Case in Point

Genetic Heart Failure in an Active-Duty Soldier

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A 45-year-old soldier who presented to the emergency department with heart failure underwent a cardiac MRI, revealing prominent trabeculations consistent with left ventricular noncompaction.

Left ventricular noncompaction (LVNC) is a rare disorder that is variably classified as a primary genetic cardiomyopathy (CM) by the American Heart Association.[1] It is mostly believed to be a congenital abnormality, characterized by the arrest of the typical embryonic myocardial maturation process with the subsequent retention of the trabecular myocardial structure, which defines the early embryonic heart.[2]

During very early embryonic development, the left ventricular (LV) myocardium is composed of a loose network of fibers separated by deep recesses, which link it with the LV cavity. At 8 weeks of prenatal development, gradual compaction of these fibers occurs, and LVNC is thought to result from the arrest of this normal process.[2,3] Significant variability in myocardial involvement exists, ranging from panventricular to isolated apical involvement, likely related to time of arrest of this maturation process.[4] The decreased contractile capability and inadequate epicardial coronary system communication of this trabecular endocardium is thought to lead to the clinical manifestations of LVNC.[1-7]

This report describes the case of a 45-year-old male soldier who presented with a unique case of heart failure, diagnosed via cardiac magnetic resonance imaging (MRI).

CASE STUDY

The patient presented to the San Antonio Military Medical Center emergency department in mid-2011 with increasing dyspnea for several weeks. He also reported significant lower-extremity and scrotal edema. Although the patient had been previously healthy, his recent medical history was remarkable for a severe combat injury suffered while on duty with the U.S. Army in Afghanistan: He was involved in an explosion from an improvised explosive device in August 2009. He was medically evacuated to the U.S., where he required multiple hospitalizations and surgeries. Prior to his current presentation, the patient had been briefly hospitalized for hospital-acquired pneumonia. During this hospitalization, he first noted abnormal swelling of his legs, a finding that was initially attributed to the large sodium load he had received with his IV antibiotics.

DIAGNOSIS

The patient's vital signs on presentation were notable for 100/83 mm Hg blood pressure, 103 beats per minute (bpm) heart rate, and 18/min respiratory rate with a saturation of 100% on 4 liters of oxygen by nasal cannula. He was conversant but tachypneic and had to pause frequently to catch his breath. His neck veins were notably distended with jugular venous pulsations visible to the angle of the jaw with the patient at 30 degrees. His heart sounds were normal without an S3, but his lungs were notable for bilateral crackles over the lower- to mid-lung fields. He had profound bilateral upper and lower extremity and scrotal pitting edema. He had no lymphadenopathy or skin rashes.

On presentation, the patient's laboratory results were remarkable for a 444 pg/mL brain natriuretic peptide. A chest X-ray revealed bilateral basilar opacities. An electrocardiogram showed normal sinus rhythm

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(70 bpm), with normal axis and poor R-wave progression across the precordium. An echocardiogram was performed and notable for a moderately dilated left ventricle with severely depressed systolic function of 10% to 15%, and elevated pulmonary artery pressures. Subsequently, the patient was referred for a coronary angiography, which showed no evidence of coronary atherosclerosis. A cardiac MRI was then performed to evaluate for nonischemic CM, which revealed prominent trabeculations in both ventricles, but most notably in the left ventricle, consistent with a diagnosis of LVNC.

The patient was treated with diuretics, beta-blockers, and an angiotensin-converting enzyme (ACE) inhibitor with improvement in his heart failure symptoms. He was started on systemic anticoagulation with warfarin for his severely depressed LV function. His hospital course was complicated by frequent, nonsustained ventricular tachycardia (VT), and he was referred to the electrophysiology service for implantation of an automated intracardiac cardioverter/defibrillator (AICD) for primary prevention of sudden cardiac death. His clinical course was otherwise unremarkable, and he was discharged after 8 days with complete resolution of his symptoms.

DISCUSSION

The clinical presentation of LVNC is typically due to complications of ventricular dysfunction, including heart failure, arrhythmias, and cardioembolic events. Retrospective studies have shown much variability in the frequency of these complications, likely due to selection bias in earlier studies. These earlier studies had suggested a frequency of heart failure > 50%, but recent studies have shown a more modest frequency of 30% to 35% of affected patients.

Even greater variance has been found in the frequency of arrhythmias, but most studies have shown a frequency of at least 20% for VT. Poor blood flow in the deep intertrabecular recesses in patients with LVNC is additionally thought to lead to a predisposition for mural thrombus formation with an elevated frequency of systemic embolic events, ranging from 5% to 20% among previous studies.[1-4,6,8]

Much debate remains regarding the genetic association of this condition. The unique character of the resulting myocardium suggests a distinct CM, but the significant genetic heterogeneity with sarcomere protein gene mutations associated with several other CMs, including hypertrophic and dilated CM, suggests that LVNC may simply exist on a phenotypic continuum with these other conditions.[4] Inheritance shows additional similarities to these other known CMs with autosomal-dominant and X-linked modes of transmission shown with familial forms in about 25% of patients.[5,7] This has led many to believe that screening of first-degree relatives of clinically affected patients may be appropriate.

The prevalence of LVNC in adults referred for echocardiography is about 0.014% to 1.3%.[5] A recent increase in the rate of recognition has raised concerns of possible overdiagnosis, with attempts now made to develop specific imaging diagnostic criteria. Diagnosis of LVNC is most commonly suspected (but can be missed) on echocardiography using 2-D and color Doppler imaging modalities. Echocardiographic findings supporting the diagnosis of LVNC suggested by Oechslin and colleague include:

- Presence of multiple trabeculations, particularly in the LV apex and free wall;
- Multiple deep trabeculation recesses in communication with the LV cavity, usually seen on color Doppler imaging;
- A 2-layered structure of the endomyocardium with ratio of end systolic, noncompacted endocardial layer to compacted epicardial layer > 2 in adults; and
- Absence of other congenital or acquired heart disease, particularly those causing LV outflow obstruction.[8]

Another proposed standardized method for identifying LVNC via echocardiography by Chin and colleagues focuses on trabeculae at the LV apex on the parasternal short axis and apical views.[2,3] LVNC is defined by a ratio of X/Y of ≤ 0.5, where X is the distance from the epicardial surface to the trough of the trabecular recess, and Y is the distance from the epicardial surface to the peak of the trabeculations.

Cardiac MRI is now a more common mode of imaging used for diagnosis of LVNC and often has better imaging characteristics than those of echocardiography. Using a ratio of noncompacted to compacted CM in diastole > 2.3 is suggestive of LVNC with sensitivity and specificity of 86% and 99%.[9]

The management of LVNC focuses primarily on treatment of complications, including heart failure, rhythm disturbances, and thromboembolic events. Treatment of heart failure is typically the same as for other CMs and includes medical therapy with salt restriction, diuretics, beta-blockers, and ACE inhibitors. In addition, exercise training, as tolerated, is beneficial to improve clinical status.[3,10] Electrophysiology studies are often performed in

these patients, and implantation of an AICD is typically done in cases of documented, sustained VT, presyncope with inducible VT or severally depressed ejection fraction of < 35%.[4,10] Deep intertrabecular recesses and impaired blood flow increase the risk of thrombus formation. Hence, anticoagulation with warfarin (international normalized ratio target 2.3) for those with an impaired LV ejection fraction (< 40%) should be considered for the prevention of cardioembolic events.[3,4,6,10]

SUMMARY

An active-duty solider with a history of battlefield trauma and multiple hospitalizations was admitted for symptomatic heart failure with cardiac MRI suggestive of LVNC. This condition is a phenotypic result of genetic heterogeneity with significant variability in clinical presentation and a predisposition for heart failure, ventricular arrhythmias, and systemic embolic events. The etiology of this patient's clinical presentation remains unclear, and additional research is needed to understand whether his recent trauma and multiple hospitalizations played a role in the manifestation of his disease. ●

Author disclosures

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