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Brief Report

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Pharmacologic therapy with flecainide for asymptomatic Wolff–Parkinson–White syndrome in an infant with severe left ventricular dyssynchrony

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Abstract

Some asymptomatic patients with Wolff–Parkinson–White syndrome have severe left ventricular dyssynchrony and dysfunction. We describe a patient who was given a diagnosis of Wolff–Parkinson–White syndrome in infancy and had a complete response to pharmacologic therapy with flecainide. Our findings suggest that flecainide is a suitable resynchronisation therapy for such infants.

Ventricular pre-excitation through an accessory pathway causes intraventricular dyssynchrony and left ventricular dysfunction.[1–5] Catheter ablation of the accessory pathway has been recognised to be an effective therapy that improves dyssynchrony and left ventricular function in older children.[1,2] However, catheter ablation performed for any reason in low-body-weight infants carries a very high risk.[6] Although an effective pharmacological therapy for infants with dyssynchrony-induced left ventricular dysfunction caused by pre-excitation through accessory pathway is awaited, not many cases have been reported. We report the first case of an infant with pre-excitation through accessory pathway and intraventricular dyssynchrony who had a complete response to flecainide therapy.

Case report

A previously healthy 5-month-old boy, with a body weight of 6.7 kg, was referred to our hospital for a heart murmur that was diagnosed during a routine medical checkup at 4 months of age. He had a systolic murmur (Levine I/VI), gallop rhythm, and mild hepatomegaly. Although his general condition and body weight gain were good, he was quiet and sweat profusely when he cried. A 12-lead electrocardiogram revealed delta waves, suggesting the presence of ventricular pre-excitation. The vector of the delta waves suggested a right anteroseptal pathway. Echocardiography showed paradoxical septal motion with an left ventricular ejection fraction of 40%. There was left atrial and ventricular volume overload, and the left ventricular end-diastolic dimension was 30.5 mm, with a z score of 3.1. The patient was admitted and received diuretics. No supraventricular tachycardia was detected on continuous monitoring over the course of several days. We considered the main cause of left ventricular dysfunction to be pre-excitation through accessory pathway, and some form of treatment was required for the accessory pathway. Because of the low body weight (6.7 kg), catheter ablation was considered a risky procedure. We therefore decided to initially try a pharmacologic therapy. Flecainide was slowly given intravenously in a carefully monitored setting. When the dose of flecainide reached 13 mg/m^2, the delta wave on the 12-lead electrocardiogram disappeared owing to a conduction block in the accessory pathway, and the paradoxical septal motion improved on echocardiography. Flecainide remained effective for about 8 hours, and then the delta wave reappeared. There was no exacerbation of the left ventricular ejection fraction or signs of heart failure. Oral flecainide (20 mg/m^2/day) was administered, and the dose was increased. When the dose reached 40 mg/m^2/day, he was free of delta waves all day, and the gallop rhythm and heart murmur had disappeared at the time of discharge. A period of 4 months after discharge, the left ejection fraction was 67%, and intraventricular motion was completely synchronised; treatment with diuretics was discontinued. In the years ahead, we will consider catheter ablation after the body weight has increased (Figs 1 and 2).

Discussion

Dyssynchrony-associated left ventricular dysfunction secondary to ventricular pre-excitation in patients with asymptomatic Wolff–Parkinson–White syndrome has been reported in

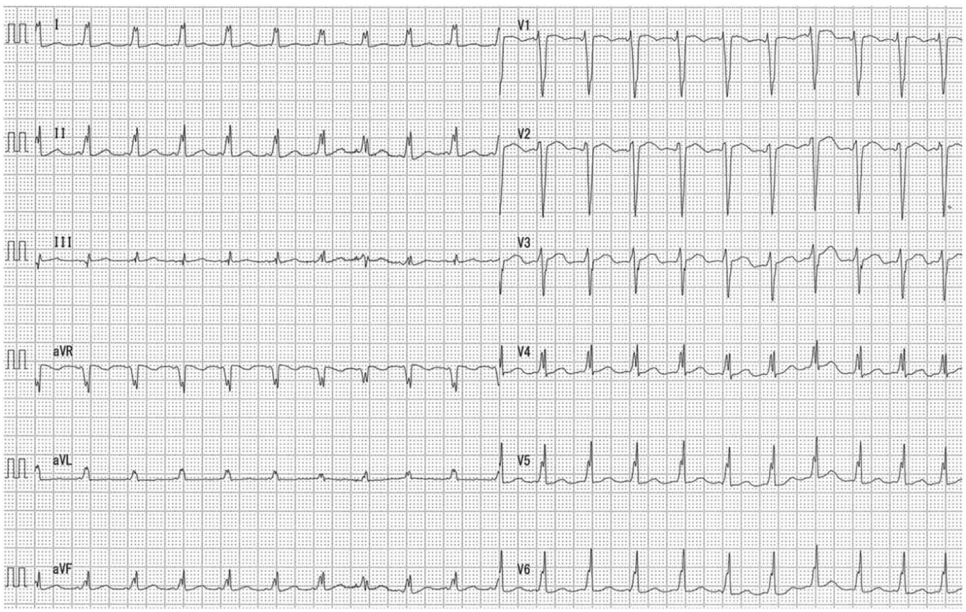

Figure 1. Electrocardiogram at the first examination, showing pre-excitation with delta waves positive in leads in I, II, aVF, V4, V5, and V6 and negative in lead III, showing a V1 rS pattern, suggesting the presence of right anteroseptal accessory pathway.

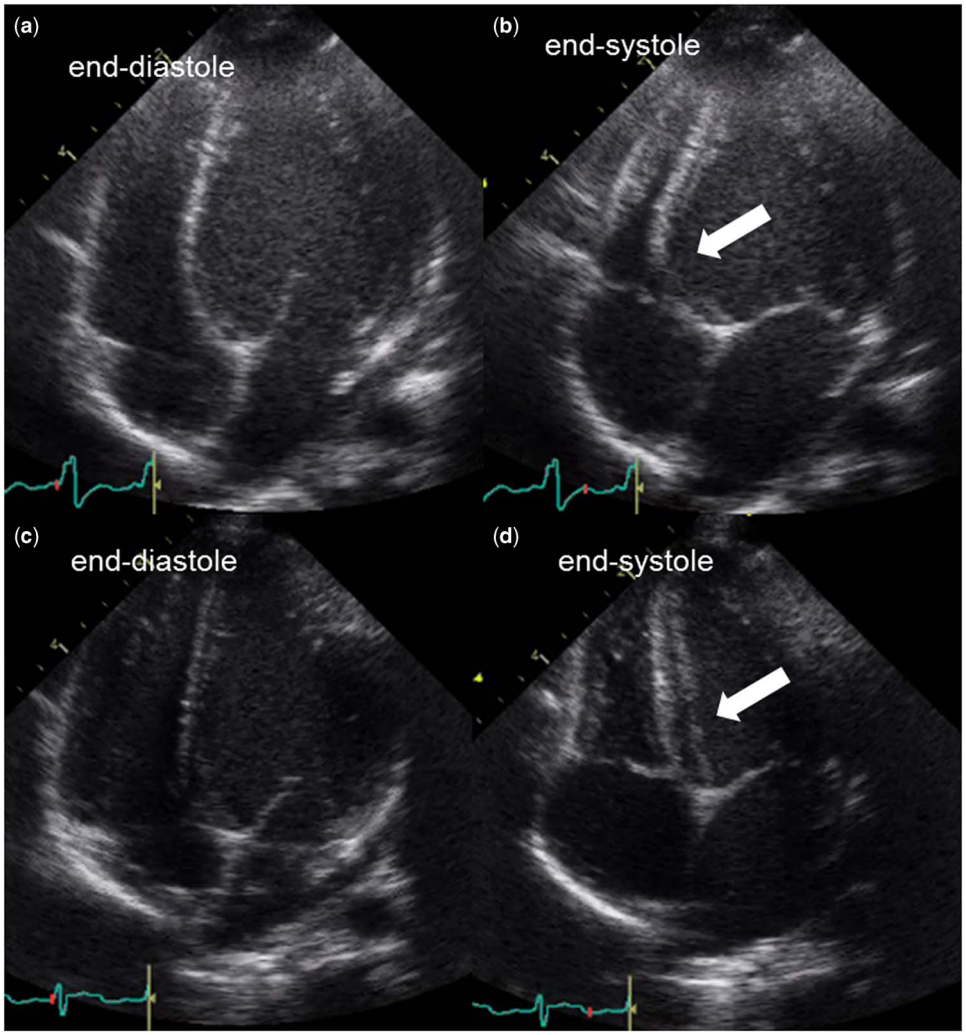

Figure 2. Echocardiographic four-chamber views (a), (b), captured at the first examination. b) Abnormal movement of the basal septum (arrow), similar to an aneurysm at end-systole. (c) and (d) 4 months after flecainide therapy, showing normalisation of septal motion.

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Table 1. Summary of reports on patients in whom asymptomatic Wolff–Parkinson–White syndrome with severe left ventricular dyssynchrony and dysfunction was diagnosed before 2 years of age.

References	Age		Resynchronisation	Course to resynchronisation	Other therapy	Recovery of LV function (months)
	Diagnosis (months)	Resynchronisation (months)				
Cadrin-Tourigny et al[4]	3.5	3.5	Amiodarone	—	Furosemide	24
	5	10	Amiodarone	LV function↓ considered HTx	Digoxin Captopril Furosemide	10
Kwon et al[2]	1	59	CA	Remain poor LV function	—	—
	5	97	CA	Remain poor LV function	Unknown	—
Peach et al[5]	15	15	Propafenone	—	—	24
Suzuki et al[7]	6	7	CA(ineffective) → Amiodarone	SVT developed Cardiac arrest	Milrinone Spironolactone Furosemide βblocker	15
Kim et al[8]	3	60 (CA was done at almost the same time)	Amiodarone (effective) → CA	Remain poor LV function SVT developed	—	—
Kwon et al[3]	day 0	1(Amiodarone) 4.5(CA)	Amiodarone (ineffective) → CA	LVDd↑ Sign of heart failure	—	—

CA = catheter ablation; HTx = heart transplantations; LV = left ventricle; LVDd = left ventricle end-diastole dimension; SVT = supraventricular tachycardia

several recent studies.[1–5] In these studies, right-sided septal accessory pathway was recognised as the main cause of left ventricular dyssynchrony.[1,2] In our patient, the vector of the delta wave on 12-lead electrocardiogram suggested involvement of a right anteroseptal pathway. To our knowledge, similar cases have rarely been diagnosed in infants, and only eight cases have been reported previously (Table 1).[2–5,7,8] In these patients, a long time elapsed between the diagnosis of left ventricular dyssynchrony and the initiation of resynchronisation therapy, such as catheter ablation and pharmacologic treatment. Some of the patients received anti-failure therapy with diuretics, beta-blockers, angiotensin-converting enzyme inhibitors, and digoxin before resynchronisation therapy began, but all patients poorly responded to treatment. Moreover, left ventricular function worsened or arrhythmias such as supraventricular tachycardia developed in some patients before the initiation of resynchronisation therapy. As previously hypothesised, the cause of left ventricular dysfunction is not only the movement of dyskinetic segments associated with a functional aneurysm but also pathological ventricular remodelling secondary to myocardial perfusion defects, changes in coronary blood flow, and regional molecular abnormalities.[9] Moreover, a causal relation between dyssynchrony-associated left ventricular dysfunction and dilated cardiomyopathy has been reported.[3,8–10] Because we considered early resynchronisation therapy essential, we wanted to start resynchronisation therapy at the same time that anti-failure medication was begun.

Previous studies have reported the effectiveness of catheter ablation for accessory pathway in older children and adults.[1,2] In contrast, reports on catheter ablation in infants are rare, and low body weight and an age of several months are associated with increased procedural and ablation risks. Pharmacologic therapy is a suitable treatment for infants, but only five cases in which pharmacologic therapy was tried have been reported. Amiodarone (five cases) [3,4,7,8] and propafenone (one case) [5] have been used, and treatment was successful in four patients given amiodarone and the patient given propafenone. We report the first case to our knowledge to successfully respond to flecainide. Similar to our case, three previously reported patients were given only pharmacologic therapy – without catheter ablation. All of these patients responded to treatment, and normal left ventricular function was completely restored within several months or several years.[4,5,7]

Flecainide has stronger negative inotropic activity, but is more effective than other sodium-channel blockers for conduction block of accessory pathway associated with Wolff–Parkinson–White syndrome in children. When we treat supraventricular tachycardia with poor responses to pharmacologic treatment with ATP or Ca channel blocker, which suppress atrio-ventricular conduction, we often use Na channel blocker such as flecainide in order to suppress accessory pathway directly. We recognise that we can use flecainide safety in a carefully monitored setting. Because of such experience that flecainide suppresses accessory pathway conduction promptly and absolutely, we considered to use it first in our case. In fact, we could safely use flecainide by performing continuous electrocardiogram monitoring and frequent echocardiographic assessment to detect exacerbations of congestive heart failure. We did not use amiodarone despite previous successful reports because of its adverse effects associated with long-term administration, such as interstitial lung disease, abnormal thyroid function, and corneal pigmentation.[10] In our patient, flecainide was the most suitable treatment not only in terms of efficacy but also safety.

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Conflicts of Interest. None.

Ethical Standards. All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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