JACC: CASE REPORTS VOL. 2, NO. 7, 2020

CASE REPORT

INTERMEDIATE

CLINICAL CASE

A Case of Ventricular Tachycardia Caused by a Rare Cardiac Mesenchymal Hamartoma

Zekun Feng, MD, PharmD,[a] Daniel Philipson, MD,[a] Jamar P. Uzzell, MD,[b] Ashley Stein-Merlob, MD,[a] Eric H. Yang, MD,[a,c] Holly R. Middlekauff, MD,[a] Ryan P. Lau, MD,[b] Gregory A. Fishbein, MD,[b] Jason S. Bradfield, MD,[a,c] Olujimi A. Ajijola, MD, PhD[a,c,d]

ABSTRACT

The presentation of a cardiac hamartoma, an exceedingly rare and histologically benign cardiac tumor, can be variable. We describe a case of refractory ventricular tachycardia in a patient with a cardiac mass failing multiple pharmacologic and procedural interventions, ultimately treated by cardiac transplantation and diagnosed with a mesenchymal cardiac hamartoma. (**Level of Difficulty: Intermediate.**) (J Am Coll Cardiol Case Rep 2020;2:1049–55) © 2020 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

HISTORY OF PRESENTATION

A 33-year-old woman with 3-year history of asymmetric cardiac hypertrophy and sustained ventricular tachycardia (VT) was treated with antiarrhythmic drug (AAD) therapy and placement of an implantable cardioverter-defibrillator (ICD). Prior to the current admission, she had recurrent VT despite multiple AADs (metoprolol, amiodarone, sotalol, and dofetilide), requiring several ICD shocks, prompting an unsuccessful endocardial radiofrequency catheter ablation and subcutaneous ICD array placement for elevated defibrillation thresholds. Six months prior to her current presentation, she underwent cardiac sympathetic denervation followed by renal artery denervation, given that her VT was precipitated by stress. The current admission was precipitated by symptomatic recurrent VT and a total of 22 ineffective

LEARNING OBJECTIVES

- To recognize the challenges in diagnosing cardiac hamartoma.
- To recognize the difficulties in controlling ventricular tachycardia associated with cardiac hamartoma.
- To review the treatment options reported in the literature for ventricular tachyarrhythmias associated with cardiac hamartoma.
- To review the histopathology of the rare mesenchymal cardiac hamartoma.

From the [a]Division of Cardiology, Department of Medicine, UCLA Medical Center, Los Angeles, California; [b]UCLA Department of Pathology and Laboratory Medicine, UCLA Health, Los Angeles, California; [c]Cardio-Oncology Program, Division of Cardiology, Department of Medicine, University of California-Los Angeles, Los Angeles, California; and the [d]UCLA Cardiac Arrhythmia Center, David Geffen School of Medicine, University of California-Los Angeles, Los Angeles, California. Dr. Bradfield has received speaker honoraria from Biosense Webster. Dr. Ajijola has received research grant support from Biosense Webster; and owns equity in NeuCures. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the *JACC: Case Reports* author instructions page.

Manuscript received February 18, 2020; revised manuscript received April 19, 2020, accepted April 28, 2020.

ISSN 2666-0849 https://doi.org/10.1016/j.jaccas.2020.04.038

ABBREVIATIONS AND ACRONYMS

AAD = antiarrhythmic drug

CMR = cardiac magnetic resonance

HCM = hypertrophic cardiomyopathy

ICD = implantable cardioverter-defibrillator

LV = left ventricular

VT = ventricular tachycardia

ICD shocks. A single external 200 J shock successfully converted her to sinus rhythm, and she was transferred to our center. On arrival, her heart rate and blood pressure were within normal limits. Her physical examination was unremarkable, and labs showed troponin of 11.1 ng/ml with normal electrolyte levels. A 12-lead electrocardiogram showed normal sinus rhythm with T-wave inversions in the inferior and septal leads, extreme left axis deviation, left ventricular (LV) hypertrophy, and incomplete right bundle branch block (**Figure 1A**). Prior transthoracic echocardiography revealed asymmetric inferolateral LV wall hypertrophy with myocardial enhancement measuring 19 × 45 mm and an ejection fraction of 55% to 60% (**Figures 2A and 2B**).

DIFFERENTIAL DIAGNOSIS

Atypical hypertrophic cardiomyopathy (HCM) was considered, given the atypical isolated segment involvement of inferolateral LV wall seen on transthoracic echocardiography. Benign primary cardiac tumors were considered more likely than primary malignant cardiac tumors or metastatic cardiac tumors, given the patient's age and her otherwise unremarkable medical history. Although many benign tumors present themselves early on in infancy or childhood, benign tumors including fibroma, hemangioma, lipoma, and hamartoma may also present in adulthood (1). Cardiac sarcoidosis was also considered. Diagnoses including channelopathies such as congenital long QT syndrome and catecholaminergic polymorphic VT were excluded based on electrocardiogram findings and lack of response to denervation procedures, respectively.

INVESTIGATIONS

The UCLA Institutional Review Board approved this study. The patient underwent extensive diagnostic work-up in the 3 years prior to presentation. Cardiac magnetic resonance (CMR) showed similar findings with delayed hyperenhancement and a hypokinetic center suggesting asymmetric HCM versus infiltrative process (**Figures 3A and 3B**). Coronary angiography revealed normal coronary arteries. A fluorodeoxyglucose positron emission tomography scan did not demonstrate evidence of active sarcoidosis and high-grade neoplasm. An incisional myocardial biopsy was performed, with pathology showing fibrosis and nonspecific myocardial hypertrophy. At electrophysiology study, multiple VT morphologies were induced, and ablation was unsuccessful (**Figures 4A and 4B**).

MANAGEMENT

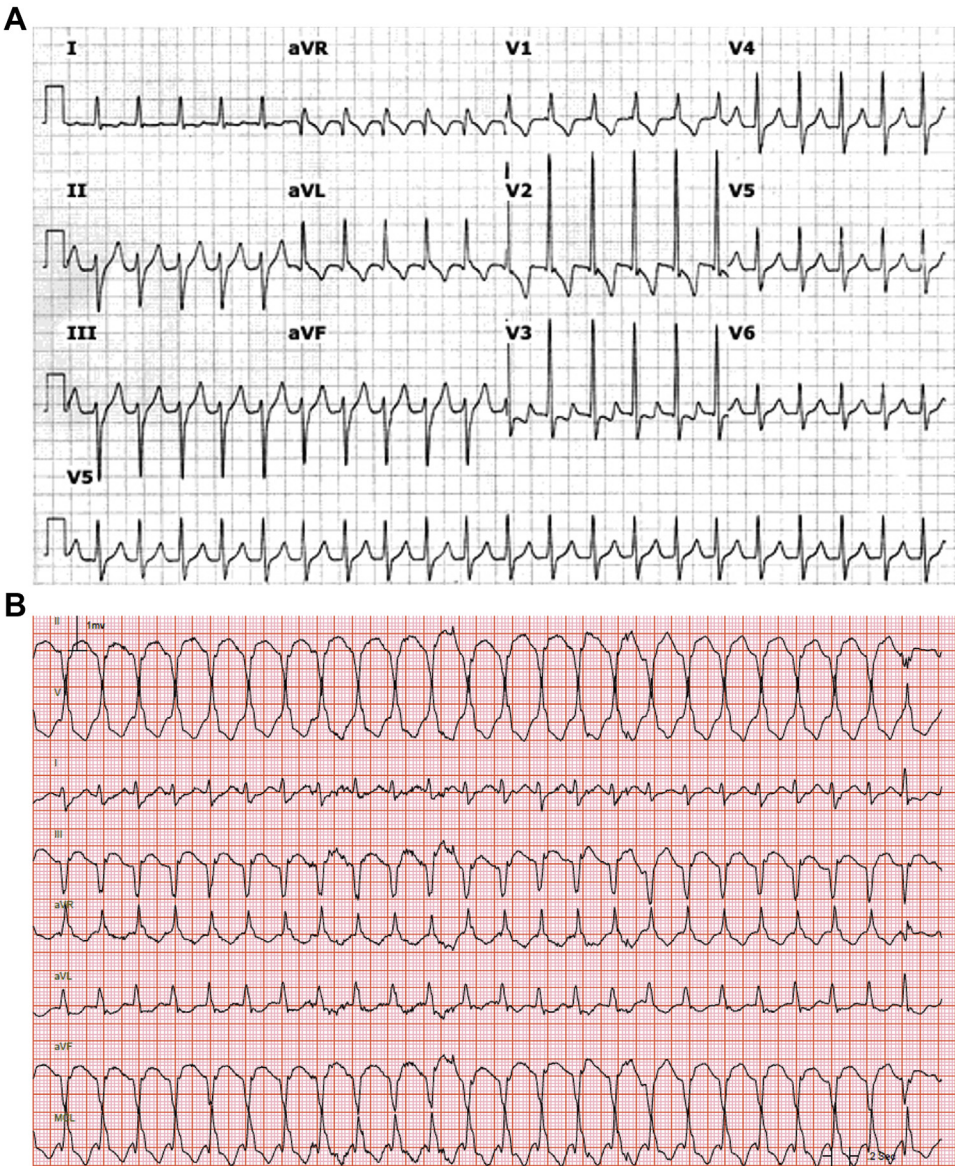
Upon arrival, oral metoprolol and intravenous lidocaine suppressed her VT, but neurotoxicity necessitated lidocaine discontinuation. Mexiletine (150 mg 3 times a day), metoprolol tartrate (200 mg twice a day), and dofetilide (250 μg twice a day) were then started. Given the difficulty in controlling her VT despite multiple antiarrhythmic therapies, failure of tachyarrhythmia suppression despite sympathetic and renal artery denervation, and multiple VT morphologies with poor ablation targets on electrophysiology study, the team felt that the myocardial enhancement seen on imaging studies was most consistent with a cardiac tumor, rather than with asymmetric HCM. Cardiothoracic surgery was consulted for debulking of the mass but was deemed not a candidate because of its large size. Stereotactic body radiation therapy to the LV was considered for drug-refractory VT but was declined by the patient. With limited noninvasive options remaining but persistent VT, she underwent orthotopic heart transplantation. The final histopathology revealed mature cardiac myocytes with fibrosis, adipose tissue, nerves, and smooth muscle, consistent with a cardiac mesenchymal hamartoma (**Figure 5D**).

DISCUSSION

Cardiac hamartomas, including rhabdomyomas and fibromas (2), are rare and typically present in the pediatric population. A mesenchymal subtype of cardiac hamartoma, as seen in our patient, is exceedingly rare, with only 1 previously reported case in the literature (2). Cardiac hamartomas present variably, ranging from asymptomatic to sudden cardiac death (2). The cardiac hamartoma literature consists of case reports, with limited treatment options for VT. Our case demonstrates the challenge in diagnosing cardiac hamartomas and the difficulty in managing associated life-threatening refractory VT.

Owing to rarity and nonspecific presentation, cardiac hamartomas are difficult to diagnose noninvasively. Differentiating cardiac hamartomas from other masses such as HCM, thrombus, or malignant cardiac tumors can be challenging, as imaging findings are often nonspecific. On echocardiography, hamartomas are reported as hyperechoic intracavitary masses with predilection for the LV (3,4). On CMR, the appearance of a hamartoma ranges from mildly hypointense to hyperintense signal on T2-weighted images, and enhancement on early and

FIGURE 1 Electrocardiogram

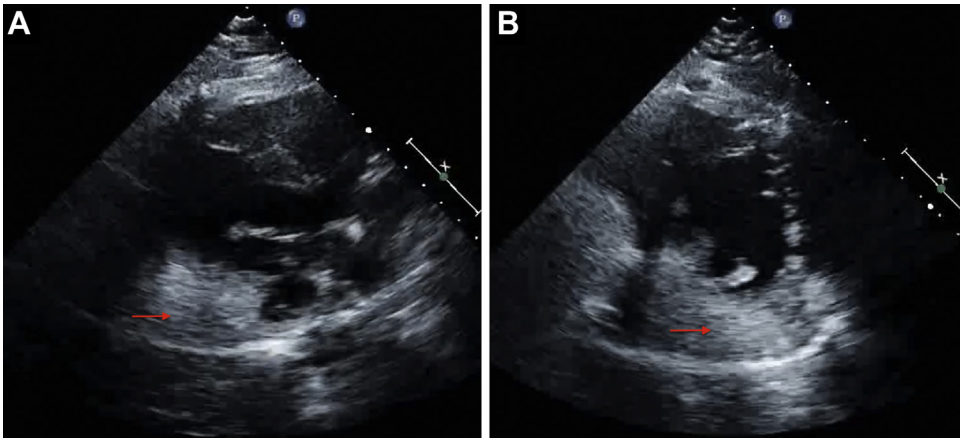


(A) Electrocardiogram at baseline showing normal sinus rhythm with extreme left axis deviation, left ventricular hypertrophy, and incomplete right bundle branch block. **(B)** Electrocardiogram during VT episode showing monomorphic wide complex tachycardia at a rate of 150 beats/min.

delayed phase post-contrast images (4). CMR may exclude thrombus or malignant lesions by first pass and delayed contrast enhancement, and regional variation in vascularity (3). Fluorodeoxyglucose positron emission tomography may also help differentiate benign from malignant lesions (4). Incisional biopsy may be inconclusive (as in this case), as the hamartoma tissue can be nonspecific and similar to the surrounding myocardium.

Given its rarity, current guidelines do not address VT management related to cardiac hamartoma. Existing published case reports of VT associated with hamartoma are mostly in the pediatric population. In a case series of 21 infants (mean 14.9 months of age) with incessant VT owing to cardiac hamartoma, AADs (lidocaine, procainamide, amiodarone, propranolol, digoxin, verapamil, mexiletine, phenytoin, and propafenone) failed in all patients (5). Surgical

FIGURE 2 Transthoracic Echocardiogram

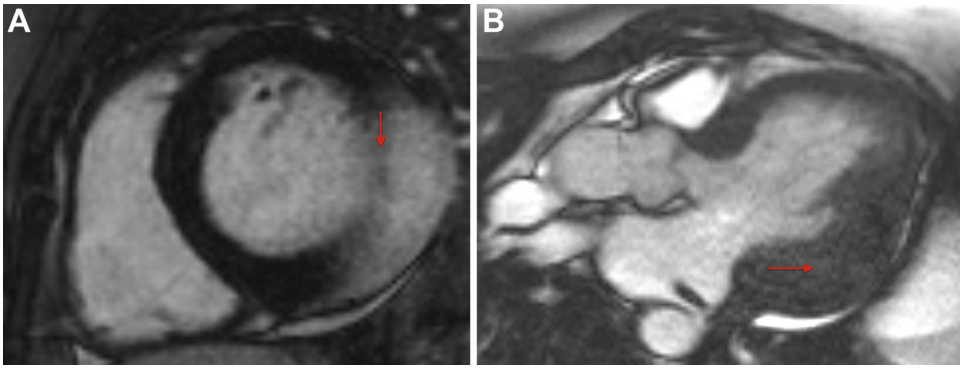


(A) Parasternal long-axis and **(B)** short-axis views of transthoracic echocardiogram demonstrating an asymmetrical and enlarged thickened inferolateral left ventricular wall **(red arrow)**.

intervention with epicardial mapping-guided resection and cryoablation resulted in complete cure of VT in all 21 pediatric patients (5). Case reports of adults with VT owing to hamartoma are limited, but all cases required surgery. For example, a 33-year-old patient underwent successful surgical resection with resolution of VT (6). A 19-year-old patient whose large hamartoma was a contraindication to surgical resection underwent successful cardiac transplantation (7). A 55-year-old patient with partial resection of cardiac hamartoma presented with a late recurrence of VT, which was successfully treated with radiofrequency catheter ablation (8). In our case, surgical debulking may have eliminated VT; however, this was contraindicated because of the size of the mass.

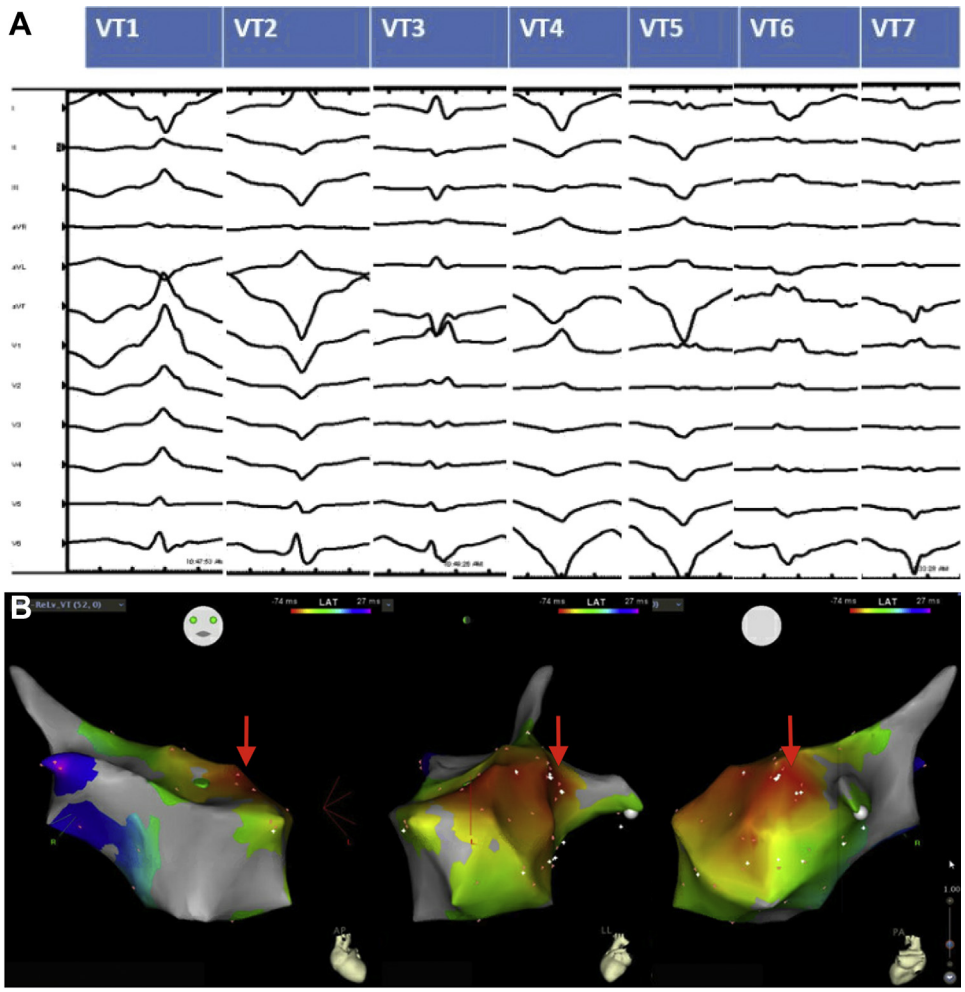
ICDs remain a cornerstone of VT therapy to reduce sudden cardiac death but do not address the underlying cause. In this case, the asymmetric hypertrophy relative to the ICD shock vector may have caused ineffective shocks, as more than 20 ICD shocks failed to cardiovert her VT, whereas 1 external shock was successful. Novel interventions such as stellate ganglion block and renal artery denervation have shown promise as adjunctive therapy for recurrent VT, especially those thought to be triggered by sympathetic activation accompanying physical or emotional stress, as in our patient (9,10). Stereotactic body

FIGURE 3 Cardiac Magnetic Resonance



Cardiac magnetic resonance in **(A)** short-axis view and **(B)** 3-chamber view showing asymmetric inferolateral wall with late gadolinium enhancement **(red arrows)**.

FIGURE 4 **Electrophysiology Study and VT Ablation**

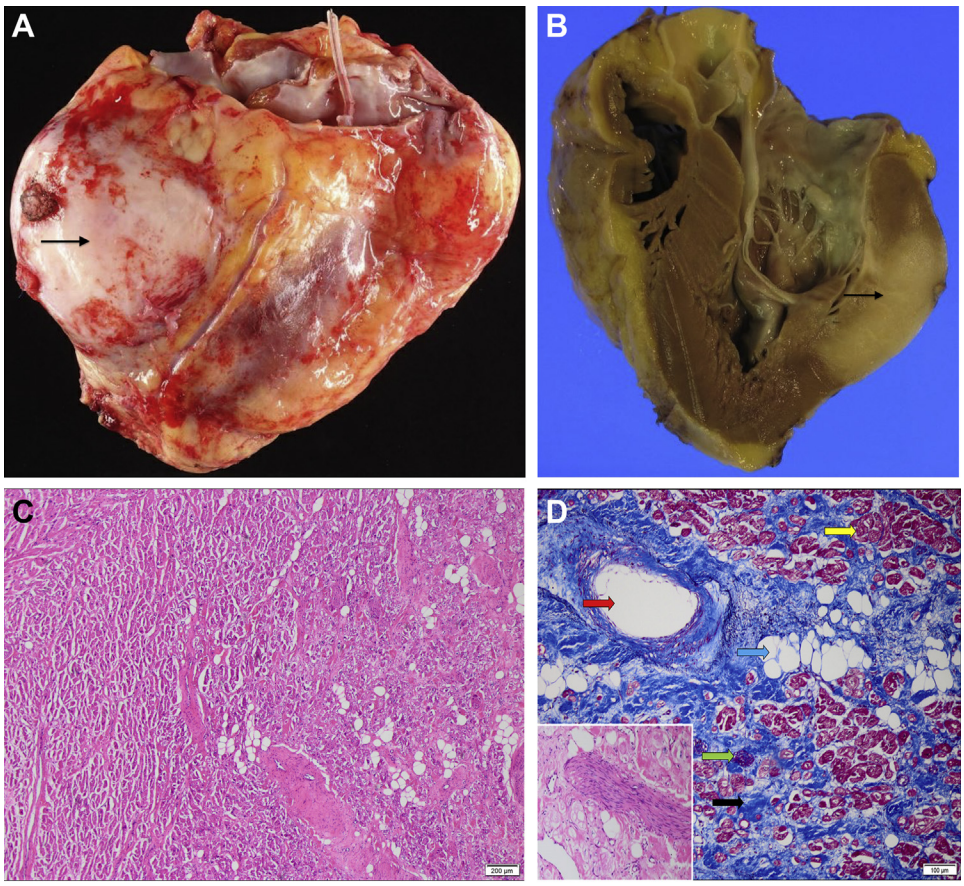


(A) Multiple ventricular tachycardia (VT) morphologies observed during electrophysiology study and programmed stimulation; VT ablation was unsuccessful due to the thickened extensive transmural scar without good endocardial targets and ineffective ablation lesions. **(B)** Activation map for VT 1 (the predominant VT morphology) showing the earliest activation (exit) site on the basal anterolateral LV (**red arrows** point to exit site). Right anterior oblique view on the **left panel**, left anterior oblique view on **center panel**, and posteroanterior view on the **right panel**.

radiotherapy is a noninvasive and reportedly effective strategy to reduce VT burden for patients with structural heart disease failing catheter ablation (11). Definitive therapy with cardiac transplantation in cases not amenable for resection is considered a therapy of last resort.

Cardiac hamartomas include hamartomas of mature cardiac myocytes, vascular hamartomas, and least commonly, cardiac mesenchymal hamartomas. Hamartomas of mature cardiac myocytes are composed of a well-circumscribed proliferation of cardiac myocytes with myofiber disarray. In contrast, HCM is characterized by a poorly demarcated area of cardiac hypertrophy most frequently located in the anterior ventricular septum, with microscopic findings of diffuse myocyte hypertrophy, focal myofiber disarray, and intramural coronary thickening (12). Vascular hamartomas are characterized by markedly abnormal vascular proliferation, whereas cardiac mesenchymal hamartomas are composed of a well-circumscribed but disorganized proliferation of cardiac myocytes, smooth muscle, blood vessels, fibroblasts, mature fat, and nerves (2). The presence of all 6 components distinguishes mesenchymal hamartoma from other benign cardiac tumors (**Figure 5D**).

FIGURE 5 Gross and Histopathology



(A, B) Gross specimen images showing thickened left ventricular wall and mass **(black arrow)**. **(C)** Histopathology slide showing the ill-defined tumor **(right side)** with an infiltrative border, along with the normal myocardium **(left side)** (hematoxylin and eosin, 40× magnification). **(D)** Tumor contains cardiac myocytes **(yellow arrow)**, fibrosis **(black arrow)**, adipose tissue **(blue arrow)**, blood vessels **(red arrow)**, and nerve tissue **(green arrow)** (trichrome a elastin stain, 100× magnification), consistent with the mesenchymal subtype of cardiac hamartoma. The **inset** shows nerve tissue (hematoxylin and eosin, 100x magnification).

FOLLOW-UP

The patient underwent uncomplicated orthotopic heart transplant and later removal of her ICD generator and leads. She continues close follow-up with her care team.

CONCLUSIONS

Benign cardiac tumors are rare, and cardiac hamartomas are among the rarest. This case report highlights the diagnostic challenge posed by the rare subtype of mesenchymal cardiac hamartoma and the therapeutic dilemma in managing associated tachyarrhythmias. Given the similarities to HCM on clinical presentation and diagnostic imaging, it is prudent to maintain an appropriate index of suspicion and to seek for an alternative diagnosis in future cases of young patients with treatment refractory VT in the setting of an atypical cardiac mass. Cardiac transplantation should remain in the diagnostic and therapeutic armamentarium—but should be used as a last resort.

ADDRESS FOR CORRESPONDENCE: Dr. Olujimi A. Ajijola, UCLA Cardiac Arrhythmia Center, David Geffen School of Medicine at UCLA, 100 Medical Plaza, Suite 660, Los Angeles, California 90095. E-mail: oajijola@mednet.ucla.edu. Twitter: @zekunfengmd.

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KEY WORDS cardiac hamartoma, electrophysiology, refractory ventricular tachycardia