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INTERMEDIATE

CASE REPORT: CLINICAL CASE

Pregnancy in Familial Left Ventricular Noncompaction-Associated Cardiomyopathy

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ABSTRACT

Left ventricular (LV) noncompaction is a phenotypic variant of LV structure; however, it also can be associated with cardiomyopathies. Pregnancy in the setting of LV dysfunction carries a risk of maternal and fetal morbidity and mortality. Multidisciplinary cardio-obstetrical care is paramount in the management of pregnancy in this unique population. (**Level of Difficulty: Intermediate.**) (J Am Coll Cardiol Case Rep 2020;2:120–4) © 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 27-year-old female patient with a history of familial, left ventricular noncompaction (LVNC)-associated cardiomyopathy presented at 20 weeks' gestation with palpitations. She was referred to our tertiary care center for cardio-obstetrics consultation.

LEARNING OBJECTIVES

- To understand the spectrum of causes of left ventricular noncompaction and its associated cardiomyopathy.
- To monitor, anticipate, and manage complications of dilated cardiomyopathies in pregnancy.
- To highlight the importance of a multidisciplinary cardio-obstetrical team for preconception counseling and peripartum management of women with existing cardiomyopathies.

MEDICAL HISTORY

The patient had a history of a familial, dilated cardiomyopathy initially diagnosed at the age of 8 and later phenotyped as LVNC-associated cardiomyopathy. She was treated with beta-blockers and angiotensin-converting enzyme (ACE) inhibitors and maintained a left ventricular ejection fraction (LVEF) of 52%. Family history was significant for a familial cardiomyopathy most consistent with an autosomal dominant pattern of inheritance (**Figure 1**). The patient and her family had undergone genetic testing with mapping of susceptibility to chromosome 1q32 without any subsequent molecular genetic testing. She had a history of a prior spontaneous miscarriage at 8 weeks' gestation. She had not been previously counseled about the risks of pregnancy given her cardiomyopathy.

DIFFERENTIAL DIAGNOSIS

Palpitations during pregnancy are not uncommon and may manifest for the first time during pregnancy as a result of increased plasma volume and cardiac

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Informed consent was obtained for this case.

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output, higher resting heart rate, increased arrhythmic potential due to atrial and ventricular stretch, as well as direct hormonal effects on the conduction system. An atrial tachyarrhythmia was considered, but there was greater concern for a ventricular dysrhythmia because of patient's known cardiomyopathy.

INVESTIGATIONS

The electrocardiogram demonstrated normal sinus rhythm without any abnormalities. Transthoracic echocardiogram (TTE) at 22 weeks' gestation demonstrated a mildly dilated and diffusely hypokinetic left ventricle (LV) (LVEF 47%) with prominent LV trabeculations and a ratio of noncompacted to compacted (NC/C) myocardium of 2.6 in end-systole at the inferior and lateral mid-ventricular level. There was no evidence of intraluminal thrombus (Figure 2). Cardiac magnetic resonance imaging performed before conception demonstrated mild LV dysfunction (LVEF 49%) with an NC/C myocardium ratio >2.3 in the mid-inferior, apical inferior, and mid-lateral segments, suggestive of LVNC phenotype (Figure 3).

MANAGEMENT

The patient was seen in consultation by the multidisciplinary Cardiovascular Disease and Pregnancy Service at our institution consisting of maternal fetal medicine, cardiac anesthesia, and cardiology. Ambulatory electrocardiogram monitoring demonstrated rare premature ventricular contractions without sustained supra or ventricular tachyarrhythmias. ACE inhibitor therapy had been discontinued preconception and beta-blockade was continued throughout pregnancy. She was monitored closely for complications associated with LVNC-associated cardiomyopathy, including heart failure (HF), arrhythmias, and thromboembolism. She was initiated on low-dose aspirin given higher risk of formation of intracardiac thrombi and associated hypercoagulability of pregnancy; however, therapeutic anticoagulation was deferred. She was referred for genetic counseling and testing given the potential implications for transmission of her phenotype to her fetus. Fetal echocardiogram demonstrated no cardiac abnormalities. She developed progressive dyspnea

ABBREVIATIONS AND ACRONYMS

ACE = angiotensin-converting enzyme

HF = heart failure

LV = left ventricle

LVEF = left ventricular ejection fraction

LVNC = left ventricular noncompaction

NC/C = noncompacted to compacted

TTE = transthoracic echocardiogram

FIGURE 1 Family Pedigree

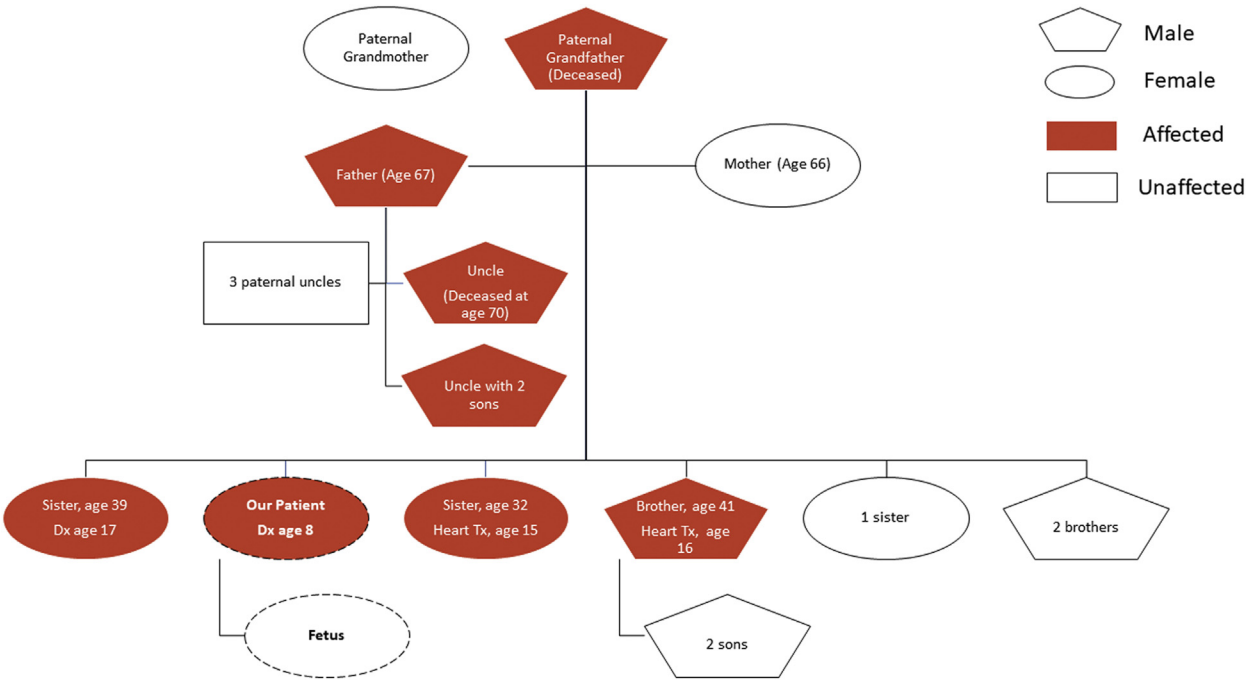
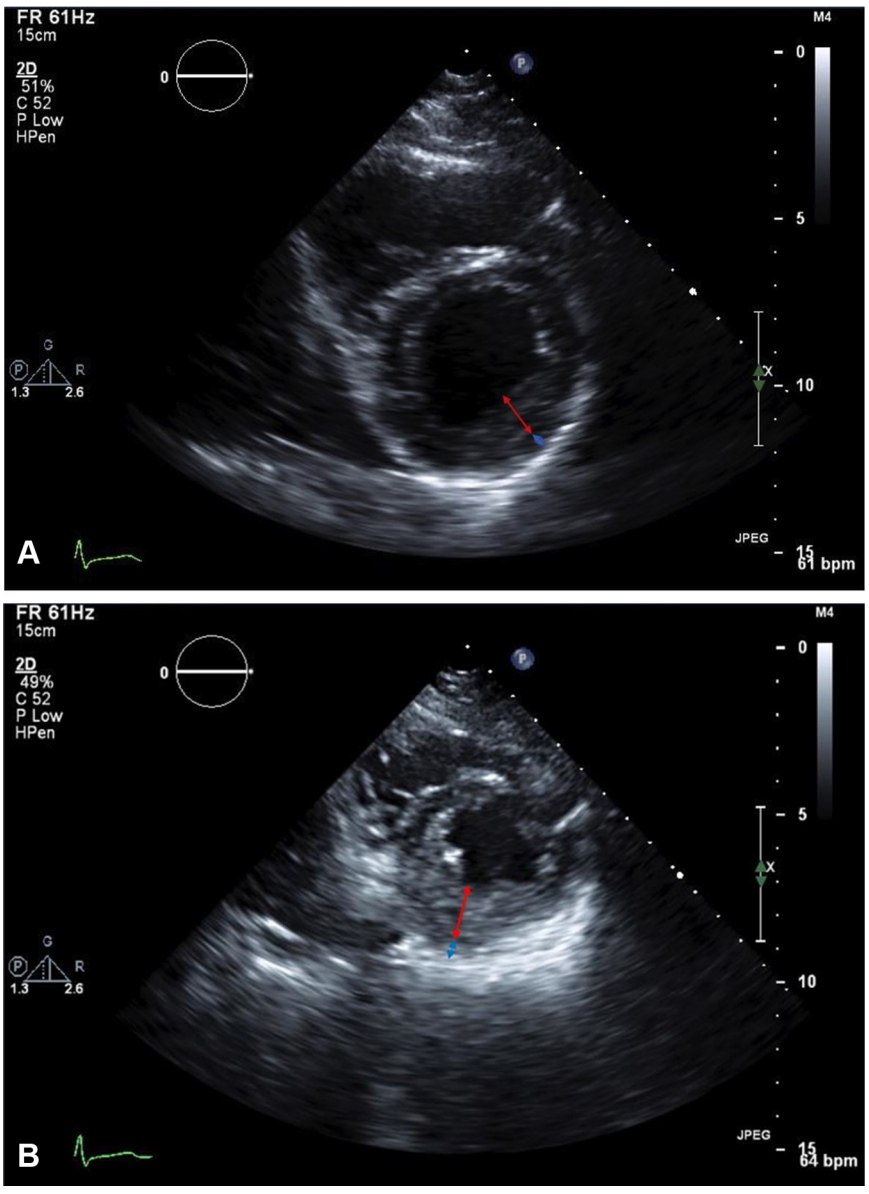


FIGURE 2 Transthoracic Echocardiogram at 22 Weeks' Gestation



Parasternal short axis of the mid **(A)** and apical **(B)** left ventricle demonstrating a thick layer of noncompacted myocardium **(red)** compared with compacted **(blue)** myocardium (ratio >2.3 at end-systole) most prominent in the inferior and inferolateral segments.

and clinical HF prompting initiation of diuretic therapy. Repeat TTE at 36 weeks demonstrated a decline in LVEF to 35% with progressive LV dilation (Table 1). The decision was made for induction of labor at 37 weeks' gestation with central venous pressure monitoring with cardiac anesthesia present at the time of induction.

DISCUSSION

LVNC is now increasingly recognized as a phenotypic variant of LV structure characterized by the prominence of LV trabeculations, deep intertrabecular recesses, and a thin, compacted layer of myocardium (1). The spectrum of LVNC ranges from a normal

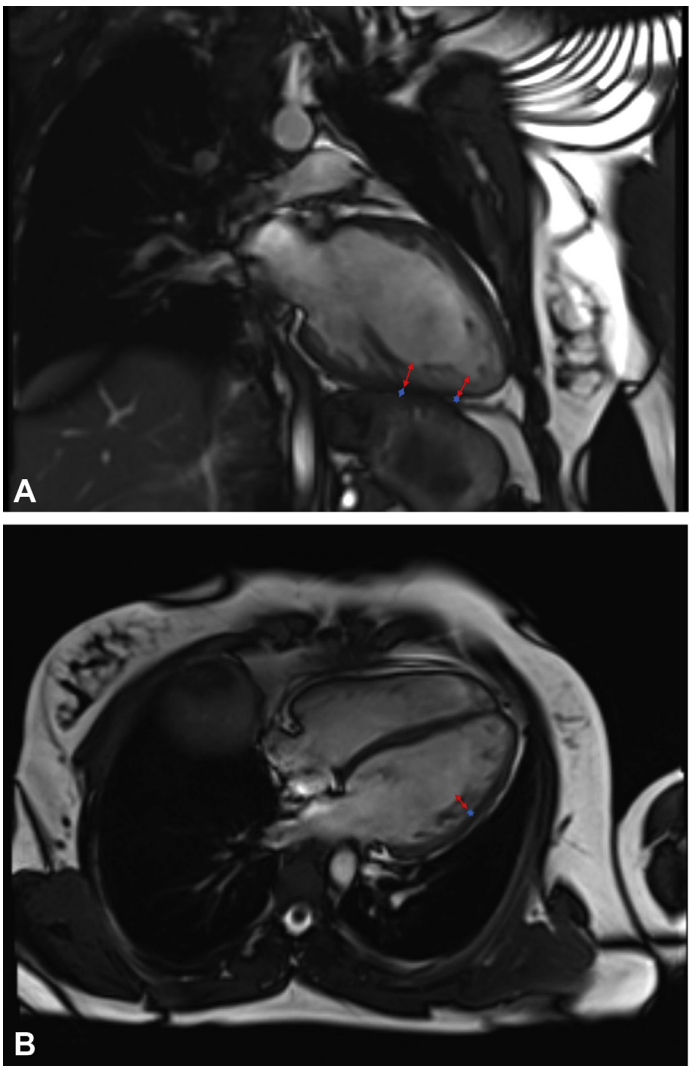
variant in LV structure in the setting of normal LV function, acquired LVNC in the setting of changes in LV mechanical loading conditions (i.e., athletes, pregnancy), and genetic LVNC syndromes associated with chromosomal anomalies, congenital heart disease, and/or cardiomyopathies (1).

The most widely used criteria for the diagnosis of LVNC rests on the presence of a high ratio (>2.3) of NC/C layers of the LV wall using TTE; however, these criteria lack specificity and no consensus criteria exist for the gold standard diagnosis of LVNC (2). Cardiac magnetic resonance imaging has shown low specificity and high prevalence of LVNC phenotype among a healthy population (3). In addition, pregnancy has been shown to induce de novo LV trabeculations in approximately a quarter of women of whom a proportion will meet criteria for LVNC (4).

There are several case reports describing the outcomes of patients with LVNC-associated cardiomyopathy; however, the risks of pregnancy in this cohort are most closely associated with the underlying primary cardiomyopathy (5). Pregnancy is poorly tolerated among some women with preexisting dilated cardiomyopathies. Among this group, the risk of adverse cardiac events is most intimately associated with the severity of preconception LV dysfunction (LVEF <30%) and/or New York Heart Association functional class III or IV. Pregnancy also carries some risk of irreversible deterioration in LV function postpartum (6,7). Because of these risks, expert consensus guidelines recommend periconception counseling in all patients with a history of cardiomyopathy (6). In addition, patients with a history of familial cardiomyopathy should undergo preconception genetic counseling with consideration of genetic testing, as most of the genes associated with LVNC cardiomyopathy have overlap with other cardiomyopathies and are associated with an autosomal dominant pattern of inheritance.

There exist no guidelines in relation to the specific pharmacological care of LVNC-associated cardiomyopathy during pregnancy. HF is the most common complication, which can be managed with diuretics, beta-blockers, and vasodilators with avoidance of ACE inhibitors, angiotensin receptor blockers, mineralocorticoid receptor antagonists, and ivabradine, which are contraindicated antepartum due to their teratogenicity. Beta-1 selective blockers are favored to minimize beta-2 mediated uterine relaxation and peripheral vasodilation; however, most beta-blockers, particularly atenolol, have been associated with fetal growth restriction (6).

FIGURE 3 Cardiac Magnetic Resonance Imaging



Vertical **(A)** and horizontal **(B)** long axis views at end-diastole showing representative measurements of thickness of the noncompacted trabeculated **(red)** to compacted myocardium **(blue)** ratio >2.3 in the mid-inferior **(A)**, and apical inferior **(A)**, and mid-lateral **(B)** segments.

The optimal strategy for managing thromboembolic risk in this population is unclear, and as a result, shared decision making should play a central role in determining the most appropriate treatment choice. Anticoagulation with either low-dose warfarin (<5 g/day) or dose-adjusted low molecular weight heparin, should, however, be prescribed in those with prior cardioembolic event or intracardiac thrombus, and may be considered in patients with atrial fibrillation and impaired LV function. The mode of

TABLE 1 Transthoracic Echocardiogram Changes in LV Chamber Dimensions and Systolic Function

Gestational Age	LV Internal Diameter Dimension Diastole, mm	LV Internal Diameter Dimension Systole, mm	LVEF, %
22 weeks	58	38	47
36 weeks	62	48	35
Postpartum (16 weeks)	59	48	39

LV = left ventricle; LVEF = left ventricular ejection fraction.

delivery should be discussed in a multidisciplinary fashion by the cardio-obstetrical team and the patient. In patients with stable HF, vaginal delivery remains the preferred method; cesarean delivery is usually reserved for obstetrical indications. Continuous central venous pressure monitoring with intensive care unit-level care should be considered for patients with HF or at high risk for developing HF at the time of delivery for guidance with fluid management. The development of cardiogenic shock and intractable HF are cardiac indications for cesarean delivery (6).

Despite improvement in perinatal and cardiovascular care over the past decade, the rates of maternal mortality continue to increase in the United States. Women with known cardiovascular disease represent a unique population who benefit from the care of a specialized cardio-obstetrical team for preconception planning, peripartum care, and postpartum risk reduction (8).

FOLLOW-UP

The patient underwent successful induction of labor at 37 weeks culminating in an uncomplicated vaginal delivery. TTE postpartum on ACE inhibitor and beta-blocker therapy demonstrated persistent LV dysfunction (LVEF 39%) with a decrease in LV chamber size (Table 1). She was counseled regarding risks of a recurrent pregnancy. Her CARPREG (Cardiac Disease in Pregnancy Study) 2 risk score was 5, which estimated her risk of an adverse cardiac event (primarily HF and/or arrythmia) at 41% for a subsequent pregnancy (9). Her daughter did not carry the genetic variant and with the desire for continued family building, she is planning a gestational carrier pregnancy.

CONCLUSIONS

LVNC is an LV phenotypic variant that can be associated with a cardiomyopathy. Women with existing dilated cardiomyopathies are at risk of peripartum complications and irreversible LV dysfunction requiring careful preconception counseling and peripartum care.

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