



Case Report

Landiolol suppression of electrical storm of torsades de pointes in patients with congenital long-QT syndrome type 2 and myocardial ischemia

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ABSTRACT

A 76-year-old man who had been diagnosed with long-QT syndrome type 2 had frequent syncopal attacks. The electrocardiogram was monitored, and frequent torsades de pointes (TdP) was detected despite administration of conventional medications: oral propranolol, verapamil, intravenous magnesium sulfate, verapamil, and lidocaine. In contrast, 2 μ g/kg/min landiolol could completely suppress TdP. Subsequently, an implantable cardioverter defibrillator was placed, and he was diagnosed with silent myocardial ischemia using myocardial perfusion scintigraphy and coronary angiography. This is the first case report wherein landiolol effectively suppressed TdP due to long-QT syndrome with silent myocardial ischemia.

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1. Introduction

Landiolol, an ultra-short-acting, β 1-supersensitive intravenous β -adrenergic blocker, is effective for controlling rapid heart rate in patients with atrial fibrillation or flutter (AF/AFL) with LV dysfunction [1] and immediate recurrence of AF after radiofrequency catheter ablation [2]. Landiolol is applicable not only for atrial tachyarrhythmias, but also for some life-threatening ventricular tachyarrhythmias [3,4].

Congenital long-QT syndrome (LQTS) is characterized by QT prolongation on electrocardiogram (ECG) and polymorphic ventricular tachycardia named torsades de pointes (TdP), resulting in syncope or sudden cardiac death [5]. In long-QT type 2 (LQT2), β -blockers can prevent TdP in almost 60%–70% of the patients; however, some experience an electrical storm of TdP even after receiving a full of medications. Here, we report a case of LQT2 with an electrical storm of TdP due to a silent myocardial ischemia, wherein landiolol suppressed the arrhythmias.

2. Case report

A 76-year-old man had syncopal attacks with remarkable QT interval prolongation (QT > 600 ms) since he was 62 years old. Along with the LQT on ECG, a *KCNH2* mutation (e.g., 7 c.1930 G > T p.V644F) was identified using genetic tests, a mutation also present in his son, grandson, and granddaughter, all were diagnosed with LQT on ECG (Supplemental Figure); thus, he was diagnosed with LQT2. Subsequently, he was administered propranolol (30 mg/day) and verapamil (120 mg/day); however, he was admitted to our hospital because of repetitive syncopal attacks and convulsions. ECG at admission showed a QT prolongation (Fig. 1A), but laboratory results were within normal limits (serum [K⁺] level = 4 mEq/l). ECG monitoring after admission showed frequent TdP (Fig. 1B), and intravenous administration of magnesium sulfate (2 g), verapamil (5 mg), lidocaine (50 mg), and serum [K⁺] correction was unable to suppress TdP. Although infusion of 1 μ g/kg/min landiolol did not have an effect, a concentration of 2 μ g/kg/min was able to completely suppress frequent TdP without significant change of the QT-interval (Fig. 1B, C). Landiolol did not change the blood pressure, but the heart rate slightly reduced (minimum, 53 beats per minute [bpm]); therefore, we performed temporary pacing at 80 bpm. No arrhythmias occurred after landiolol administration and pacing; thus, landiolol was gradually

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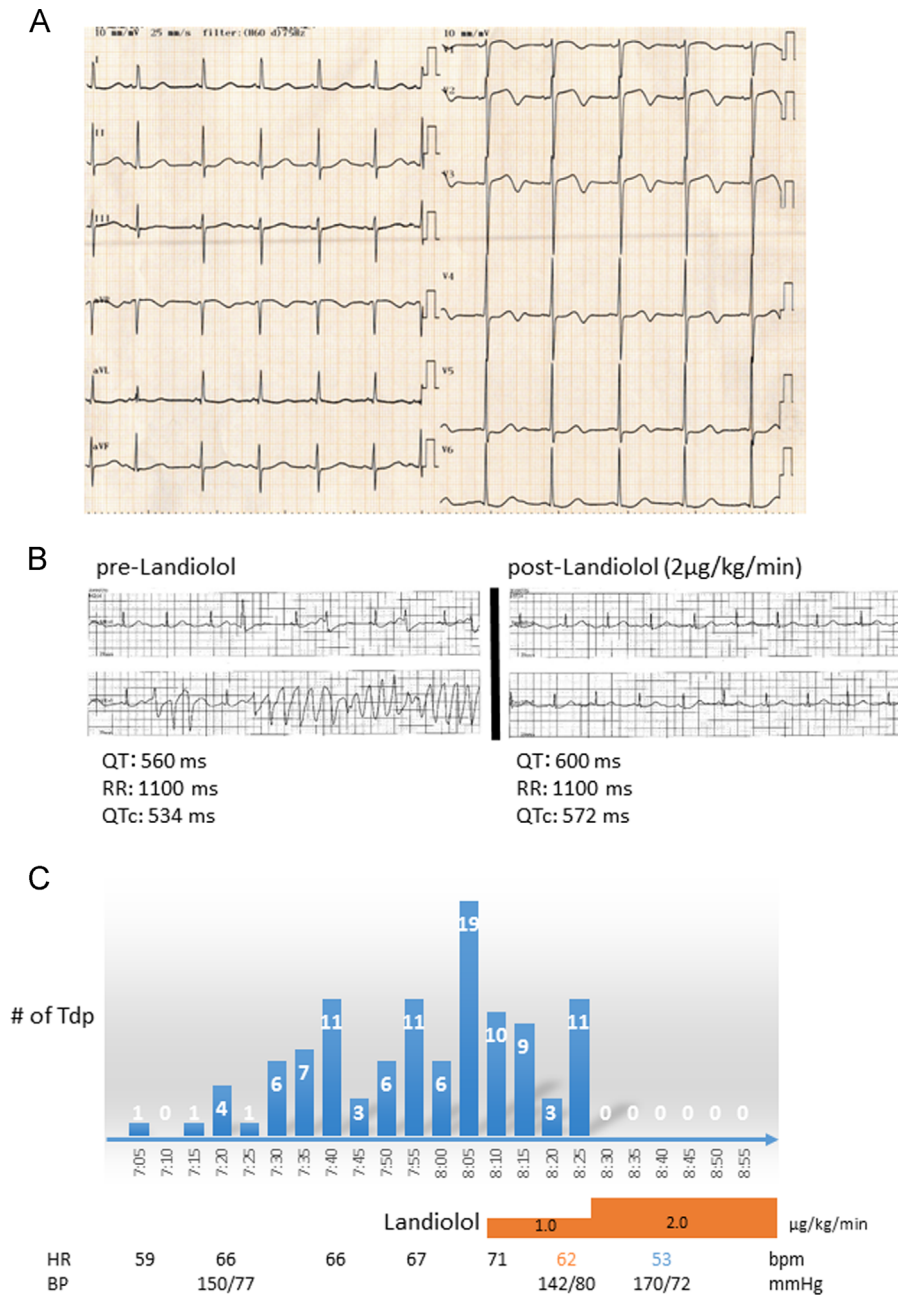


Fig. 1. A: 12-lead ECG on admission, RR=840 ms, QT=560 ms, QTc=608 ms. B: ECG monitoring before and after landiolol therapy. HR=heart rate, BP=blood pressure.

tapered off and replaced with 2.5 mg/day bisoprolol. Landiolol was stopped on the 4th day, and an implantable cardioverter defibrillator (ICD) was placed (AAI-DDDR: 80–120 bpm).

Cardiac echocardiography revealed a significantly reduced left ventricular (LV) contraction (LVEF: 20%–25%), myocardial perfusion scintigraphy showed a perfusion redistribution in the infero-septum and antero-septum area of the LV (Fig. 2A, arrow), and coronary angiography revealed 90% stenosis at #6 in the left anterior descending (LAD) artery and 75% stenosis at #1 and #4 PD in the right coronary artery (RCA) (Fig. 2B), which were consistent with the ischemic area. Percutaneous coronary intervention was performed in both LAD and RCA regions. After one-year follow-up, LVEF was normalized (> 50%). Atrial pacing with 2.5 mg/day bisoprolol shortened the QT (QTc) interval to 422 (484) ms, and no arrhythmic event occurred.

3. Discussion

Landiolol is considered to be useful not only for atrial tachyarrhythmias [1,2], but also for ventricular tachyarrhythmias [3,4]; however, evidence for the effect of landiolol for TdP in LQTS is limited. Most of the LQTS-related cardiac events, such as syncope and TdP, occur at a younger age, but some experience events at the middle or elderly age due to some additional triggers, such as bradycardia, hypokalemia, and drugs. In this case, silent myocardial ischemia and reduced LV contraction may increase arrhythmogenicity by increased Ca^{2+} leakage from the ryanodine receptor. Furthermore, the failing heart and myocardial ischemia may increase and/or decrease action potential duration (APD) by changing several ion channel functions, whereas conduction velocity in the ischemic border area is reduced; thus, increased

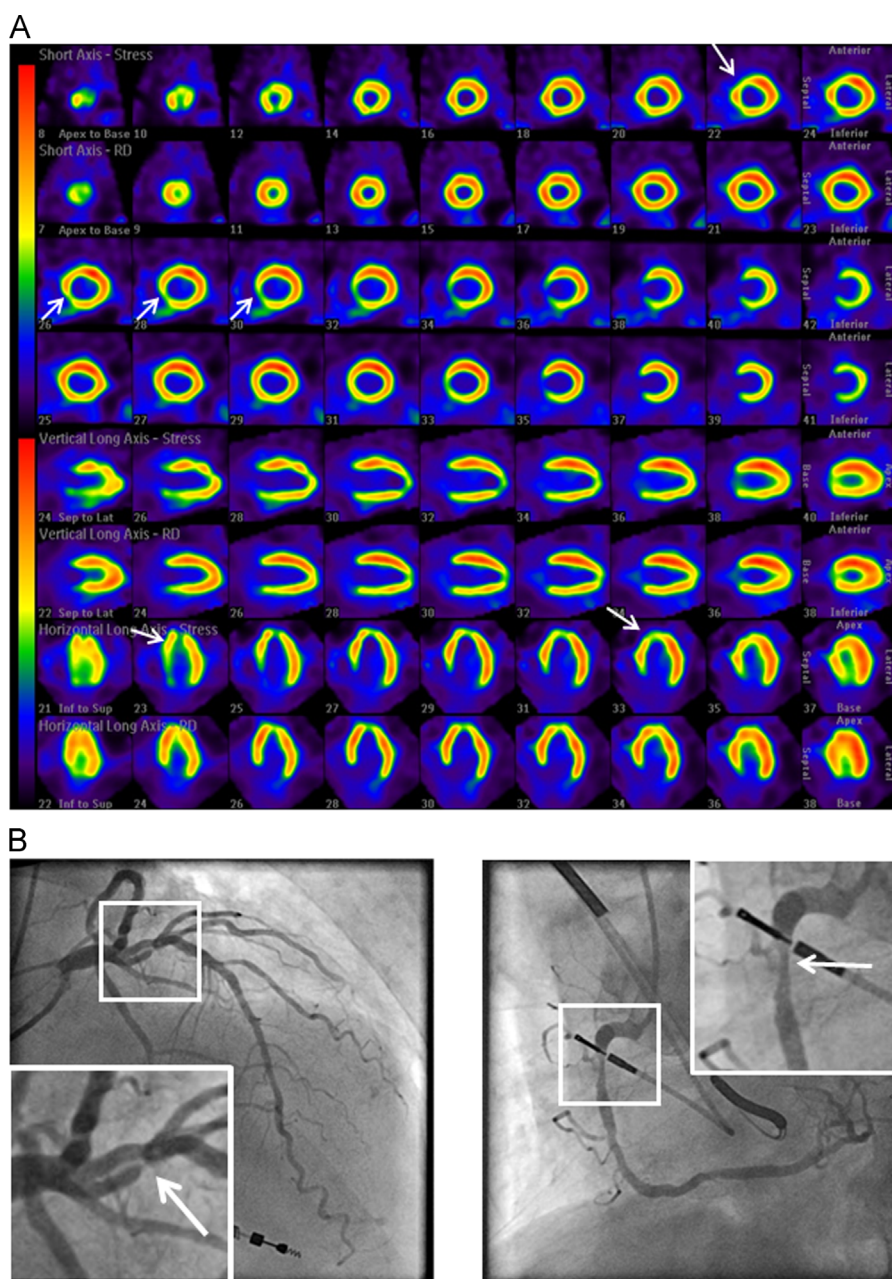


Fig. 2. Myocardial ischemia detected by myocardial perfusion imaging using Tl-201:74MBq scintigraphy (A), and coronary angiography for LAD (left) and RCA (right) (B).

dispersion of APD and conduction delay worsen the substrate of reentrant arrhythmias.

Beta-blockers regulate phosphorylation of Ca^{2+} handling proteins by not increasing the intracellular $[\text{Ca}^{2+}]$, resulting in suppression of early afterdepolarization, a trigger of lethal ventricular arrhythmias, without changing the QT interval. Low-dose landiolol may directly inhibit Ca^{2+} transient alternans and Ca^{2+} leakage by suppression of RyR2 hyper-phosphorylation [6]. Thus, landiolol might play an important role, not only as a β 1-blocker, but also by having a direct effect on RyR2 and diastolic Ca^{2+} leakage, resulting in suppressed TdP in this case. However, β -blockers also suppress sinus node function, which may induce bradycardia that might often aggravate TdP in LQT2. Therefore, temporary pacing or pacing from ICD could suppress bradycardia and shorten the QTc interval (from 533 to 484 ms) and prevent sudden cardiac death.

Based on the 2012 ACCF/AHA/HRS guidelines for device-based therapy of cardiac rhythm abnormalities [7], ICD therapy is not indicated for patients with a completely reversible disorder in the absence of structural heart disease. Furthermore, the 2014 EHRA/HRS/APHRS Expert Consensus on Ventricular Arrhythmias [8] recommended a wearable defibrillator for re-evaluation of LVEF after 90 days of revascularization. In patients with LVEF > 35%, ICD implantation is not necessary, but patients may have a benefit only under medical treatment. Thus, in this case, we should have used a wearable defibrillator for 3 months and re-evaluated the indications of ICD.

However, this patient was diagnosed not only with a coronary arterial disease, but also with LQT2. This *KCNH2*-V644F mutation is located in segment 6 (S6) of the *KCNH2* (HERG) channel, indicating a higher risk of cardiac events because of the S5-pore-S6 lesion compared with other non-pore lesions [9,10]. Although revascularization

could perfectly normalize coronary perfusion and LVEF, a risk for LQTS still existed. He has also a significant family history, with his son, grandson, and granddaughter having the same *KCNH2* mutation and repetitive syncope due to TdP even after beta-blocker medications. Thus, ICD has already been indicated for his son and grandson. Based on the 2012 JCS guideline for diagnosis and management of patients with long-QT and Brugada syndromes [11] and the 2013 h/EHRA/APHRS Expert Consensus Statement on the Diagnosis and Management of patients with Inherited Primary Arrhythmic Syndromes [12], ICD indication for patients with LQT with repetitive syncope even after adequate beta blocker therapy is class IIa. In contrast, this patient had been syncope-free for > 14 years under medical treatment until the events described in this report; thus, indication for ICD in this patient was only class IIb.

Conflict of interest

Takeshi Aiba has received consulting fees from Ono Pharmaceutical. The other authors declare no conflict of interest related to this study.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at <http://dx.doi.org/10.1016/j.joa.2017.05.007>.

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