Isolated Non-Compaction of the Ventricular Myocardium Associated With Long QT Syndrome
—— A Report of 2 Cases ——

Kiyoshi Ogawa, MD; Yoshihiro Nakamura, MD; Kazuhiro Terano, MD; Tatsuya Ando, MD; Takashi Hishitani, MD; Kenji Hoshino, MD

Isolated non-compaction of the ventricular myocardium (INCVM) is a relatively newly defined clinicopathologic entity. INCVM is clinically accompanied by depressed ventricular function, arrhythmias, and systemic embolization. We report two cases of INCVM with long QT syndrome (LQTS). In both cases the QT interval was over 0.55 s with episodes of torsades de pointes, and prominent ventricular trabeculations and deep intertrabecular recesses were detected by 2-dimensional echocardiography. Both cases had the KCNH2 mutation. To the best of our knowledge, this is the first report investigating INCVM with LQTS. (Circ J 2009; 73: 2169–2172)

Key Words: Cardiomyopathy; Long QT syndrome; Myocardium

Isolated non-compaction of the ventricular myocardium (INCVM) is a relatively newly defined disorder of the endomyocardium characterized by prominent ventricular trabeculations and deep intertrabecular recesses. Clinical manifestations include a depressed left ventricular (LV) function, ventricular arrhythmia, and systemic embolization. INCVM has been reported to be associated with several electrocardiographic changes such as ST depression and flat or negative T waves, bundle branch block, and Wolff-Parkinson-White (WPW) syndrome. To the best of our knowledge, a long QT interval has not been reported on previously.

We report 2 cases of INCVM with long QT syndrome (LQTS).

Case Report

Patient 1
The patient was a boy aged 1 day old, who had no family history of sudden death or arrhythmia, and electrocardiograms (ECGs) of his parents showed no abnormality. He was born normally in a maternity hospital at the gestational age of 38 weeks. The Apgar score was 8 points at 1 min.

When he was admitted to our hospital, his condition was severe. His respiratory rate was 60 breaths/min and heart rate was 130 beats/min. His systolic blood pressure was 60 mmHg. His head and face was edematous. No heart murmur was audible. Hepatosplenomegaly was not recognized.

Blood gas analysis indicated severe metabolic acidosis; the base excess was –9.2 mmol/L and pH was 7.305. Both AST and CK were elevated. In particular, CK was as high as 2,830 IU/L. Mild hypocalcemia (7.8 mg/dl) was present and other serum electrolytes including magnesium (2.3 mg/dl) were within normal limits. A physical examination and laboratory data showed marked stress during gestation or circulatory shock of an unknown cause. A chest X-ray revealed cardiomegaly, and the cardiothoracic ratio (CTR) was 68%.

The ECG on admission showed left bundle branch block (LBBB) and a long QT time (Figure 1). An echocardiography showed that the ventricular myocardium was thickened and that the endocardial trabeculation was prominent at the apex, especially in the right ventricle. There were no congenital heart defects, and the ejection fraction of the left ventricle (LVEF) was 10%.

A few minutes after supplemental calcium infusion, polymorphic ventricular tachycardia (VT) with torsades de pointes and sustained VT were detected on an ECG monitor (Figure 1). Lidocaine 1 mg/kg was infused initially, but it was ineffective. Even though cardioversion was performed several times, it had only a transient effect on resolving polymorphic and sustained VT. After 1 mmol/kg MgSO4 was administered, sustained VT was resolved, and MgSO4 was infused at a rate of 0.1 mmol·kg⁻¹·h⁻¹ to prevent sustained VT with torsades de pointes.

After VT was resolved, the LVEF was gradually improved to 60% and the CTR based on a chest X-ray was normalized at the age of 4 days. An ECG showed a narrow QRS pattern, not a bundle branch block, and QTc was still prolonged to 0.59 s at the age of 5 days. Twenty-four-hour Holter ECG at the age of 9 days showed an intermittent narrow QRS in the majority of LBBB patterns. The hypertrophic trabeculation mostly at the apex of ventricles became gradually more apparent in the LV endocardium (Figure 2). The thickness of the LV posterior wall was 4 mm. There was no thrombus in the apical intertrabecular spaces. These findings are con-
consistent with the echocardiographic criteria of INCVM proposed by Oechslin et al.\textsuperscript{5} Both INVCN and prolonged QT intervals are still seen in the boy, who is now 7 years old (Figure 3). Genetic analysis revealed a KCNH2 (LQT2) missense mutation (A561V).

**Patient 2**

A 5-year-old boy presented to our hospital with symptoms of generalized tonic convulsion during sleep. An electroencephalogram (EEG) demonstrated spikes and sharp waves in the right posterior brain regions. He was diagnosed with epilepsy and started treatment with phenobarbital. Three months later, a repeat EEG showed no abnormal spikes, and a prolonged QT interval was suspected based on a ECG recorded in the EEG. Twelve-lead ECG revealed that the QTc time was 0.59 s (Figure 4). T wave alternans and torsades de pointes were detected by a repeat 24-h Holter ECG. The QT interval remained unchanged after the discontinuation of phenobarbital. The CTR by chest X-ray was 42%. A prominent trabecular meshwork of the apical, lateral, and inferior wall of the left ventricle was observed by 2-dimensional echocardiography (Figure 2). There were no congenital heart defects, and the LVEF was 74%. The serum electrolytes were within normal limits (calcium, 9.0 mg/dl; magnesium, 2.0 mg/dl). Genetic analysis revealed the mutant KCNH2 (D501N).

Written informed consent was obtained from the parents of each patient, as stipulated in the Declaration of Helsinki.

**Discussion**

Isolated non-compaction of the ventricular myocardium is characterized by the presence of prominent ventricular trabeculations and deep intertrabecular recesses within the...
left ventricle, sometimes also affecting the right ventricle and interventricular septum. Because of an increasing awareness and interest in this disorder, and advances in echocardiographic imaging, reported cases have increased. Ritter et al showed that the prevalence of INCVM is 0.05% in all adult patients examined using transthoracic echocardiography. Therefore, INCVM might not be so rare as was initially estimated. Genetic linkage analysis of the 2 families mapped INCVM to the Xq 28 region near the locus of Barth syndrome, a genetic condition comprising dilated cardiomyopathy, skeletal myopathy, neutropenia, and a short stature. Although the etiology of INCVM has not been fully investigated, this rare disorder is thought to result from an arrest in endomyocardial morphogenesis during the embryonic period. During early embryonic life, the heart is a loose interwoven meshwork of muscle fibers. The developing myocardium gradually condenses, and the large spaces within the trabecular meshwork flatten or disappear. Kohl et al described a case where INCVM could be recognized on an echocardiographic study at 23 weeks of gestation; thus supporting the developmental hypothesis. In contrast, Bleyl et al demonstrated that echocardiographies obtained between 24–30 weeks of gestation in 3 members of a family who subsequently developed INCVM did not show the characteristic findings of INCVM. They suggested that echocardiographic changes associated with INCVM might develop postnatally, and INCVM did not result from the developmental arrest of the myocardium. The ECG of the previously reported patients with INCVM showed ST depression and flat or negative T waves, bundle branch block, WPW syndrome, and various patterns of arrhythmia. A high incidence of WPW syndrome was found in children. A long QT interval accompanied by INCVM has not yet been reported. LQTS occurs as an inherited or sporadic disorder, or it might be acquired. The cellular mechanism behind the lengthened QT interval recording on surface ECG is prolonged ventricular action potentials. Recent genetic studies have shown that congenital LQTS is an electrical disease caused by the mutation of genetic coding for specific ion channels.

A small number of newborns show transient long QT intervals, and the interval returns to normal within 1 year. Manoach et al showed that the ECG of newborn mice with a prolonged QT interval is similar to that of mouse embryos in the intermediate stage, while the ECG in normal newborns resembles that of the prenatal fetus. Fein et al demonstrated a good correlation between the number of undifferentiated myoblasts in the ventricular walls and typical prolongation of the QT interval in rats and mice. On the basis of these results, Manoach et al suggested that prolongation of the QT interval might be caused by the delayed or incomplete differentiation of myocardial cells. Our cases...
showed the ECG pattern and endomyocardial morphology during the embryonic period.

Recently, Shi et al reported the cardiac sodium channel mutation delQKP 1507-1509 in a family with LQT 3 and dilated cardiomyopathy.\textsuperscript{12} Although our 2 cases of LQT2 and INCVM had a different mutation of \textit{KCNH2} (A561V in the pore region, and D501N in the non-pore region), the mutation of \textit{KCNH2} might cause LQT2 and INCVM. The precise mechanism of the association between INCVM and LQT2 is unclear.

The success rate of $\beta$-blocker therapy is reported to be lower among LQT2 and LQT3 patients than among LQT1 patients. Our cases might have a higher risk of life-threatening cardiac events. Although an implantable cardioverter-defibrillator (ICD) should be considered in high-risk patients with LQTS, ICD therapy in pediatric patients involves complications such as infections, lead malfunctions, inappropriate shocks, and psychological effects. Careful follow up is needed.

We reported 2 cases of INCVM with LQTS. We propose that in the differential diagnosis of LQTS, INCVM should also be considered.

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References