

Suppression of cardiac memory–related severe form of torsades de pointes by landiolol in a patient with congenital long QT syndrome type 2



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Introduction

Although earlier studies reported the benefit of antibradycardia pacing in patients with recurrent syncope or cardiac arrest, ventricular pacing without implantable cardioverter-defibrillator (ICD) implantation is associated with a significant risk of recurrent sudden cardiac arrest and death in patients with long QT syndrome (LQTS).¹ Cardiac memory is usually a benign phenomenon of persistent T-wave abnormalities appearing during normal ventricular activation after a period of altered ventricular activation.² Few case reports have suggested the proarrhythmic effect of cardiac memory in patients with congenital LQTS.³ The proarrhythmic effect of cardiac memory and the efficacy of beta-blockers in suppressing torsades de pointes (TdP) due to cardiac memory remain unclear. We present a case of a 41-year-old patient with LQT type 2 who had cardiac memory–related Tdp that was suppressed by landiolol.

Case report

A 41-year-old woman had been experiencing episodes of syncope with remarkable QT interval prolongation since the age of 18 years (Figure 1). Her father and paternal grandmother had QT prolongation and her paternal grandmother had TdP requiring a shock from an automated external defibrillator at the age of 75 years (Supplemental Figures 1 and 2). Her paternal great-grandfather died suddenly at age 47 years. Genetic testing in the 41-year-old case patient revealed a mutation in *KCNH2* (c.3103delC). The previous study identified the mutation in the cohort of patients with LQTS as pathogenic.⁴ Therefore she was diagnosed with LQTS type 2 (LQT2). At the age of 24 years, a single-chamber ICD was implanted for primary prevention. At that time,

KEY TEACHING POINTS

- Cardiac memory in changing pacing mode may cause marked longer QTc and torsades de pointes (TdP) in patients with long QT syndrome (LQTS).
- In patients with congenital LQTS, we may have to consider atrial lead implantation for avoiding proarrhythmic effects related to ventricular pacing.
- Landiolol may be worth considering as the drug of choice for the treatment of Tdp in congenital LQTS.

the dual-chamber ICD was not yet available. Although she was treated with bisoprolol (3.75 mg/day) and mexiletine (300 mg/day), she had occasional episodes of syncope and ICD shocks due to the Tdp or ventricular fibrillation during exertion. Because of increasing sinus bradycardia, the percentage of ventricular pacing increased from 70% to 100% by age 38 years. Her slight fatigue and mildly elevated brain natriuretic peptide levels were of concern, as was the percentage of ventricular pacing, and resulted in an upgrade to a dual-chamber ICD with the addition of an atrial lead, discouraging ventricular pacing. Although electrocardiography revealed atrial paced rhythm with long QT interval and T waves discordant with the QRS axis, she had no episodes of syncope or ICD therapy (QT, 480 ms; QTc, 519 ms).

Three years later she had an atrial lead fracture. The atrial lead revision was planned for 4 months later and the device reprogrammed to VVI. However, after 2 months she had an appropriate shock for TdP. Electrocardiography revealed right ventricular apical paced rhythm with markedly longer QTc than that at 2 months earlier (from 539 ms to 647 ms) and giant T waves concordant with the QRS axis (Supplemental Figure 3). Her plasma potassium (4.3 mmol/L), magnesium (2.0 mg/dL), and corrected calcium levels (2.2 mmol/L) were within their normal ranges. Her echocardiogram at the time was normal with normal systolic left ventricular function. Reimplantation of the atrial lead was

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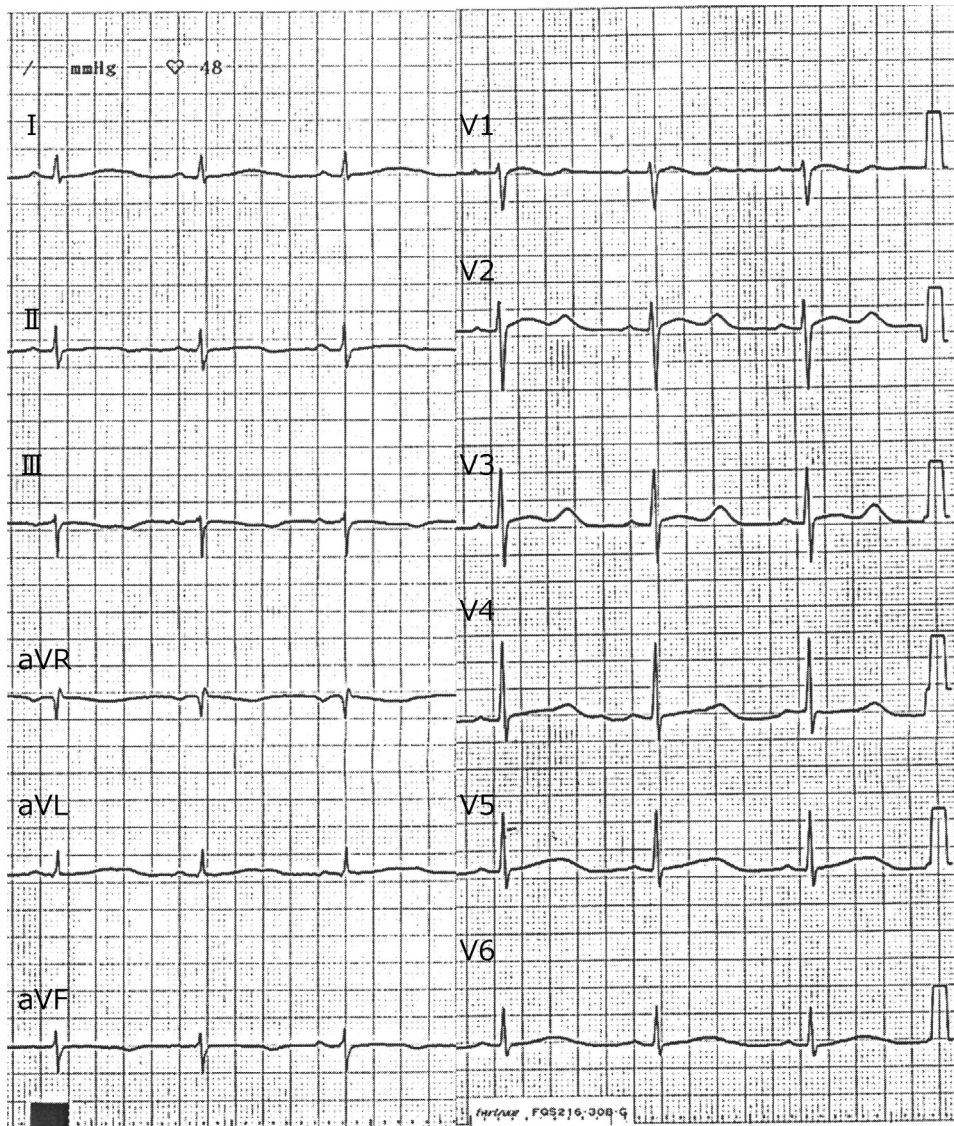


Figure 1 Baseline electrocardiogram at the age of 18 years (heart rate, 48 beats/min; QT, 600 ms; QTc, 537 ms).

planned at 10 days after admission. Programming the device with a higher pacing rate (VVI 90 ppm) suppressed the Tdp in the interim. She underwent atrial lead reimplantation under general anesthesia with propofol and dexmedetomidine, and the pacing mode was reprogrammed to dual chamber (DDD 70 ppm) just after the procedure. Around 4 hours after the procedure, she had a Tdp electrical storm (Figure 2). The electrolytes were normal (plasma potassium level was 4.1 mmol/L, magnesium 1.7 mg/dL, and corrected calcium levels 2.2 mmol/L). Device programming with a higher pacing rate (DDD 90 ppm) and intravenous administration of magnesium sulfate failed to suppress the Tdp. Subsequently, administration of landiolol was started at 3 $\mu\text{g}/\text{kg}/\text{min}$ and increased to 6 $\mu\text{g}/\text{kg}/\text{min}$, which completely suppressed the Tdp without changing the QT interval (Figure 3A). Around 1 week later, she continued the bisoprolol therapy (3.75 mg/day) with tapering and discontinuation of the landiolol therapy, and had no further episodes of Tdp. After 9 months

without ventricular pacing, the giant negative T waves returned to their stationary state (Figure 3B).

Discussion

Although cardiac memory is usually a benign phenomenon, this case suggests that caution should be used when changing pacing mode in patients with LQTS. Only 1 previous report described the proarrhythmic effect of cardiac memory in a patient with congenital LQTS.³ One of the ion channel changes of cardiac memory has been previously reported to be a transcriptionally induced reduction in potassium (IKr) channels.⁵ Di Cori and colleagues³ suggested that cardiac memory might be potentially risky in patients with a baseline IKr loss of function. Repolarization abnormalities might be revealed owing to cardiac memory after changing the pacing mode, so the effect of cardiac memory in changing the pacing mode, especially in patients with LQT2, must be considered.

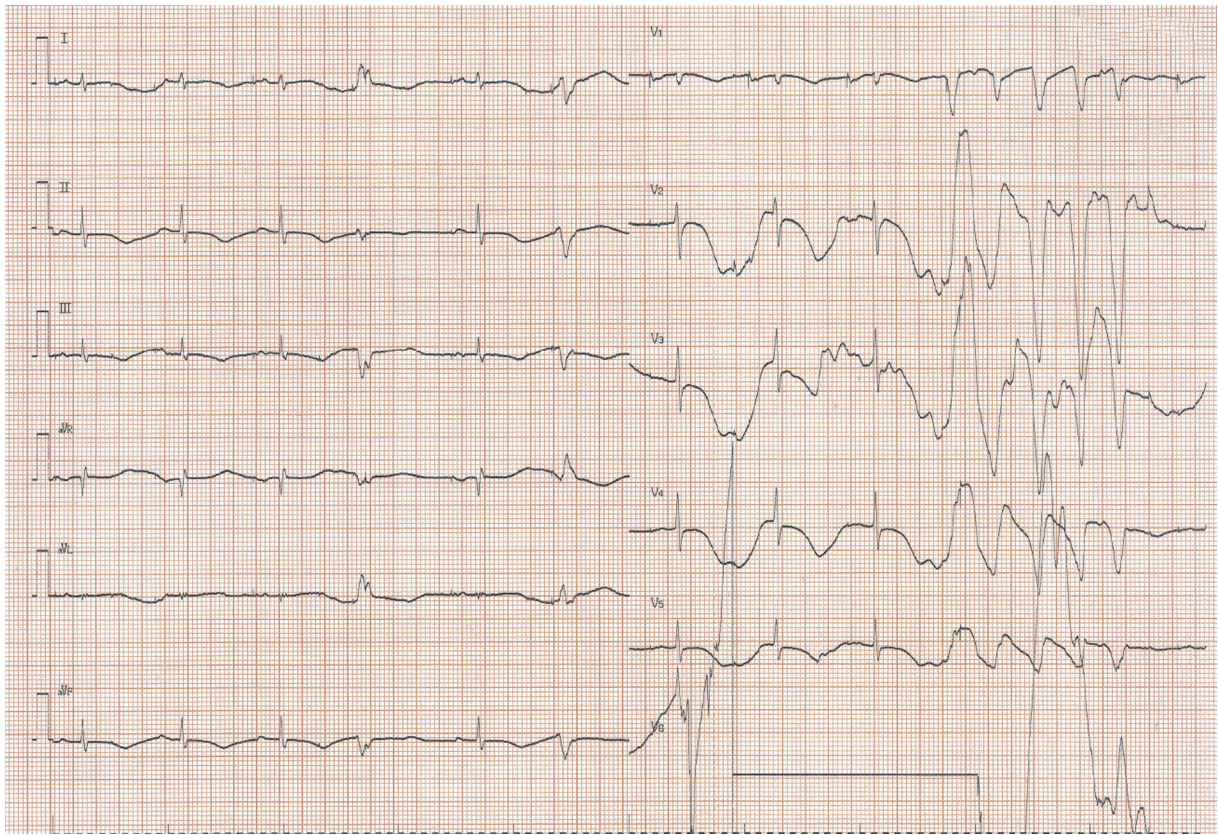


Figure 2 Twelve-lead electrocardiogram obtained during the torsades de pointes electrical storm, after reprogramming to the DDD mode. The premature ventricular contraction on the T wave induced polymorphic ventricular tachycardia.

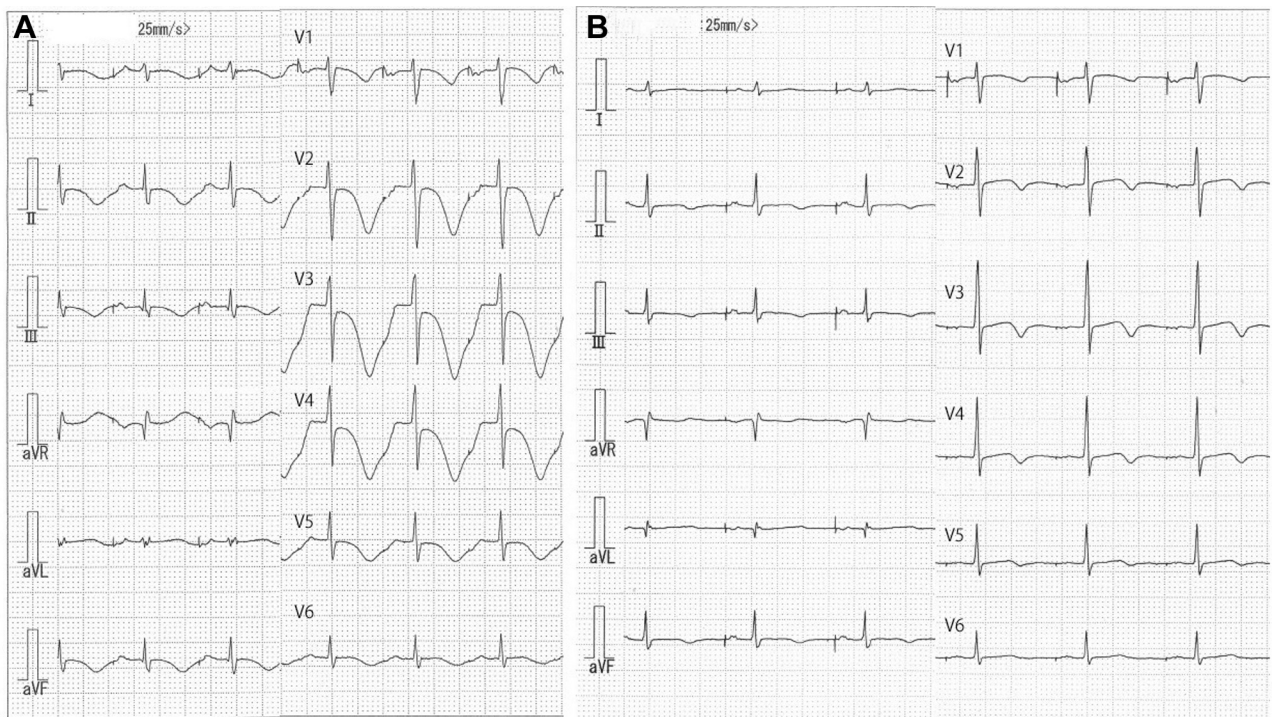


Figure 3 Twelve-lead electrocardiograms in the DDD mode: **A:** after administration of landiolol; **B:** 9 months after the torsades de pointes (Tdp) storm. Administration of landiolol had no effect to the prolongation of the QTc interval, but suppressed the Tdp electrical storm.

This is the first reported case of suppression of cardiac memory–related Tdp with landiolol in a patient with LQT2. Beta-blockers have been shown to either decrease or prevent an increase in transmural dispersion of repolarization in response to strong sympathetic stimulation, a mechanism that contributes to its antiarrhythmic effect.⁶ Although only few reports have indicated the efficacy of landiolol for Tdp in congenital LQTS, beta-blockers have a preventive effect on Tdp in patients with congenital LQT1 or LQT2.⁷ Moreover, a previous study suggested that low-dose landiolol inhibits Ca²⁺ leakage through the ryanodine receptor (RyR2) by selectively suppressing RyR2 phosphorylation. Landiolol might be superior to other beta-blockers owing to its direct effects on RyR2 and diastolic Ca²⁺ leakage.⁸ Landiolol may be worth considering as the drug of choice for the treatment of Tdp in congenital LQTS, especially in the acute phase, because landiolol is ultra-short-acting, unlike other beta-blockers such as propranolol.

Eighteen months after the atrial lead reimplantation, the patient required ventricular lead reimplantation owing to lead fracture. Under the same conditions as the previous procedure of atrial lead implantation (ie, general anesthesia with propofol and dexmedetomidine, oral drugs, and baseline lower pacing rate), she underwent the ventricular lead implantation. However, the QT interval was stable during the procedure during the atrial pacing. This case is important because it demonstrates the effect of cardiac memory through the difference in clinical course between the atrial and ventricular lead reimplantations.

Several studies have reported not all beta-blockers are equal for risk reduction in long QT.⁹ For LQT2, nadolol was reported to show superior efficacy. Therefore, the use of nadolol in this patient from the onset may have made the disease less malignant.¹⁰

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Appendix Supplementary data

Supplementary data associated with this article can be found in the online version at <https://doi.org/10.1016/j.hrcr.2020.03.013>.

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