CASE REPORT

Replacement of an Implantable Cardioverter-Defibrillator (ICD) with a New Standard Subcutaneous ICD System in a Patient with Jervell and Lange-Nielsen Syndrome

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Summary

A 7-year-old female suffering from syncope attacks and deafness was genetically diagnosed with Jervell and Lange-Nielsen syndrome (JLNS). A transvenous-designed shock lead and implantable cardioverter-defibrillator (ICD) were atypically implanted subcutaneously, because the patient’s body was small. Six years after implantation, we confirmed the patient’s eligibility for a subcutaneous ICD (S-ICD) based on electrocardiogram screening. The implanted ICD system was replaced with a new standard S-ICD system. Implantation of the S-ICD may be considered a reliable and safe option in young patients with JLNS, even if their electrocardiograms show remarkable prolongation of the QT interval and T-wave alternans.

Key words: Long QT syndrome, KCNQ1

The implantable cardioverter-defibrillator (ICD) is an established treatment and is increasingly recommended in children with congenital heart diseases or inherited arrhythmia syndromes.1,2) An entirely subcutaneous ICD (S-ICD) has recently become available worldwide. However, it is unknown whether the S-ICD operates reliably and safely in children with Jervell and Lange-Nielsen syndrome (JLNS), which is characterized by significant prolongation of the QT interval and abnormal T-wave morphology.

Here, we present the first case of JLNS who underwent replacement of an atypically subcutaneously implanted transvenous-designed ICD (TV-ICD) system with the new standard S-ICD system.

Case Report

A 7-year-old female was admitted because of syncope attacks that occurred during exercise. Her resting electrocardiogram (ECG) showed remarkable prolongation of the QT interval and T-wave alternans (Figure 1A). Her QT and corrected QT (QTc) intervals were 530 and 686 ms, respectively. She had no abnormal physical examination except for severe bilateral sensorineural hearing loss. The patient’s echocardiography and biochemical tests, including serum electrolyte levels, were all normal. After the patient was clinically diagnosed with congenital long QT syndrome (LQTS), she was started on the β-blocker propranolol, and the dose was subsequently increased to 90 mg/day.

A genetic analysis of our patient identified two different mutations in the potassium voltage-gated channel subfamily Q member 1 gene (KCNQ1, NM_000218.2) as follows: c.502G>A (p.Gly168Arg) and c.115G>T (p.Glu39Ter) (Figure 1B and C). Both mutations were previously reported as causative of JLNS.3,4) No mutation was found in other LQTS-causative genes (KCNH2, SCN5A, KCNE1, KCNE2, or KCNJ2). None of the family members had hearing loss, syncope episodes, or a cardiac event. However, her two grandmothers, mother, and younger sister had slight prolongation of the QT/QTc intervals on ECGs (Figure 1D, a-b and d-f). Genetic screening revealed a heterozygous p.Gly168Arg mutation in her father, and a heterozygous p.Glu39Ter mutation was found in her mother and sister (Figure 1D). Therefore, this proband was a compound heterozygote for the two KCNQ1 mutations and diagnosed with JLNS.

Implantation of an ICD was planned in our patient because the prognosis of JLNS patients is very poor due to ventricular tachyarrhythmias, even if they are treated with β-blocker.5) Since her body was still small (height, 121 cm; weight, 22 kg), implantation of a typical TV-ICD system could have created trouble during the growth process. The so-called entirely S-ICD system was not yet available for use in Japan (2011). Hence, a TV-designed shock lead was placed in a subcutaneous position on her

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back and connected to an abdominally implanted ICD generator. An epicardial pacing/sensing lead was attached to the right ventricle wall with a small epigastric incision (Figure 2A and B). A delivery of 25 J was able to defibrillate ventricular fibrillation (VF), which was induced by the ICD generator. After an increase in the patient’s weight was noted during follow-up, the treatment was switched from propranolol to atenolol (50 mg/day). No ventricular tachycardia or VF episodes were observed during the 6 years after ICD implantation. Furthermore, no appropriate or inappropriate ICD shocks occurred during that time. Because of the ICD battery depletion, an exchange of the ICD generator was necessary within one year. As the patient grew to 156 cm tall and 46 kg (weight), chest radiographs revealed that the subcutaneous shock lead had shifted to her left lateral chest and the heart no longer fell centrally within the shock vector among the ICD generator and two defibrillation shock coils (Figure 2C and D). It was thus suspected that appropriate ICD defibrillation could not be provided. After informed consent, her parents chose a revision operation with the new standard S-ICD system (EMBLEM™; Boston Scientific Co. St. Paul, MN, USA), which became available in Japan in 2017. The interrogation data obtained from the implanted ICD showed limited backup pacing (0% pacing rate) over 6 years of follow-up. According to a 24-hour Holter ECG, the patient’s sinus rhythm was maintained at 58-108 bpm, and there was never bradycardia, a long pause, or pacing beat. For surface ECG screening for the S-ICD, the Boston Scientific Co. ECG screening tool was used to determine eligibility for the S-ICD.5) We analyzed ECG recordings simulating the following three sensing vectors of the S-ICD: primary, secondary, and alternate vectors (Figure 3). In spite of QT prolongation, all of the sensing vectors of the screening ECG in the supine and standing positions were eligible for S-ICD. As the intensity of exercise increased, the amplitude of the T-waves grew large, the QT/QTc intervals extended more than 500/600 ms, and the QT ends overlapped with the next P-waves. Thus, the QRS-T complexes in the primary and alternate vectors became ineligible for S-ICD (Figure 3). However, a serial QRS-T complex in at least one vector (the secondary vector) fit the preimplant screening criteria. Under general anesthesia, the subcutaneously implanted shock lead was pulled out via an incision line at the left lateral chest. After the abnormally implanted ICD generator was removed, a new S-ICD system was implanted with the 2-incision technique6) (the preceding incisions at her left lateral chest and a small incision next to the xiphoid process; Figure 2E and F). Her QT intervals were markedly extended during an exercise test after implantation of the S-ICD, but no problems were detected in any of the three sensing vectors. In the managements with exercise restriction and medication, S-ICD discharge for ventricular tachyarrhythmia and S-ICD sensing difficulty have not been observed.
**Figure 2.** Posterior-anterior and lateral view chest radiographs. A transvenous-designed shock lead and implantable cardioverter-defibrillator (ICD) were implanted subcutaneously when the patient was 7 years old (A, B). The ICD system, which was placed subcutaneously in the patient until she reached 12 years old (C, D), was replaced with a new subcutaneous ICD (E, F).

**Figure 3.** Electrocardiograms of the three vectors during the exercise screening test for the subcutaneous implantable cardioverter-defibrillator. Part of the T-waves in the primary and alternate vectors protruded out of the criteria region (arrows).
over a 24-month follow-up period.

Discussion

LQTS is a hereditary arrhythmia disease caused by mutations in genes encoding cardiac ion channels, including the potassium channel \( \text{KCNQ1} \). Autosomal-dominant inheritance is usually observed in LQTS, but autosomal-recessive inheritance can be rarely observed in LQTS patients accompanied by sensorineural deafness; the former is Romano-Ward syndrome and the latter is JLNS. In this report, the proband was diagnosed with JLNS as a compound heterozygote for two \( \text{KCNQ1} \) mutations. JLNS is suggested to be more severe than Romano-Ward syndrome. Schwartz, et al., reported that cardiac events occurred in 51\% of JLNS patients who were prescribed \( \beta \)-blocker therapy; more than half of the events were life-threatening. Therefore, these data suggest that ICD implantation was necessary in our JLNS patient with syncope episode.

Nonetheless, our patient’s body was still small at the time of the first operation and was expected to grow. Implanting a TV lead in a small body often results in problems not only at the time of the implantation but also after growth. Additionally, an ICD system which does not involve intravascular or intracardiac space is preferable when considering possible device removal in the future. Because the S-IDC system was not available for use in Japan at that time, we performed an operation using a TV lead that was placed subcutaneously (as described by Stephenson, et al.). Six years after the operation, the configuration of the ICD generator and defibrillation coils shifted away from the heart during somatic growth. Kaltman, et al. reported that an 8-year-old patient with LQTS had an appropriate successful shock for VF by the abdominal TV-ICD generator with subcutaneous finger arrays. However, 2 years later, an ICD discharge failed to defibrillate the VF, largely because of the increased weight of this patient (from 33 to 44 kg). At an appropriate time, it is necessary to exchange the initial ICD configuration with the conventional TV-ICD system or the current S-IDC system. S-IDC has become commercially available worldwide, and a few S-IDC implantations in children have been reported. The S-IDC generator has a higher power output (80 J) for defibrillation than the TV-ICD generator (40 J). However, the S-IDC generator is larger than that of the TV-ICD; thus, skin erosion on the axillary pocket may occur in a small body. The smallest patient previously described receiving the S-IDC was 13.5 kg, but the non-standard method of S-IDC implantation was used. McLeod, et al. described two children who weighed 34 and 35 kg, respectively, who were treated safely with common implantation of S-IDC. Therefore, the timing of replacement to the standard S-IDC in our patient, whose weight was 46 kg, was suitable in consideration of her body size.

We considered additional two points prior to S-IDC implantation in our patient with JLNS. One was whether the S-IDC system could avoid T-wave oversensing when the QT intervals were markedly prolonged and when the T-wave became prominent during exercise. It was reported that young patients with primary electrical diseases were at an increased risk of inappropriate shocks; 25\% of the patients received inappropriate shocks due to T-wave oversensing by S-ICDs. We can predict the sensing abnormality of the S-IDC by preoperative ECG screening. In the preoperative screening test of our patient, the QRS-T complexes became ineligible based on the criteria in two of the three vectors during exercise. However, no abnormal sense was found in any of the three sensing vectors after S-IDC implantation. It is likely that the criteria for S-IDC screening will have sufficient margins not to cause sensing trouble. Nonetheless, in children with JLNS who show a morphology change in the QT or T-wave by sympathetic stimulation, preoperative ECG screening during exercise is particularly important. Second, it was important to confirm that there was no bradycardia in the recipient of the S-IDC which had no pacing lead. Long R-R intervals may facilitate prolongation of the QT intervals and, as a result, ventricular tachyarrhythmias (e.g., torsade de pointes and VF). Fruh, et al. reported that atrial pacing by a pacemaker or TV-ICD could prevent life-threatening tachyarrhythmias in JLNS children during long-term follow-up. Because our patient did not have any bradycardia, fortu- nately, we chose S-IDC rather than TV-ICD implantation. This is the first report, to our knowledge, to describe the implantation of an entirely subcutaneous ICD system in a JLNS patient. Our patient was eligible for S-IDC implantation based on cautious preoperative screening and did not have any difficulties after S-IDC implantation. Implantation of the current S-IDC system may be considered a safe and satisfying option in young patients with LQTS, including JLNS, even if they show significant QT prolongation and T-wave alternans.

Disclosures

Conflicts of interest: The authors have no conflict of interest to disclose.

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