Arrhythmogenic right ventricular cardiomyopathy in monozygotic twin sisters, and persistent left superior vena cava in one complicating implantation of ICD

Aritmojenik sağ ventrikül kardiyomiyopatisi bulunan tek yumurta ikizi kız kardeşler ve birinde ısrarcı sol üst vena kava sendromu ile komplike ICD implantasyonu

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Summary– Arrhythmogenic right ventricular cardiomyopathy (ARVC) is an inherited cardiomyopathy characterized histologically by fibro-fatty replacement of heart muscle, and clinically by ventricular arrhythmias and right ventricular dysfunction. This report presents monozygotic twins with ARVC, suggesting a genetic abnormality as the most probable cause.

Özet– Aritmojenik sağ ventrikül kardiyomiyopatisi kalp kasının histolojik olarak fibroz-yağlı doku ile yer değiştirdiği ve klinik olarak ventriküler aritmi ve sağ ventrikül fonksiyonu bozukluğu ile karakterize kalıtsal bir kardiyomiyopatidir. Burada biz aritmojenik sağ ventrikül kardiyomiyopatili tek yumurta ikizlerini sunuyoruz; hastalığın en olası nedeni olarak genetik anormallik gözükmektedir.

Arrhythmogenic right ventricular cardiomyopathy (ARVC) is an inherited cardiomyopathy. It is characterized histologically by fibro-fatty replacement of heart muscle, and clinically by ventricular arrhythmias and right ventricular dysfunction.[1] Sudden death or syncope may be the first manifestations, while in other cases the disease may be asymptomatic.[2] Familial ARVC is a genetic disorder transmitted with reduced penetrance and variable phenotypic expression.

In this report, we present monozygotic twins with ARVC, which suggests a genetic abnormality as the most probable cause.

CASE REPORT

A 20-year-old woman (Patient 1) presented with near syncope after exercise. During admission, her monozygotic twin sister (Patient 2) was also invited for diagnostic testing. Echocardiography (ECG) showed T wave inversions in lead V1 to V6 in the absence of a complete right bundle branch block (RBBB); duration of the QRS complex was 110-120 ms in lead V1 and 80 ms in lead V6 in both patients (Figure 1).

Abbreviations:

ARVC	*Arrhythmogenic right ventricular cardiomyopathy*
ECG	*Echocardiography*
PLSVC	*Persistent left superior vena cava*
RV	*Right ventricles*

On ECG, both patients had severely dilated right ventricles (RV) with reduced ejection fraction (EF); left ventricles were normal. Cardiac magnetic resonance imaging (MRI) confirmed severe RV dilation with thin free walls, and also showed fatty tissue in the left ventricle in both patients (Figure 2). These findings fulfilled the criteria for a diagnosis of ARVC.[3]

Electrophysiological (EP) testing failed to induce ventricular arrhythmias in either patient. Due to the positive family history and LV involvement, ICD implantation was planned in both patients for primary prevention of sudden death. During the initial left subclavian puncture, Patient 2 was seen to have a persistent left superior vena cava (PLSVC) draining into a dilated coronary sinus. An active fixation lead with

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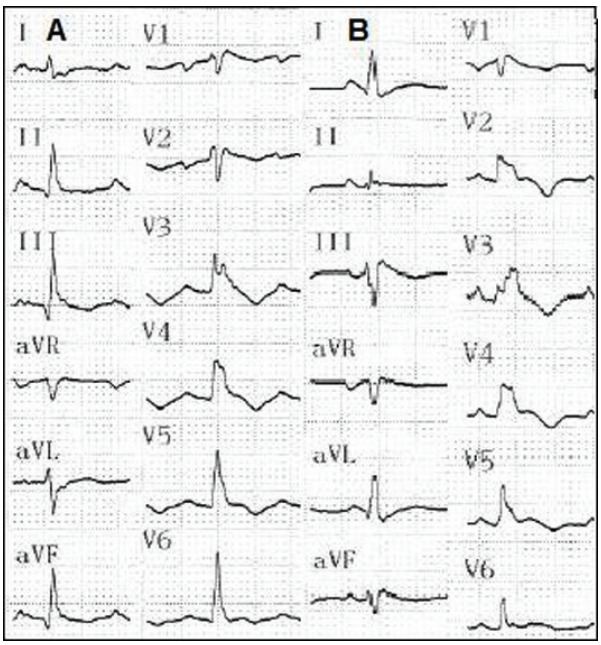

Figure 1. Sisters IA and IB electrocardiograms. Normal sinus rhythm. T wave inversions in V1 to V6. rSr' in lead V1-V4. Duration of QRS complex: ~110 ms in lead V1 and 80 ms in lead V6.

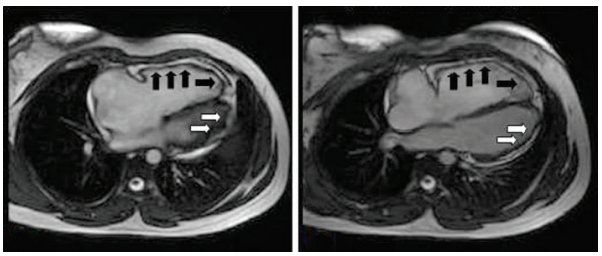

Figure 2. FIESTA (Fast Imaging Employing Steady State Acquisition) sequence cardiovascular magnetic resonance images from the sisters with ARVC indicate fat infiltration at the outflow tract, free wall, and apex of the right ventricle and thinning of the underlying myocardial wall (black arrows) and a thinned lateral wall of the left ventricle (white arrows) due to fatty replacement.

standard stylets was advanced through the PLSVC and coronary sinus into the RV without any complications (Figure 3).

DISCUSSION

Although significant progress has been made in recent years in our knowledge of ARVC, its etiology is still uncertain. In familial cases of ARVC, autosomal dominant inheritance with different penetrance and expression has been reported, and accounts for approximately 50% of cases.[4]

The most common thoracic venous anomaly is PLSVC, which occurs in 0.3% of the population.[5] To the best of the authors' knowledge, this is the first report of PLSVC in a case with ARVC in monozygotic twin sisters. This condition is usually asymptomatic, and may be detected incidentally by venography during device implantation, as in our case. Transvenous advancement of the lead through the PLSVC, coronary sinus and right atrium to the right ventricle can be technically challenging, as the tip of the lead tends to deflect away from the tricuspid annulus. This limited maneuverability adds to the difficulty in finding a right ventricular implantation site with sufficient voltage in ARVC. Manual reshaping of the stylet into a U-shape and forming a loop in the right atrium using the right atrial free wall for support with some specific maneuvers usually works well in these circumstances. As there is no reported specific link between genetic disorder and PLSVC, only one of the twin sisters had this anomaly.

The inflammatory process has been suggested as playing a role in cases of ARVC because of the com-

Table 1. Similarities and differences of phenotype of monozygotic twin

Patient	Symptoms/arrhythmia	ECG	RV morphology	LV involvement	Ventricular arrhythmia in EPS	Differences in environmental factors
1	Near syncope, PVBs		Enlargement, dysfunction	+	No	No
2	Near syncope		Enlargement, dysfunction	+	No	No

PVBs: Premature ventricular beats.

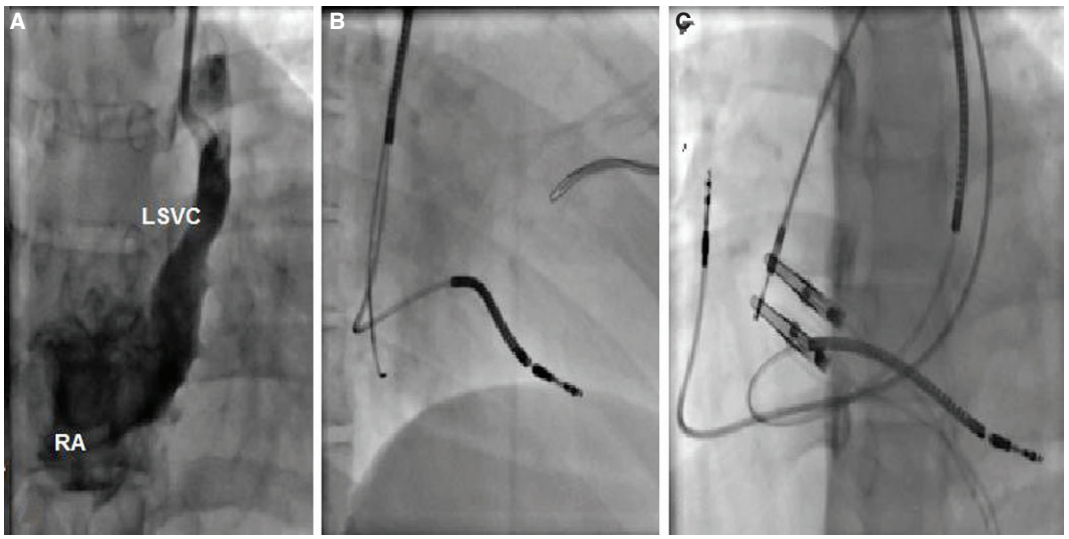

Figure 3. **(A)** AP projection demonstrating a LSVC. **(B)** RAO 30° view demonstrating lead advanced into the coronary sinus via a PLSVC, and an active fixation RV lead directed into the apex. **(A)** LAO 30° view demonstrating the RV lead placement.

mon finding of inflammatory infiltrates in the myocardium, suggesting that ARVC is a consequence of myocarditis.[6] Some cases have also been identified with cardiotropic viruses in the myocardium. However, the role of inflammation in disease pathogenesis remains unknown, particularly as to whether these viruses contribute to disease or the diseased myocardium is more prone to virus infection.[7]

Table 2. **Summary of twins with ARVC reported in literature**

Author	Patient	Symptoms/arrhythmia	ECG	RV morphology	LV involvement
Non-Identical					
Wlodorska	IA	VT, PVBs	Wide QRS in V1	Enlargement, bulges	–
	IB	Asymptomatic	Normal	Enlargement, bulges	–
	IIA	Asymptomatic	Wide QRS in V1	Enlargement	–
	IIB	Asymptomatic	Normal	Enlargement, bulges	–
Buja	1	Syncope, VT	LP+	Enlargement, bulges	
	2	PVBs	LP–	Enlargement, bulges	
Solenthaler	1	Syncope, HF, VT, SD	Neg T in V1-3	Enlargement, bulges	+
	2	VT	Neg T in V1-3	Enlargement	–
Identical					
Hiraoka[10]	A	PVBs	Neg T in V1-3	Enlargement, bulges	–
	B	PVBs	Neg T in V1-3 Wide QRS in V1	Enlargement, bulges	–
Indik[11]	A	HF, AFib, nsVT	Neg T in V1-3 Epsilon wave in V1	Enlargement, dysfunction	–
	B	HF, nsVT	Neg T in V1-3 Epsilon wave in V1	Enlargement, dysfunction	–

PVBs: Premature ventricular beats; AFib: Atrial fibrillation; HF: Heart failure; VT: Ventricular tachycardia; nsVT: Nonsustained VT; SD: Sudden death; LP: Late potentials.

The mechanism by which male gender results in greater risk of some expressions of ARVC is not known. The cardioprotective features of estrogens due to inhibition of myocardial cell apoptosis has been documented.[8] This theory would explain why the disease is more common in males.

The arrhythmias are characteristically provoked by adrenergic stimulation such as physical exercise.[9] The majority of patients with ARVC are susceptible to adrenergic stimulation and the frequent induction of arrhythmia by isoprenaline infusion suggests a role for catecholamines.[10] The role of sympathetic stimulation in provoking arrhythmias in ARVC possibly accounts for the high frequency of this situation in individuals who die during exertion.

In addition to a genetic cause of ARVC, hormonal, infectious or inflammatory, apoptotic and physical exercise theories have been proposed either as the cause of or as environmental factors facilitating gene expression. The relative influence of genetics and environmental factors can be best assessed by studies of twins with the disease, when it is possible that different phenotypes are a result of environmental factors.

Our observations are compatible with those of Hiraoka and Indik, in that findings and courses of the disease are similar in monozygotic twins.[11,12] Neither of our patients had any history of myocarditis or exposure to toxins. The findings strongly suggest a genetic cause for ARVC.

In conclusion, this is the first report of PLSVC in a case with ARVC in monozygotic twin sisters. Limited maneuverability of the lead tip caused by PLSVC adds to the difficulty in finding an appropriate implantation site with good voltage in cases with ARVC. Specific techniques are required to overcome these challenges.

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