International Journal of Arrhythmia

CASE REPORT Open Access

Accessory pathways in monozygotic twins with different clinical phenotypes: a case report

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Abstract

Background The atrioventricular reentrant tachycardia (AVRT) is the most common tachycardia associated with accessory pathways (APs). Although sporadic Wolff-Parkinson-White (WPW) syndrome has been well-described, AP occurrence in identical twins with WPW syndrome remains rarely reported.

Case presentation We report a case of 14-year-old monozygotic twin brothers referred for an electrophysiology (EP) study. Twin A presented with recurrent symptomatic narrow complex tachycardia after exercise, noted for 3 years. His 12-lead surface electrocardiogram (ECG) did not show ventricular pre-excitation. However, an orthodromic AVRT utilizing a concealed right posteroseptal AP was found and successfully ablated. AVRT did not recur 12 months after the procedure. Twin B was asymptomatic. During his medical examination for firefighter volunteerism, his 12-lead ECG showed a spontaneous ventricular pre-excitation. EP study revealed a short anterograde right midseptal AP, which was then successfully eliminated by catheter ablation. His 12-lead ECG showed no ventricular pre-excitation recurrence 12 months after the procedure.

Conclusions These identical twin brothers had a right-side AP in almost the same place but showed completely different phenotypes. This case clearly illustrates the difficulty in understanding genetic contribution in the origin of atrioventricular APs. Environmental exposure could play a role in their clinical presentations and AP electrophysiological properties.

Keywords Wolff-Parkinson-White syndrome, Accessory pathways, Atrioventricular reentrant tachycardia, Identical twins, Electrophysiology study, Catheter ablation

Background

Accessory pathways (APs) represent the substrate for atrioventricular reentrant tachycardia (AVRT) and are the second most common cause of paroxysmal supraventricular tachycardia (SVT). These atrioventricular (AV) associations are caused by incomplete embryological development of the AV annuli, without complete separation of the atria and the ventricles. Most APs conduct both anterogradely and retrogradely. Other APs conduct in single direction more frequently in retrograde ($\leq 50\%$) and rarely in anterograde ($\leq 10\%$) approach [1]. Cases of familial Wolff-Parkinson-White (WPW) syndrome with autosomal dominance are rarely reported [2, 3]. WPW syndrome can be associated with cardiomyopathy, particularly hypertrophic cardiomyopathy (HCM). PRKAG2 gene mutations are the well-characterized genetic cause of familial WPW syndrome associated with HCM [4–6].

Generally, genetic underpinnings are more difficult to establish in familial WPW syndrome. WPW syndrome in a set of identical twins suggests a genetic involvement in AP genesis. In this report, we describe the case

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of 14-year-old identical male twins, one with a concealed pathway and the other with a pre-excitation without symptoms. They both exhibited a right-sided AP in almost the same location but had a different phenotype.

Case presentation

We report the case of 14-year-old monozygotic twin brothers who were referred for an EP study and possible ablation therapy on the same day. They were born from an uncomplicated pregnancy by normal spontaneous delivery. Their parents are healthy, with no palpitation and cardiac problem history, and no family member had an AP. On admission, the twins' physical examination was unremarkable. However, twin A reported having post-exercise recurrent paroxysmal palpitation at 180 beats per minute (bpm) for 3 years, sometimes associated with discomfort. A 12-lead surface ECG showed sinus rhythm at 82 bpm and normal PR interval (159 ms), without evidence of ventricular pre-excitation (Fig. 1A). Transthoracic echocardiography and 24-h ECG monitoring were uneventful. However, an orthodromic AVRT was suspected because of having a twin. Twin B was asymptomatic and only sought medical examination to certify that he was fit to undergo strenuous exercises for firefighter volunteerism. His 12-lead ECG revealed sinus rhythm with a short PR interval (95 ms) and a large pre-excitated QRS (149 ms). The delta wave was negative in leads III and V1 and R/S transition between V1 and V2. The delta wave's onset was positive, with an R wave in lead II and a small R wave in lead aVF, suggesting a right midseptal AP (Fig. 1B). Furthermore, transthoracic echocardiography and 24-h ECG monitoring were uneventful.

EP study was performed using right femoral venous access. We inserted a decapolar catheter (Inquiry Steerable Diagnostic Catheter, Abbott, St Paul, MN, USA) into the coronary sinus (CS) to record and stimulate left atrial activity. We also placed a quadripolar catheter (Inquiry Steerable Diagnostic Catheter, Abbott, St Paul, MN, USA) directly across the tricuspid valve for His-bundle activity recording as well as ventricular pacing from the right ventricular floor. Additionally, a 7 Fr steerable quadripolar catheter with a 4-mm tip electrode (Biosense Webster, Diamond Bar, CA, USA) was used for mapping along the tricuspid annulus and performing radiofrequency ablation.

Twin A

At baseline, the EP study demonstrated normal AH (106 ms) and HV (46 ms) intervals, with no spontaneous anterograde pre-excitation. The anterograde effective refractory period (ERP) of the AV node (AVNERP) was 390 ms (153 bpm). During ventricular stimulation at a cycle length of 600 ms, we observed a concentric retrograde atrial activation, with the earliest at CS 9–10. The ventriculoatrial (VA) interval was measured at 80 ms. The retrograde atrial conduction was non-decremental in ventricular extrastimulation, suggesting a right-sided concealed AP. Aggressive atrial burst pacing was also introduced until the atrioventricular Wenckebach point, but it did not induce any tachycardia. Intravenous isoprenaline perfusion (1 µg/min and titrated up to 3 µg/min, with the underlying sinus

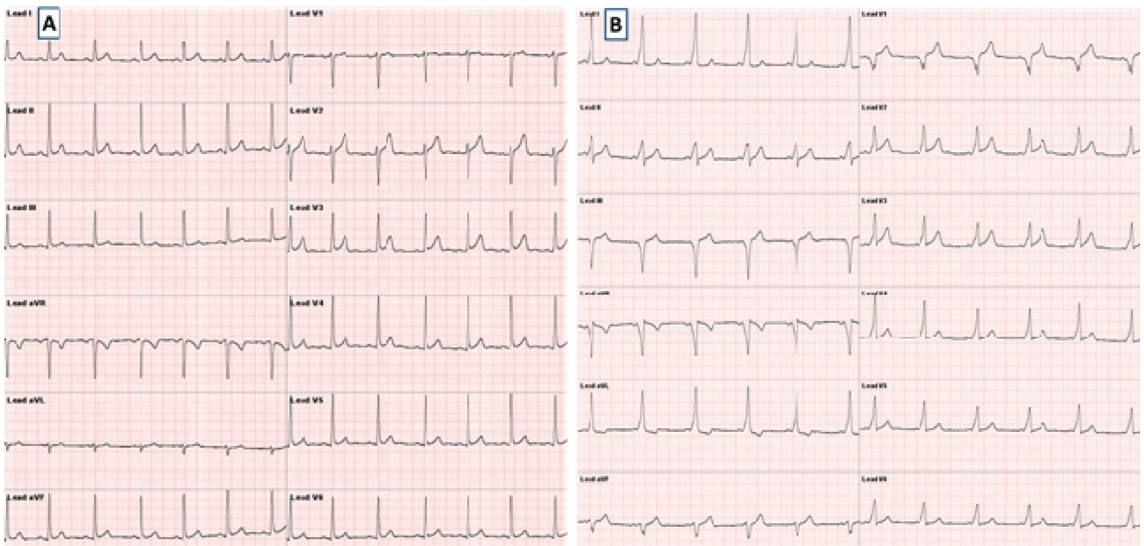

Fig. 1 **A:** 12-lead surface electrocardiogram at admission was normal in twin A without evidence of ventricular pre-excitation. **B:** 12-lead surface electrocardiogram at admission in twin B showed a right midseptal ventricular pre-excitation

rhythm markedly accelerated) could not reveal anterograde AP conduction. However, atrial stimulation under isoproterenol perfusion repeatedly induced a stable SVT (cycle length: 296 ms) (*Fig. 2*). The shortest VA interval was 80 ms, with earliest atrial activation at CS 9–10. The patient tolerated orthodromic reciprocating tachycardia poorly; thus, we had ablated this AP in sinus rhythm with ventricular pacing.

During right ventricular pacing, the earliest retrograde atrial activation was at 04.00 o'clock on the tricuspid annulus in the right posteroseptal position below the CS ostium (Fig. 3A). A single radiofrequency application delivered on the site during ventricular pacing abolished AP conduction in 3.7 s, with VA interval increase from 78 to 170 ms (Fig. 4A).

After waiting for 30 min, AP retrograde conduction did not recur. In addition, atrial pacing at baseline and under

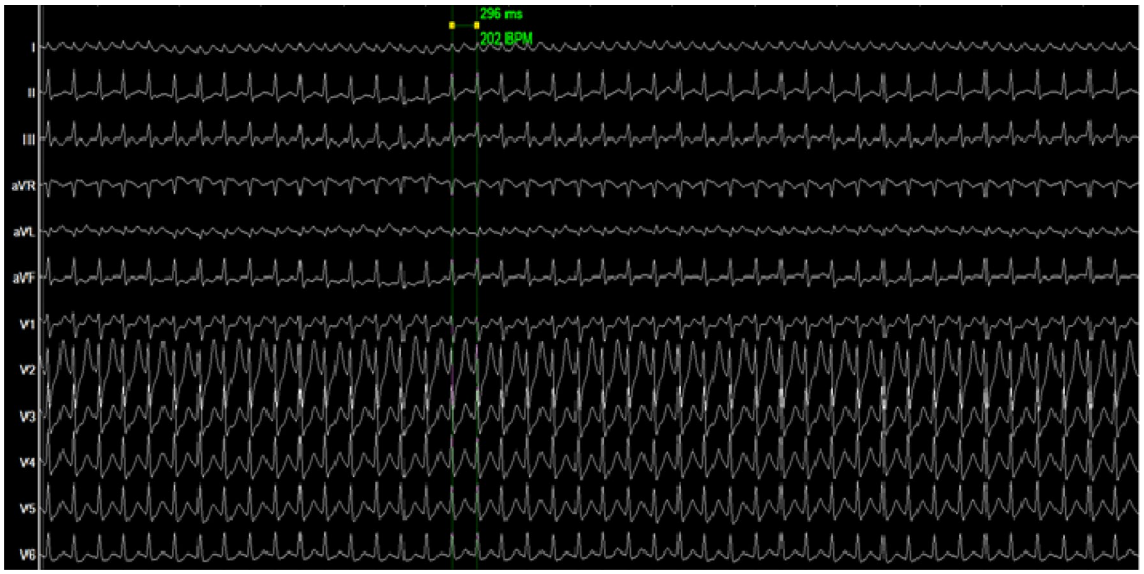

Fig. 2: 12-lead surface electrocardiogram showed a stable supraventricular tachycardia (cycle length: 296 ms) induced by atrial stimulation under isoproterenol perfusion during electrophysiology study

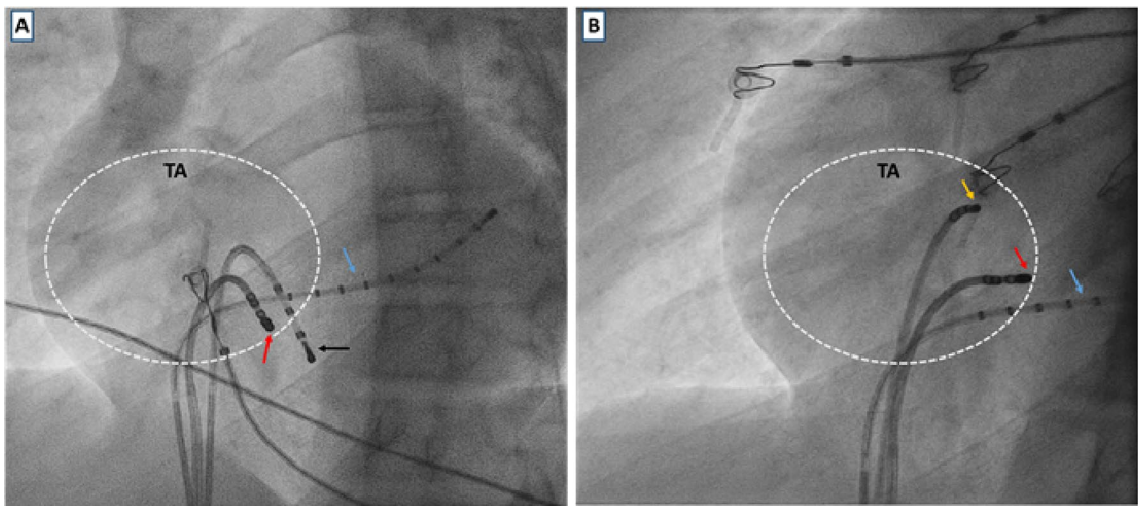

Fig. 3 **A:** Left anterior oblique fluoroscopic image showing a successful ablation site (red arrow) in twin A. A decapolar catheter is placed in the coronary sinus (blue arrow). A quadripolar catheter in the right ventricle is shown in black. **B:** Left anterior oblique fluoroscopic image showing a successful ablation site (red arrow) in twin B. A quadripolar catheter is located at the His-bundle (orange arrow). A decapolar catheter in the coronary sinus is shown in blue. Dashed circle represents the approximate location of the tricuspid annulus. TA = tricuspid annulus

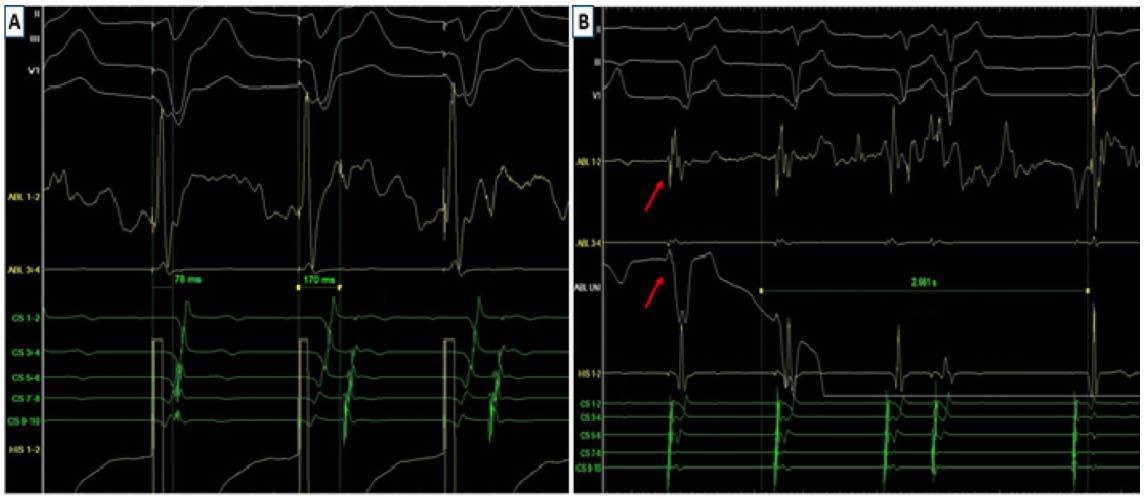

Fig. 4 Electrophysiology study in identical twins. **A:** Abolition of right posteroseptal accessory pathway in 3.7 s during ventricular pacing with increased ventriculoatrial interval from 78 to 170 ms in twin A. **B:** Abolition of right-sided midseptal anterograde accessory pathway in 2.6 s with classic atrioventricular fusion on ablation catheter (red arrows) in twin B. CS = coronary sinus; HIS = His-bundle; ABL = ablation catheter at the successful site of accessory pathway ablation; UNI = unipolar

isoprenaline could not induce any tachycardia. Intravenous adenosine (10 mg) administration also did not reveal VA conduction through a retrograde AP.

Twin B

At baseline, the EP study showed a normal AH (122 ms) interval and an HV of 30 ms with spontaneous anterograde pre-excitation. During ventricular stimulation at 600 ms, a concentric retrograde atrial activation was observed, with the earliest at CS 9–10, and a short VA interval. In ventricular extrastimulation, retrograde atrial conduction did not increase gradually, suggesting a right-sided AP.

The AP anterograde ERP was 300 ms (200 bpm) at baseline and below 250 ms under isoprenaline infusion.

Subsequently, this asymptomatic patient, who had a short AP ERP of 250 ms or less and high-risk hobbies (volunteer firefighter), underwent catheter ablation.

Atrial and ventricular burst pacing or programmed extrastimulation at baseline and under isoprenaline infusion did not induce arrhythmia. With careful mapping of the tricuspid annulus, the earliest ventricular activation during pre-excitation was at 03.00 o'clock on the tricuspid annulus in the right midseptal position above the CS ostium (Fig. 3B). When radiofrequency was delivered in this location, the right-sided midseptal AP was abolished in 2.6 s (Fig. 4B). After this catheter ablation via the right-side approach, the delta waves disappeared, the AV conduction decreased, and the earliest retrograde atrial activation was observed on the His-bundle electrogram. AP anterograde or retrograde conduction did not recur after 30 min. Moreover, intravenous adenosine (10 mg) infusion after the catheter ablation confirmed the anterograde and retrograde AP conduction interruption.

During follow-up at 12 months, AVRT did not recur in both twins, and their ECG results were normal.

Discussion

We reported a case of 14-year-old monozygotic twin brothers with AP. They presented a right-side AP in almost the same location but showed completely different phenotypes. Familial WPW syndrome with or without cardiomyopathy has been well-described in the literature. The genetic inheritance pattern in WPW syndrome appears to be autosomal dominant [2, 3]. Familial WPW was previously reported in a mother and her son, with identical anatomical location of AP, further proving that WPW syndrome is hereditary [7]. Molecular genetic studies revealed that several genes cause a rare familial WPW syndrome associated with structural cardiac disease (HCM and Ebstein's anomaly) or systemic disease (mitochondrial syndromes, metabolic myopathies, and storage disorders) [8]. *PRKAG2* is the most described gene involved in familial WPW syndrome causing HCM with glycogen accumulation and ventricular pre-excitation [4–6]. Despite important advances in understanding the mechanism of the WPW pattern in these rare genetic disorders, the genetic basis of WPW in individuals without cardiomyopathy remains unclear. Unlike familial WPW syndrome, sporadic isolated WPW syndrome does not involve *PRKAG2* gene mutations [9]. However, rare de novo and inherited genetic variants were recently

reported in children with isolated WPW without cardiomyopathy or other systemic disease, thereby opening new perspectives for genetic research for sporadic WPW syndrome [10].

Identical twins with sporadic WPW syndrome have been reported. An older report described a different AP location in 10-year-old identical twin sisters [11]. According to some recent case reports, most twins with this condition have a similar AP location; hence, genetic factor may be significant in AP genesis [12, 13]. However, Lu et al. showed that their phenotypes differ in terms of clinical manifestations and electrophysiological properties of AP [13], as shown in our case. Our patients had a right-sided AP located in almost the same place, that is, in the posteroseptal position below the CS ostium and in the midseptal position right above the CS ostium. However, twin A had an asymptomatic manifestation of AP, whereas twin B had concealed AP. Differing forms of ventricular pre-excitation in identical twins highlight the difficulty in understanding genetic contribution in the origin of AV APs.

Conclusions

The inheritance pattern of WPW is more complex, with possibly monogenic causes in some families with syndromic pre-excitation and mainly oligogenic or polygenic causes with environmental exposure. This notion could explain the phenotype difference in some identical twin brothers. Finally, if an AP is diagnosed in one of the twins, we recommend that the other(s) should have at least an ECG.

Abbreviations

AP	Accessory pathways
AV	Atrioventricular
AVNERP	Effective refractory period of the atrioventricular node
AVRT	Atrioventricular reentrant tachycardia
CS	Coronary sinus
ECG	Electrocardiogram
EP	Electrophysiology
ERP	Effective refractory period
HCM	Hypertrophic cardiomyopathy
SVT	Supraventricular tachycardia
VA	Ventriculoatrial
WPW	Wolff-Parkinson-White

Acknowledgements

Not applicable.

Author contributions

HM conceived and designed the case study and drafted the manuscript with SF and LJ. TC, MK, and AS managed the patient. LJ was responsible for critically revising the manuscript. All authors read and approved the final manuscript.

Funding

The authors declare there is no funding source to disclose.

Availability of data and materials

Not applicable.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

All data generated is anonymized.

Competing interests

The authors declare no conflict of interest for this article.

Received: 23 December 2022 Accepted: 2 March 2023
Published online: 03 April 2023

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