CASE REPORT

Improvement in Dyssynchrony with Pharmacological Ablation of Right-Sided Accessory Pathway-Induced Cardiomyopathy in Infants

Mai Sekine, MD, Satoshi Masutani, MD, Tomohiko Imamura, MD, Yoichi Iwamoto, MD, Shota Muraji, MD, Shigeki Yoshida, MD, Hirotaka Ishido, MD and Naokata Sumitomo, MD

Summary

Right-sided accessory pathways in patients with Wolff-Parkinson-White (WPW) syndrome may cause cardiac dyssynchrony and dilated cardiomyopathy, with a characteristic septal shape, irrespective of any supraventricular tachycardia episodes. We report on two infants (13 and 5 months), whose right-sided accessory pathway-induced dilated cardiomyopathy was successfully treated by flecainide for the first time. After the flecainide administration, an abnormal aneurysmal dilation of the basal interventricular septum was almost restored to normal, and the decreased ejection fraction recovered. Flecainide use may be an important therapeutic option for this entity to avoid catheter ablation during infancy.

Key words: Wolff-Parkinson-White syndrome, Na channel blocker, Secondary dilated cardiomyopathy, Preexcitation

Wolff-Parkinson-White (WPW) syndrome is characterized by a manifest atrio-ventricular accessory pathway that might cause paroxysmal supraventricular tachycardia (PSVT) or sudden death due to rapid ventricular conduction of atrial fibrillation (pseudo ventricular tachycardia) that degenerates into ventricular fibrillation. Some patients with right-sided accessory pathways may develop left ventricular dyssynchrony and cardiac dysfunction, which may result in secondary dilated cardiomyopathy (DCM) irrespective of the existence of PSVT episodes.1-4 We here report on two infants whose accessory pathway-induced DCM was successfully treated by flecainide.

Case Report

Patient 1: A male infant (13 months, 8.3 kg) was referred to our center for evaluation of a heart murmur that was detected during a vaccination. His past, developmental, and family histories were unremarkable. His general condition, including his oral intake, was fine. There were no abnormalities of the vital signs or physical symptoms suggesting heart failure at rest. However, when crying, sweating occurred, and a systolic ejection murmur (Levine II/VI) at the second left sternal border was audible. The chest X-ray showed an enlarged heart shadow with a cardiothoracic ratio of 0.61 and mild pulmonary congestion. The electrocardiogram exhibited sinus tachycardia with a heart rate of 192 and a delta wave due to a right anterior accessory pathway (Figure 1A). An echocardiogram demonstrated mild to moderate tricuspid and mitral regurgitation. In addition, aneurysmal dilation, thinning of the basal intraventricular septum (Figure 1D), and a reduced ejection fraction (EF, 36%) were noted. A mild right ventricular outflow tract obstruction (3 m/second) seemed to be the origin of his heart murmur. Radial strain imaging, using 2-dimensional speckle tracking echocardiography in the parasternal short axis view at the papillary muscle level, revealed apparent dysynchrony: the anterior and septal wall contractions faster than the inferior and lateral wall (Figure 2A).

There was no evidence to indicate a general or metabolic disorder potentially causing dilated cardiomyopathy. The infant's detailed history indicated no suspected episodes of PSVT, such as sudden abrupt irritability or pale face. Consequently, the right anterior accessory pathway-induced DCM was most likely to account for his condition. Considering his preserved general condition, we decided to start medical therapy to inhibit the accessory pathway conduction.

An intravenous flecainide (2 mg/kg) injection over 10 minutes successfully eliminated the delta waves (Figure 1B, C). We then started 4.8 mg/kg of oral flecainide. After flecainide administration and its titration (9.4 mg/kg), his condition remained healthy, and the abnormal aneurysmal dilation of the basal interventricular septum was almost...
restored to normal (Figure 1D). His ejection fraction recovered month-by-month (EF 43% at two months of treatment). Two months after the flecainide treatment, we started carvedilol in addition to flecainide. Four months after the flecainide, his EF increased to 49%, and the left ventricular dyssynchrony improved (Figure 2B).

**Patient 2:** A female infant (5 months, 6.3 kg) was referred to our center for evaluation and treatment of decreased feeding and heart murmur. Her past, developmental, and family histories were unremarkable except for a late preterm birth (gestational age of 35 weeks and 6 days and birth body weight of 1946 g). Her oral intake and amount of urine decreased. Her heart rate was 120 bpm and respiratory rate 40 per minute. A systolic regurgitant murmur (Levine II/VI) was audible at the apex. A chest X-ray revealed an enlarged heart shadow with a cardiothoracic ratio of 0.52. An electrocardiogram exhibited delta waves due to a right anterior accessory pathway (Figure 3A). An echocardiogram demonstrated mild mitral regurgitation. In addition, a distinctive dilation, thinning of the basal intraventricular septum, distinct interventricular septum bulging (Figure 3D), reduced EF, 23.7%, and paradoxical interventricular motion were noted (Figure 4A).

The infant’s detailed history indicated no suspected episodes of PSVT, such as sudden abrupt irritability or pale face. Consequently, right anterior accessory pathway-induced DCM was most likely to have accounted for her condition. Considering her preserved general condition, we decided to try medical therapy to inhibit the accessory pathway conduction.

To confirm the acute effect of the drug, we slowly injected flecainide intravenously. When we gave her 5 mg of flecainide (0.8 mg/kg), the delta waves disappeared (Figure 3B, C). Two weeks after we started the oral flecainide (7.1 mg/kg), her distinct interventricular septum bulging almost recovered (Figure 3D), and the paradoxical interventricular motion (Figure 4A) and left ventricular dyssynchrony (Figure 4B) recovered. Her EF increased (36.7%), the cardiothoracic ratio decreased to 0.46 on the chest X-ray, and her heart murmur disappeared.

**Discussion**

To the best of our knowledge, these two infants, without a history of PSVT attacks, were the first patients reported in which their dyssynchrony caused by
Figure 2. Dyssynchrony of the left ventricular wall motion in patient 1. A: Radial strain imaging using two-dimensional speckle tracking echocardiography in the parasternal short axis view at the papillary muscle level showing apparent dyssynchrony. B: Radial strain imaging after a four-month treatment showing an improvement in the dyssynchrony. The anterior (ANT) and septal wall (inferoseptal [I-S], anteroseptal [A-S]) contracted faster than the inferior (INF) and lateral wall (inferolateral [I-L], anterolateral [A-L]).

Figure 3. Electrocardiogram and echocardiogram in patient 2. A: The electrocardiogram on admission showing positive delta waves in leads I, II, aVL, and V3 to V6, and rS pattern in V1, that may suggest a right anterior accessory pathway. B: Electrocardiogram after flecainide loading. The delta waves disappear after an injection of flecainide. C: The electrocardiogram change during the flecainide injection. The delta waves disappear during the flecainide injection. D: Morphological change before and after the flecainide therapy. Before the therapy, distinctive dilation of the basal interventricular septum was noted. The basal dilation returns almost to normal two months after the therapy.
preexcitation-induced DCM was successfully controlled by using flecainide. Accessory pathways, which induce DCM, usually exist on the right side. Right-sided accessory pathways cause an abnormal interventricular septal motion, similar to that observed in the left bundle branch block, which typically causes left ventricular dyssynchrony and dysfunction. Our two patients had right anterior accessory pathways diagnosed by characteristics including positive delta waves in leads I and II, isochronic or negative deflections in lead III, and an rS pattern in lead V1. Accessory pathway-induced DCM, in the previously reported cases and in our cases, is characterized by uneven dilation, thinning, and aneurysmal formation of the basal interventricular septum (Figures 1D, 3D), which is completely different from the morphology in typical DCM. It has been reported that the elimination or block of accessory pathway conduction by catheter ablation or amiodarone subsequently improves the cardiac function. Consequently, cardiac dyssynchrony due to an accessory pathway seems responsible for such left ventricular dilation and functional impairment in accessory pathway-induced DCM.

Although flecainide, a group Ic Na channel blocker, inhibits the accessory pathway conduction in WPW syndrome, to the best of our knowledge, there has been no report of the usefulness of flecainide for accessory pathway-induced DCM. Although flecainide use has been associated with an increase of proarrythmic events in adult patients with acute recurrent myocardial infarctions, and with an increase in cardiovascular hospitalizations in adult patients with atrial fibrillation, flecainide use has been reported effective and safe in the pediatric population even in those with a reduced EF. Nevertheless, we still have to take care when using flecainide in patients with a severely impaired cardiac function because of its negative inotropic effect. However, in infantile cases with accessory pathway-induced DCM without severe heart failure, as in our cases, we believe that cautious flecainide use should be the first therapeutic option because of the potential risk of catheter ablation and potential side effects of amiodarone.

Figure 4. Echocardiographic change before and after the flecainide therapy. A: M-mode echocardiographic change before and after the flecainide therapy. Before the therapy, paradoxical interventricular septal motion on the M-mode echocardiography in the long-axis view is noted. The interventricular septal motion is restored two weeks after the therapy. B: Radial strain imaging, using 2-dimensional speckle tracking echocardiography in the parasternal short axis view at the papillary muscle level shows apparent dyssynchrony before the flecainide (upper panel), and, consequently, the dyssynchrony disappears after the flecainide treatment.
There is also the possibility of spontaneous loss of ventricular preexcitation during the follow-up. Given the relatively high ablation risk during infancy, we can wait for the patients’ growth before catheter ablation until they are a relatively safe age and body size (e. g. 4 years, 15 kg). As a limitation of this report, there were some differences in the dosage and titration of the flecainide between the two cases, probably due to drug metabolism, but both were within the reported recommended range.

Because accessory pathway-induced DCM is rare, a multicenter prospective accumulation of cases is warranted to clarify the nature and to construct an evidence-based algorithm for this disease entity.

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References