

Resolution of cardiomyopathy with catheter ablation of right anterolateral accessory pathway



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Introduction

The association between accessory pathways (APs) and cardiomyopathy (CMP) was described first in congenital heart disease as Ebstein's anomaly and hypertrophic CMP.¹ Later, tachycardia-induced CMP was discovered in patients with APs and frequent tachyarrhythmias.² More recently, the occurrence of CMP with a lack of tachyarrhythmia in patients with APs was described mainly in the pediatric population.³ In this case we report the finding of left ventricular (LV) dyssynchrony and dysfunction in an adult patient with refractory large cell lymphoma who also had a right anterolateral AP. The CMP resolved after successful ablation, enabling the administration of life-saving stem cell transplantation. Additionally we highlight the differences of AP-induced CMP in adults and children.

Case report

A 44-year-old man with asymptomatic ventricular pre-excitation and anaplastic large cell lymphoma presented with a third relapse. Previous therapy included chemotherapy (cyclophosphamide, doxorubicin, vincristine, etoposide, prednisone, and brentuximab vedotin), radiation therapy, and autologous stem cell transplantation. He received salvage therapy with brentuximab vedotin and ICE (ifosfamide, carboplatin, and etoposide) with a plan for allogeneic stem cell transplant. An echocardiogram (Echo) revealed a new CMP with left ventricular ejection fraction (LVEF) of 20%–25%, severe global hypokinesis, and LV dyssynchrony. Baseline Echo prior to chemotherapy 3 years ago had shown an LVEF of 50%–55%, and a repeat Echo 15 months ago had shown an LVEF of 45%–50%. The electrocardiogram (ECG) showed sinus tachycardia of 102 beats per minute with full pre-excitation, PQ interval of 96 ms, QRS duration of 152 ms, with left bundle branch block (LBBB)

KEY TEACHING POINTS

- Accessory pathway (AP)-induced cardiomyopathy (CMP) is underdiagnosed, and can be initially diagnosed during adulthood.
- AP-induced CMP should be considered as a contributing factor for CMP, even in the presence of other causes, by careful examination of the electrocardiogram for evidence of right-sided pre-excitation.
- All right-sided APs, including anterolateral APs, can cause left ventricular (LV) dysfunction.
- Even with the lack of tachyarrhythmias or high-risk AP conduction properties, these pathways should be ablated as first-line therapy for restoring LV synchronization, owing to high procedural success rates with future improvement in LV function.
- QRS normalization post successful ablation can result in LV function improvement even in the presence of a combined CMP.

morphology (Figure 1A). Baseline ECG prior to chemotherapy demonstrated a QRS duration of 100 ms with minimal pre-excitation. The patient had NYHA class II symptoms of congestive heart failure, but denied any palpitations and had no history of any tachyarrhythmias. A 48-hour Holter monitor demonstrated persistence of ventricular pre-excitation throughout the recording. Despite guideline-directed heart failure therapy for 5 months, the patient failed to improve. Relapsed anaplastic large cell lymphoma, anaplastic lymphoma kinase-negative, carries a poor prognosis of less than 1 year survival. Allogeneic stem cell transplantation was his only hope for long-term survival, but this therapy required an LVEF $\geq 40\%$. Although the patient was thought to have a chemotherapy-induced CMP, it was postulated that the LBBB-appearing QRS complex from the right-sided AP may also be contributing to the low LVEF. Therefore, he underwent an electrophysiology

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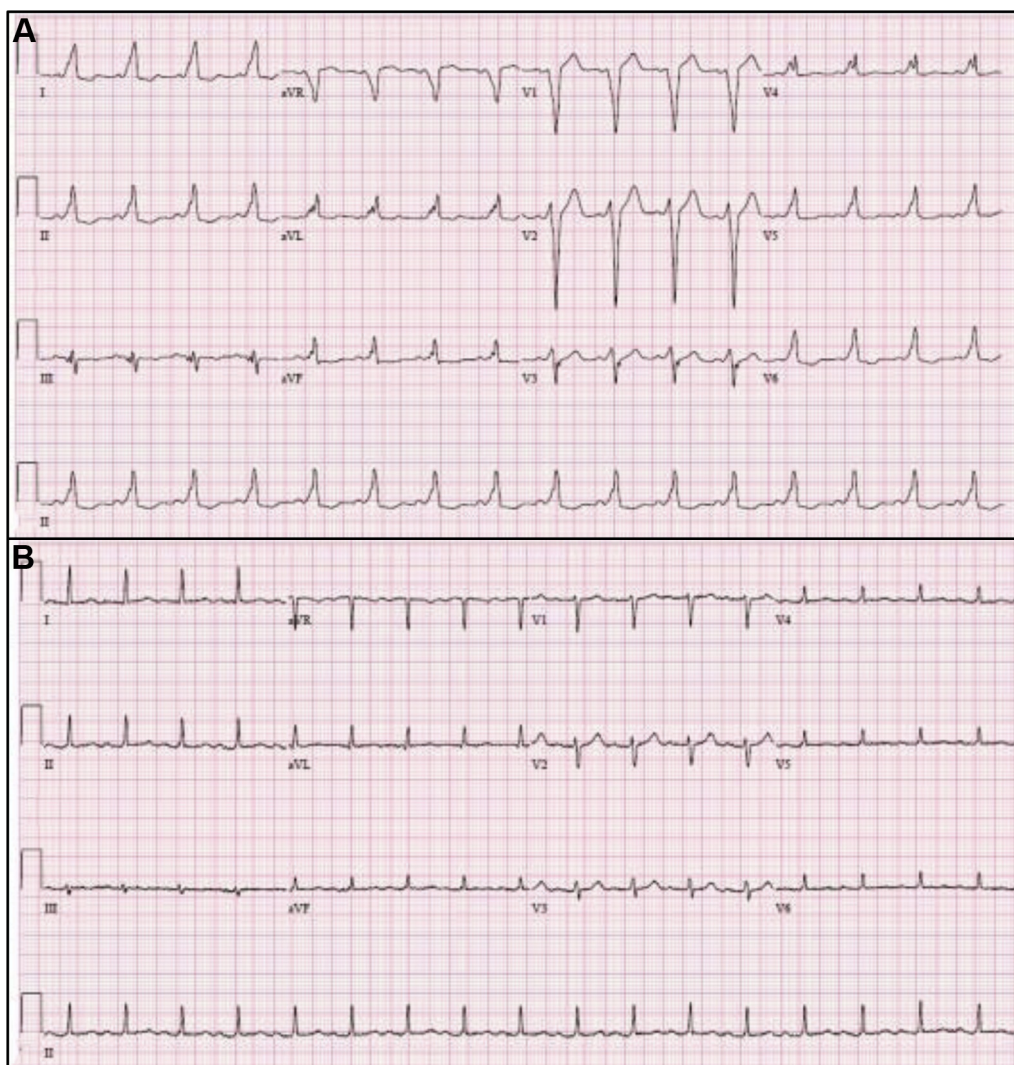


Figure 1 **A:** Electrocardiogram (ECG) prior to ablation demonstrating overt pre-excitation with a wide QRS and left bundle branch block morphology. **B:** ECG post ablation demonstrating a PQ interval of 196 ms and a narrow QRS of 80 ms.

study and ablation of the AP in order to resolve LV dyssynchrony and potentially improve his LV function. The AP Wenckebach cycle length (CL) was 340 ms, and AP effective refractory period at basic CL of 500 ms was 300 ms. HV interval was 0 ms when conducting over the AP, and 47 ms in the absence of AP conduction. When anterograde conduction over the AP was blocked and occurred only over the atrioventricular (AV) node, QRS duration was 80 ms with a normal morphology. The retrograde ventriculoatrial block CL was 290 ms. No arrhythmias were induced with atrial and ventricular burst pacing or programmed extrastimulation. A 3-dimensional map of the tricuspid annulus was made during sinus rhythm and showed a right-sided anterolateral AP. Radiofrequency (RF) lesions delivered at this location resulted in abolition of AP function in 2.3 seconds. Postablation AH interval was 96 ms and HV interval 47 ms. ECG 1 month post ablation was normal, with a PR interval of 196 ms, QRS duration 80 ms with a normal morphology (Figure 1B). An Echo performed 1 month post ablation

showed improvement in LVEF to 43%, with Strain Echo demonstrating the resynchronization of the LV contraction (Figure 2). Because of the improvement in LVEF, he underwent allogeneic stem cell transplantation and achieved remission from his lymphoma.

Discussion

This patient presented with a combined etiology for his CMP: chemotherapy-induced cardiotoxicity caused by ifosfamide and doxorubicin, in addition to LV dyssynchrony due to a right-sided AP, which likely exacerbated his chemotherapy-induced CMP. Furthermore, the degree of pre-excitation was possibly affected by the chemotherapy, as evident by the change in QRS duration prior to and post chemotherapy, through 2 mechanisms. First, doxorubicin was reported to cause various degrees of AV block,⁴ possibly resulting in slower AV nodal conduction; and second, the heart failure resulted in sinus tachycardia; both of these

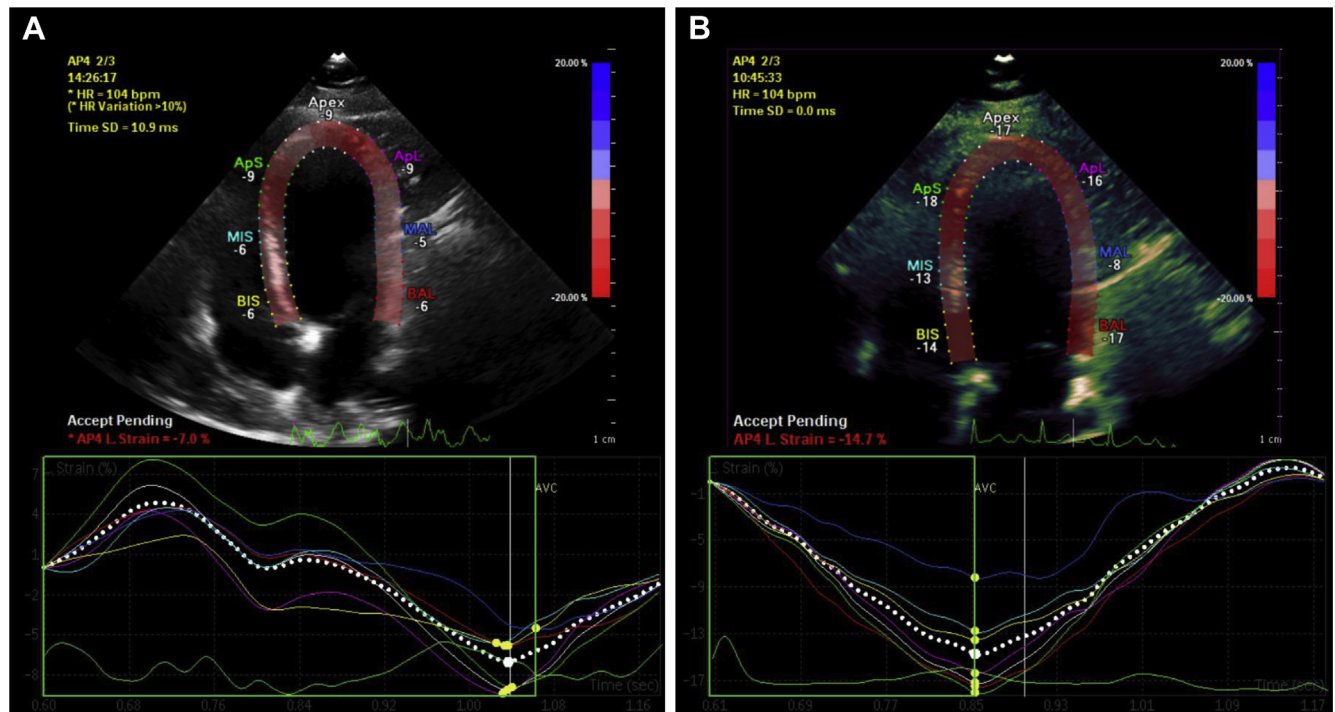


Figure 2 A: Strain echocardiogram prior to ablation demonstrating left ventricular (LV) dyssynchrony. B: Strain echocardiogram post ablation demonstrating a synchronous and improved LV function.

mechanisms resulted in a higher degree of pre-excitation. Since the right-sided AP was thought to cause LV dyssynchrony and contribute to LV dysfunction, the decision was made to perform an electrophysiology study with ablation of his AP, despite no symptoms from Wolff-Parkinson-White syndrome, no prior history of tachyarrhythmia, and AP properties that are not considered high risk for sudden cardiac death.^{5,6} The partial improvement in LV function post ablation was sufficient to enable restoring lifesaving therapy of stem cell transplantation.

The occurrence of CMP in patients with pre-excitation, and the lack of cardiac tachyarrhythmia, has been described in the pediatric population in a few case reports and small case series.^{3,7,8} In a retrospective study of 34 pediatric patients, 56% of patients with right septal or posteroseptal APs had decreased LV function and increased septal-to-posterior wall motion delay.³ In pediatric patients with septal APs, LV function was significantly lower ($53\% \pm 11\%$) than that of patients with right ($62\% \pm 5\%$) or left ($61\% \pm 4\%$) APs ($P = .001$).⁸ Catheter ablation resulted in mechanical resynchronization, reverse remodeling, and improvements in LV function. Tomaske and colleagues³ discussed the importance of septal and posteroseptal location of APs to cause LV dysfunction. The extent of the pre-excited ventricular myocardium depends on the relative timing of normal and eccentric ventricular activation. It was thought that only septal and posteroseptal APs may induce sufficiently earlier interventricular activation to cause a decrease in LV function. In left free wall pathways, the amount of pre-excited myocardium is rather small because of long

conduction time from the sinus node to the atrial pathway insertion, leading to almost-normal activation of the left ventricle through the AV node and normal conduction system. In right free wall pathways, LV activation is almost synchronous over the normal conduction system, with a pre-contraction area being limited to the right ventricular free wall. In contrast to right free wall pathways, septal and posteroseptal pathways may induce earlier interventricular activation, with substantial pre-excitation of the septum and delayed activation of the LV free wall. However, 2 case reports of adults with dilated cardiomyopathy associated with asymptomatic right posterolateral AP reported LV function improvement after RF ablation of the AP. In one report, a cardiac resynchronization therapy (CRT) defibrillator was first implanted and successful RF ablation of the AP 2 years later resulted in a near-normal LV function with the CRT pacing turned off.^{9,10} In a second report, a patient with combined ischemic CMP and a posterolateral AP had partial improvement in LVEF post ablation.¹¹ One other case report of a 20-year-old asymptomatic man with LV dysfunction, in whom AP ablation was performed owing to a short refractory period of the AP (250 ms), reported normalization of LV function after RF ablation of a right anterolateral AP.¹² An abnormal systolic motion of the interventricular septum in patient with right anterior AP was described by Chandra and colleagues.¹³ In addition, anterograde conduction with a right or septal AP was found to increase the brain natriuretic peptide level in Wolff-Parkinson-White syndrome patients with normal cardiac function.¹⁴ Our case demonstrated that ablation of a right anterolateral AP enabled improvement of

LV function. Thus, this case confirms the notion that right-sided APs, regardless of location, can cause LV dyssynchrony and dysfunction. This might be explained by different AV node conduction properties in adults, with a higher mean anterograde block CL, resulting in a greater degree of fusion and more myocardium being activated by the AP.¹⁵ This fusion causes LBBB-appearing QRS, which can mimic the pathophysiology of LBBB-induced dyssynchrony.

Conclusion

AP-induced CMP is an underdiagnosed type of CMP. Based on our case and review of the literature, we recommend considering AP-induced CMP in patients with idiopathic dilated CMP, with careful examination of the ECG for evidence of pre-excitation in the presence of LBBB morphology. All right-sided APs can potentially cause LV dyssynchrony and dysfunction. Successful ablation of these pathways with QRS normalization results in improvement of LV function even in the presence of a combined CMP. In such cases, achieving even partial improvement in LV function can further enable optimization of medical therapy. AP ablation should be attempted as first-line therapy, prior to a CRT device implantation, for restoring LV synchronization owing to high procedural success rates with future improvement in LV function, evading the need for CRT.

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