A Rare Case of Late Onset Familial Long QT Syndrome Presented with Recurrent Cardiac Arrest, Complete Heart Block, and NSTEMI

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ABSTRACT

Long QT Syndrome (LQTS) is a rare cardiac condition whose etiology is acquired or congenital. It has a wide range of clinical manifestations ranging from asymptomatic to sudden cardiac death due to malignant arrhythmia such as ventricular tachycardia. Congenital LQTS usually occurs at an early age in the form of prolonged QT interval in ECG examination, but such a condition may occur in later life. Therefore, QT interval should be assessed thoroughly to minimize the risk of iatrogenic ventricular tachycardia. A 72-year-old Javanese female with recurrent syncope episodes for 8 months was referred to the emergency department for temporary pacemaker implantation due to a complete heart block and NSTEMI. Family history revealed a first-degree family history of sudden cardiac death. She had a history of recurrent cardiac arrest due to ventricular arrhythmia and was treated with amiodarone continuous intravenous infusion in the previous hospital. During examination in the emergency department, she experienced another episode of cardiac arrest due to ventricular arrhythmia. Electrocardiogram examination pre-cardiac arrest revealed a complete heart block, atrial rate 60 bpm, ventricle rate 60 bpm, T Inversion in I, aVL, V2-V6, with prolonged QT interval (QT 616 ms, QTc 578 ms). Thus, amiodarone was subsequently stopped, and defibrillation was administered under ACLS guidelines. After the return of spontaneous circulation, revascularization was conducted due to ongoing typical chest pain and increased troponin level (117 ng/mL) to the LAD. Despite optimal revascularization and normal electrolyte level (Sodium 137 mEq/L, Potassium 3.8 mEq/L, Chloride 104.5 mEq/L), prolonged QT interval was observed in the patient until the 9th day post-revascularization and the double-chamber pacemaker implantation was conducted on patient. Thus, the prolonged QT interval subsided after double-chamber pacemaker implantation. Long QT Syndrome may occur at any period of life and may be asymptomatic. A thorough ECG examination before commencing treatment on a patient was pivotal to preventing malignant arrhythmia.

***Keywords**: Familial Long QT syndrome, cardiac arrest, myocardial infarction, cardiac pacemaker.*

INTRODUCTION

Long QT Syndrome (LQTS) has been widely known as associated with sudden cardiac death (SCD), particularly due to syncope, seizure-like activity, and malignant arrhythmia (ventricular tachycardia) as its clinical presentation. Since it was first described by Jervell and Lange-Nielsen, numerous studies reported the mutation of ion channels responsible for ventricular repolarization causing QT interval prolongation seen on electrocardiogram (ECG).[1-3] Based on the genetic examination, there are 6 phenotypes of LQTS, however, only 3 phenotypes have been described in clinical studies. The diagnostic process of LQTS requires genetic testing, however, through clinical and ECG examinations with Schwartz score, a quick assessment of LQTS can be performed especially in an emergency setting.[4] Quick assessment is necessary because there are drugs that can prolong QT interval, particularly anti-arrhythmia drugs such as amiodarone, sotalol, dofetilide, and quinidine.[5] Besides the precautionary treatment, quick assessment of LQTS is important because if left untreated it has a high risk of any cardiac events (36%) or SCD (13%).[6]

Previous studies reported that SCD was a result of ventricular arrhythmia complicating acute myocardial infarction in 20-50% of cases.[7,8] Prolonged QT interval as an independent risk of any cardiac events was reported in 21.95% of patients with Non-ST Elevation Myocardial Infarction (NSTEMI).[9] Furthermore, patients with prolonged QT interval were reported to have an increased risk of lethal arrhythmia and mortality after acute myocardial infarction (AMI).[10] Previous studies reported that QT interval duration in Non-ST elevation myocardial infarction (NSTEMI) was prolonged at the time of admission, reaching its peak at 48-72 hours and returning to normal at the time of pre-discharge.[11,12] Therefore, the possibility of myocardial ischemia as the etiology of lethal ventricular arrhythmia should be considered in an emergency setting.

Regardless of LQTS diagnosis, prolonged QT interval as an SCD risk factor at a later age (≥40 years) was considered rare, with a prevalence of 0.42% according to the Spanish cohort study, and presentation of congenital LQTS in all age groups had been reported.[13,14] Therefore, this case report aims to report a patient with late-onset congenital LQTS with incidental NSTEMI as its initial presentation. Prompt assessment of LQTS is important because LQTS patients are prone to experience SCD, or ventricular arrhythmia induced by drugs that prolong QT interval. Therefore, early detection is important to raise clinician awareness so that acquired SCD can be prevented.[15,16]

CASE ILLUSTRATION

A 72-year-old Javanese female was referred from a secondary referral hospital for temporary pacemaker implantation due to a complete heart block and NSTEMI. History taking revealed her chief complaint was typical chest pain for 10-15 minutes for 3 days before admission. Typical chest pain was preceded by syncope which occurred with moderate exercises (aerobic exercises, walking), approximately 30 seconds to 1 minute, and first experienced 8 months before admission and recurred approximately once twice syncope episodes in a month. She reported no dyspnea or asymmetrical weakness during her syncope episodes. Her past medical history was hypertension which was first diagnosed in 2022 with candesartan (16 mg). She reported that his brother died from sudden cardiac death while watching television and she had a familial history of hypertension and cancer (**Figure 1**).

She was admitted to the ICCU at the secondary referral hospital and received aspirin 300 mg and clopidogrel 300 mg as loading dose, dopamine, and enoxaparin. Within treatment, she experienced episodic cardiac arrest due to ventricular tachycardia (**Figure 2**) after exercise or increased abdominal pressure and was resuscitated according to the Advanced Cardiac Life Support (ACLS) protocol and received amiodarone 600 mg in 12 hours. Physical examination in the Emergency Room revealed she was fully alert, with normal blood pressure, on oxygen 3 pm with nasal cannula, and on dopamine infusion 3 mcg/kgBW/min, nicardipine 3 mg/h, and amiodarone 600 mg/12 hours. Physical examinations revealed fine-coarse rales on the bilateral lower lobe. Laboratory

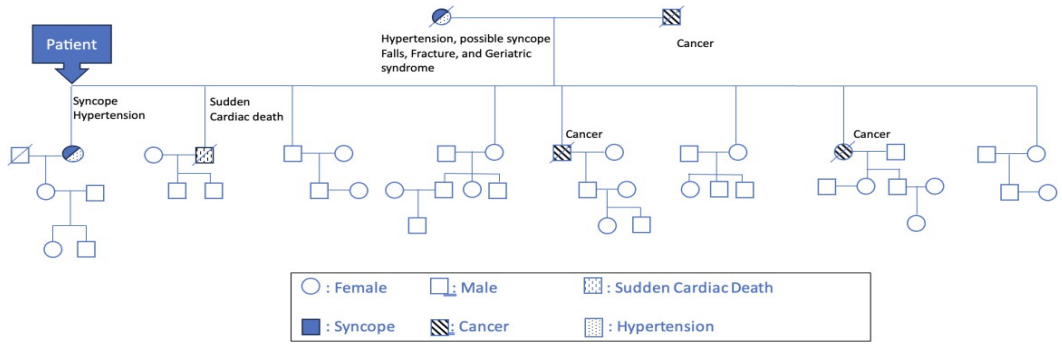

Figure 1. Family History of Patient.

parameters showed leukocytosis (17,820 cells/mm3), normal electrolyte (Sodium 137 mEq/L, potassium 3.7 mEq/L, chloride 104.5 mEq/L, calcium corrected 8.5 mg/dL, magnesium 1.96 mg/dL), elevated troponin T (117 ng/L), slightly elevated hepatic transaminase serum (AST 92 U/L, ALT 112 U/L), and acute kidney injury (Ureum 42.8 mg/dL, creatinine 1.0 mg/dL, and eGFR 56.4 ml/min/1.73m^2.

An electrocardiogram revealed the presence of a complete heart block with the persistence of prolonged QT interval (**Figure 3**). However,

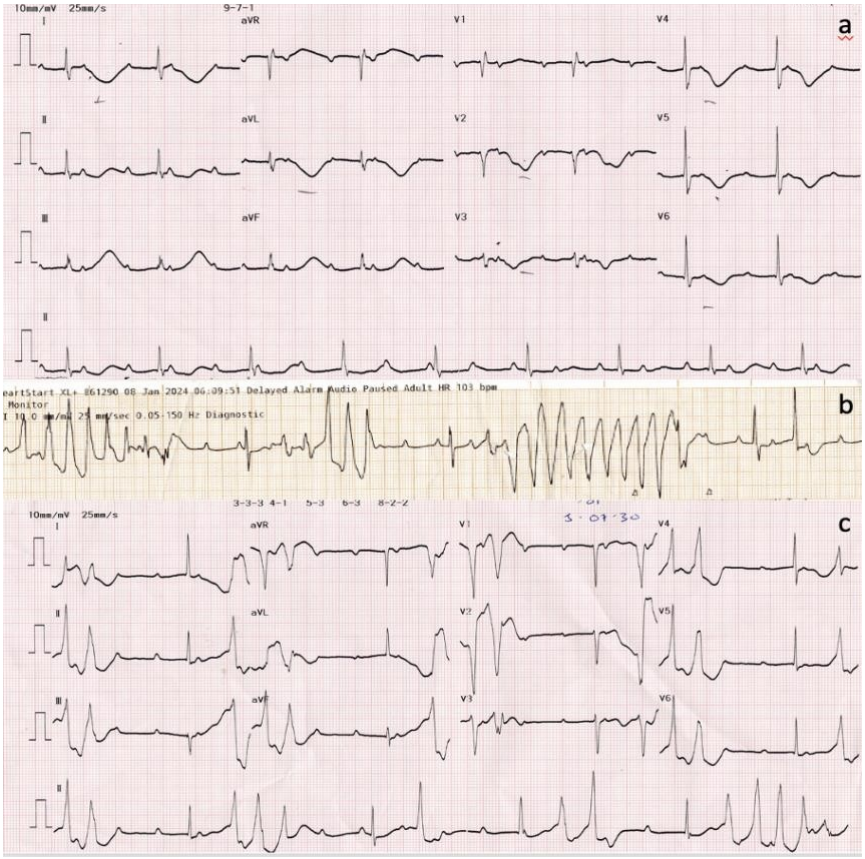

Figure 2. Electrocardiography image from the secondary referral hospital revealed (a) complete heart block, T inversion in I, aVL, V2-V6, and prolonged QT interval (QT 616 ms/QTc 578 ms) in the emergency room, (b) the presence of non-sustained multifocal ventricular tachycardia during the first episode of cardiac arrest, and (c) the presence of TAVB with polymorphic triplet premature ventricular contraction just before the patient was transported to the hospital.

she experienced multiple cardiac arrests with pulseless ventricular tachycardia and ventricular fibrillation in our Emergency Room. After stopping amiodarone, CPR, and defibrillation according to ACLS guidelines, the patient was resuscitated, and a return of spontaneous circulation (ROSC) was observed in the patient. Therefore, urgent revascularization was conducted. Coronary angiography revealed the presence of chronic total occlusion of the left anterior descending artery (LAD) osteal branch, 80% stenosis in mid left circumflex artery (LCx), and dominant right coronary artery (RCA). Therefore, stenting with drug eluting stent (DES) was conducted in LAD. Echocardiography revealed left atrial and left ventricle dilation, with mildly reduced ejection fraction (43%) and grade II diastolic dysfunction, as well as MR and TR mild.

On the 2nd day of ICCU care, she reported that her shortness of breath improved, but Torsades de Pointes (TdP) was observed in the patient at 7:00 pm (**Figure 3**). During TdP was observed, she reported no symptoms, but the monitored heart rate was around 65-70 bpm. Therefore, magnesium sulfate injection was administered during TdP under ACLS protocol. Electrolyte examination revealed normal sodium (137 mEq/L) and potassium (3.8 mEq/L). Despite normal electrolyte examination, ventricular paced rhythm with prolonged QT interval was observed in her ECG examination the following day (**Figure 4a**). Treatment re-assessment was conducted to avoid administering drugs that prolonged QT interval. Her symptoms gradually improved and 9th day after revascularization her electrocardiogram showed 2:1 beats consistent with 2nd degree AV-block Mobitz II with prolonged QT interval (**Figure 4b**).

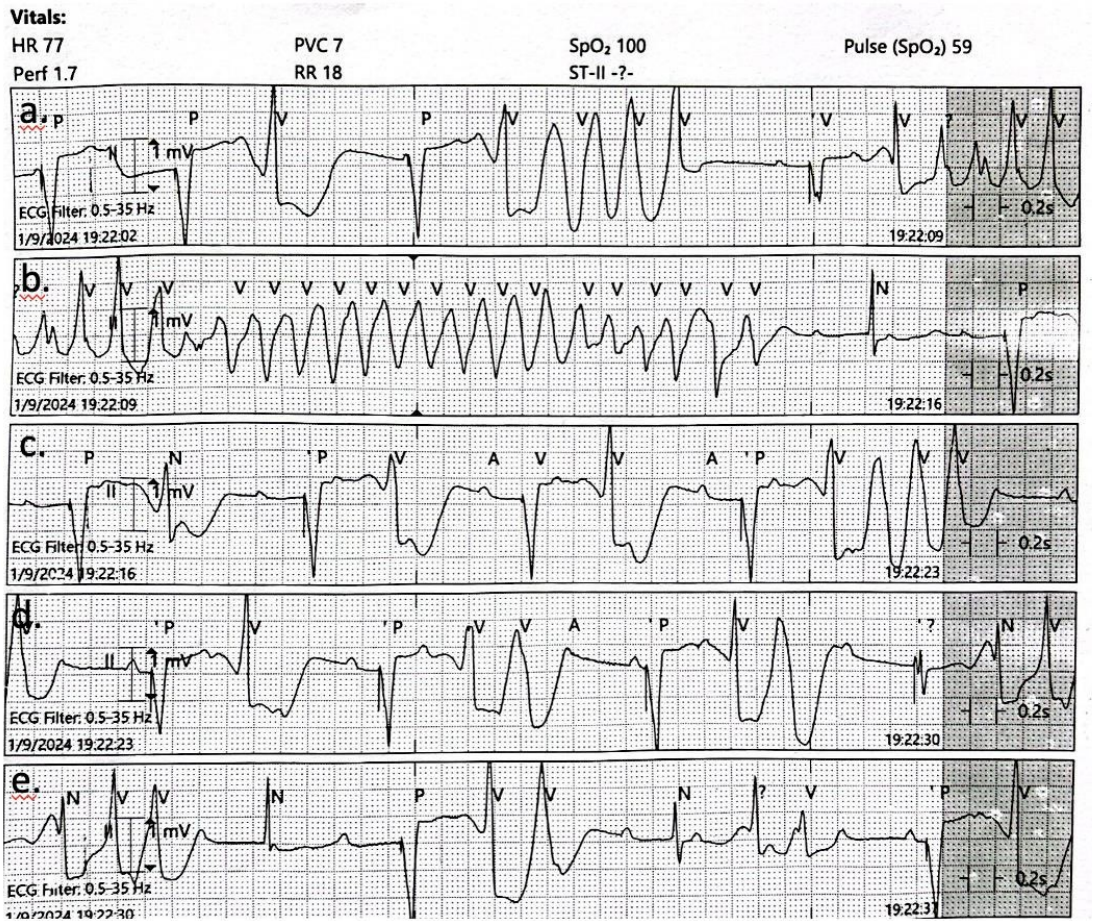

Figure 3. Ventricular arrhythmia recorded on patients on 2nd day after urgent revascularization with non-sustained ventricular tachycardia (a), Torsades de Pointes episode (b) with ventricular paced rhythm with long QT interval observed premature ventricle contraction triplet formation (c), and premature ventricle contraction couplet (d,e).

Evaluation of the possibility of congenital QT syndrome with LQTS diagnostic criteria was conducted. According to the Schwartz diagnostic criteria, her probability of LQTS was "high probability" (Schwartz Score: 8).[17] Based on her family history, clinical manifestation, and the probability of LQTS score, double-chamber pacemaker implantation instead of ICD was conducted on the patient. After pacemaker implantation, her QTc interval was markedly decreased (**Figure 5**).

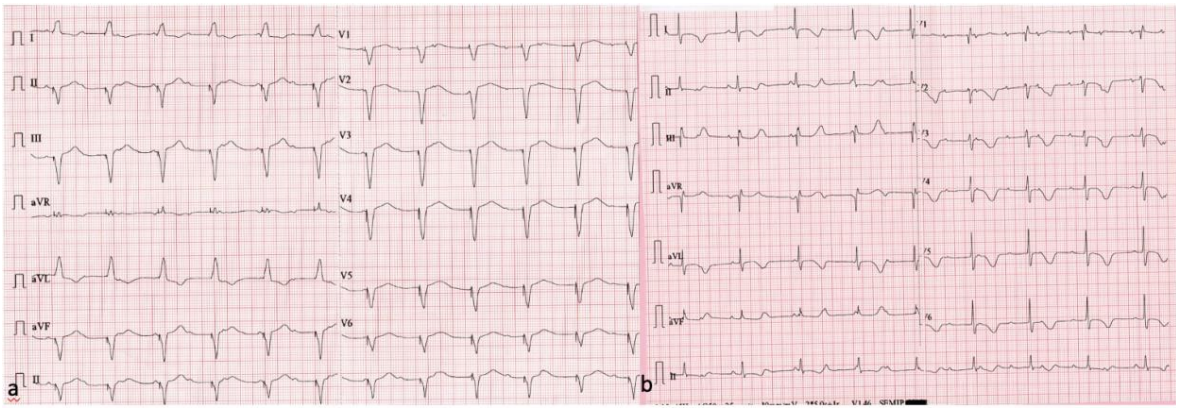

Figure 4. (a) Electrocardiogram after TdP episode showed ventricular paced rhythm with prolonged QT interval (QT 434 ms/QTc 501 ms). (b) Electrocardiogram of the patient on the 9th day after revascularization showed a two-to-one AV block with prolonged QT interval (QT 540 ms/QTc 511 ms).

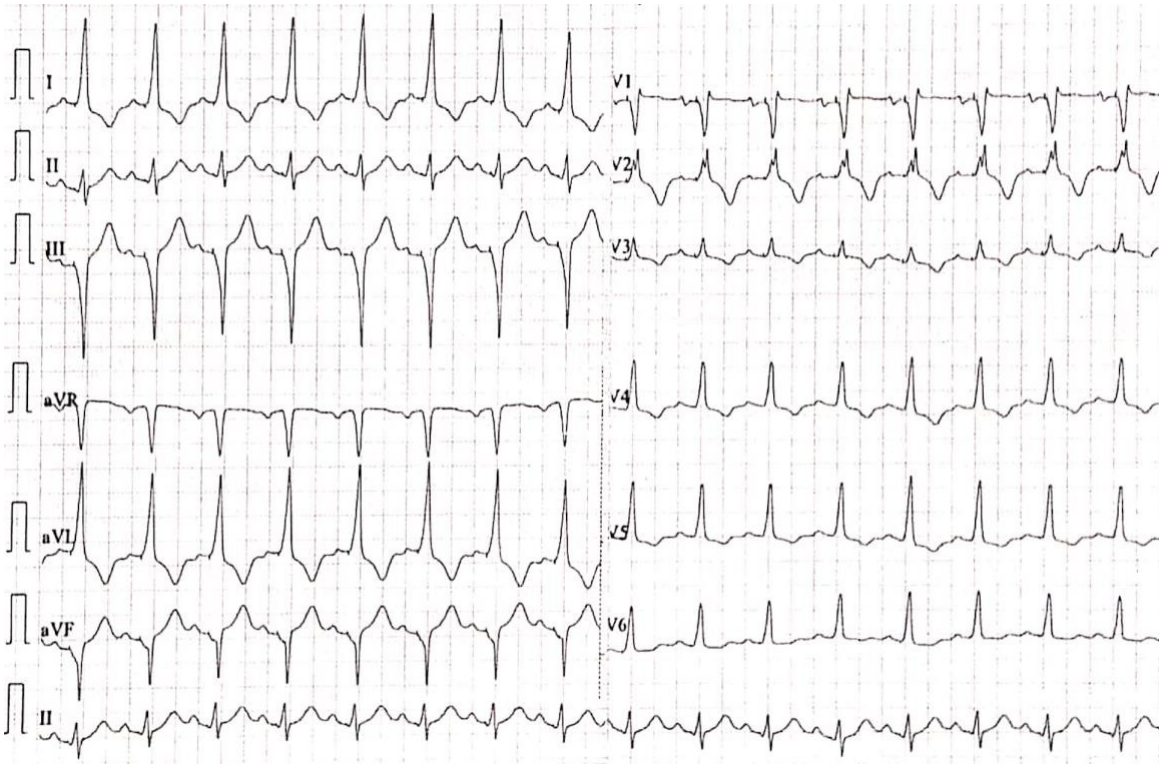

Figure 5. Electrocardiogram after double-chamber pacemaker implantation showed atrial sensed, ventricular paced rhythm with rate 100 bpm, with T inversion in V2-V6 and decreased QT interval (QT 380/QTc 464 ms).

DISCUSSION

The prevalence of LQTS is approximately 1:2000, though it was reported in the literature that its prevalence might vary from 1:5000 to 1:20.000.[18] Long QT Syndrome has been reported to have a wide range of clinical manifestations, from sudden cardiac death, early episodes of the ventricle arrhythmia to asymptomatic and might occur at a later age.[15] Previous case reports also reported that patients with congenital LQTS at a later age could experience ventricular arrhythmia due to myocardial infarction.[19] However, in this case report, the ventricular arrhythmia experienced by the patient was less likely due to myocardial infarction since the culprit lesion in this case report was different than that of the previous case's report (LAD vs RCA), the exacerbation timing in which more likely due to administering of drug which prolonged QT interval (amiodarone), and supported by the persistence of 2:1 AV block with prolonged QT interval observed until 7th day after revascularization (Figure 4). Therefore, the NSTEMI in this patient was considered a coexistence finding and the LQTS is the underlying pathology of the ventricular arrhythmia.

Schwartz's score was reported as a quick assessment tool to assess the probability of LQTS. Genetic examination in patients with a high probability of LQTS in Schwartz score should be conducted. Multiple genetic mutations have been reported in congenital LQTS according to its phenotype such as KCNQ1, HERG (KCNH2), SCN5A, etc.[17,20] However, a genetic examination of this patient was not conducted due to resource limitations and it was ineffective since the patient arrived at our intensive care with NSTEMI and frequent cardiac arrest. The patient was diagnosed with LQTS based on the latest consensus in which several clinical components are necessary such as the presence of QT interval ≥480 ms, with clinical symptoms, and high probability in Schwartz score.[21] Quick assessment and therapy were the utmost priority in this patient since she was referred to in critical condition.

Long QT syndrome has been reported to have many genotypes according to the genetic mutation involved, but the most common genotypes reported were LQTS 1 and LQTS 2.[20] Defining the possibility of LQTS subtype is pivotal to narrow the target gene to be evaluated in the genetic examination. In the clinical setting, differences in the setting of arrhythmia from history taking and ECG analysis were important to narrow the patient's LQTS subtype diagnosis, especially in health facilities with limited resources (**Table 1**).[22] In this case, differences in the setting of arrhythmia from history taking and ECG analysis were sufficient to determine the possibility of which LQTS subtype occurred in the patient (**Table 1**).[22] Congenital LQTS-1 subtype was diagnosed in this case due to her family history, the nature of syncope's onset and no pause observed in EKG during arrhythmia episode (**Figure 1**).

Treatment strategies for both congenital and acquired LQTS is to reduce risk of SCD. This can be achieved with: (1) avoid prescribing QT-prolonging drugs, (2) early detection and prevention of electrolyte abnormalities, as

Table 1. Common forms of LQTS Subtype.[22]

Variable	Genetic mutation		
	LQTS-1	LQTS-2	LQTS-3
Disease-associated gene	KCNQ1	KCNH2	SCN5A
In vitro effect	Decreased I_{Ks}	Decreased I_{Kr}	Increased plateau I_{Na}
Setting of arrhythmia	Emotional or physical stress, swimming, noise	Emotional or physical stress, sudden loud noise	Rest, sleep
Typical resting ECG	Broad T wave	Low-amplitude Twave with notching	Low isoelectric ST segment
ECG at the onset of arrhythmia	No pause	Pause	Not Established
QT change with exercise	Failure to shorten	Normal	Supranormal
QT shortening with mexiletine	No	No	Yes
Clinical response to beta-blockers	Yes	Less than LQTS1 response	Uncertain

well as (3) giving patients proper information about LQTS and the importance of avoiding its triggering factors. Furthermore, the role of long-acting non-selective beta-blockers in reducing the risk of malignant arrhythmia in LQTS has been reported in case reports and guidelines.21,23 Though beta-blocker has been reported to have no impact in QT interval, it is effective in LQTS-1 due to its adrenergic dependence.23 In this case, the clinical presentation of LQTS was complicated with NSTEMI. Thus, the treatment strategy was to treat the NSTEMI and reduce the malignant arrhythmia episode with special attention to avoid the usage of drugs which might prolong her QT interval such as amiodarone. However, we refrained from using beta-blockers in this case due to bradycardia (55-57 bpm). The prolonged QT interval persisted until the patient was discharged from hospital. Thus, to minimize the risk of SCD, an Implantable Cardioverter Defibrillator (ICD) implantation was proposed for this case.

Implantable Cardioverter Defibrillator is a mechanical device in which its' benefits have been reported in LQTS patients particularly those who survived cardiac arrest, therefore since the patient's clinical manifestation involving recurring cardiac arrests and her probability of survival is >1 year, its implantation was considered.[21,24] Therefore, ICD implantation's aim in this patient is for secondary prevention of SCD. Because of its high cost as its main drawback, double-chamber pacemaker implantation was conducted instead of ICD. In this case, pacemaker implantation was considered rare due to ICDs providing all of the pacemaker function, but pacemaker was reported to be advantageous in several clinical scenarios such as LQTS and catecholamine-induced TdP, neonates, and small infants with LQTS, LQTS patients with symptomatic bradycardia, low risk of ventricular arrhythmia, or other scenarios where ICD implantation is not preferred.[25] Her QT interval decreased remarkably after double-chamber pacemaker implantation and beta-blocker therapy, therefore lowering the risk of cardiac arrest due to ventricular arrhythmia. She was then discharged with education regarding her condition and advised to avoid medication which can prolong QT interval.

CONCLUSION

Long QT Syndrome is a serious medical condition that has been reported to have a wide variety of clinical symptoms, ranging from asymptomatic to sudden cardiac death due to malignant ventricular arrhythmia. Any prolonged QT interval in electrocardiogram should be assessed thoroughly by a physician to lower the risk of ventricular arrhythmia by choosing drugs that have no impact on QT interval. The usage of a double-chamber pacemaker can be an alternative in LQTS patients where ICD implantation is not preferred.

COMPETING INTEREST

The authors declare that there is no conflict of competing interest regarding the publication of this article.

INFORMED CONSENT

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

AUTHOR CONTRIBUTION

MY and HG contributed to writing the manuscript and being the investigator in this case report. MY contributed as a decision-maker in this case and edited the manuscript. MY contributed to drafting as well as editing the manuscript.

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