PA. Who are the long-QT syndrome patients who receive an implantable cardioverter-defibrillator and what happens to them?:data from the European Long-QT Syndrome Implantable CardioverterDefibrillator (LQTS ICD) Registry. *Circulation*. 2010;122:1272–1282

Wenjing Zhu, Xueyan Bian, Jianli Lv, From genes to clinical management: A comprehensive review of long QT syndrome pathogenesis and treatment, Heart Rhythm O2,Volume 5, Issue 8,2024,Pages 573-586,