

Case Report

Flash Pulmonary Edema: A Case and Review of Left Ventricular Non-Compaction Cardiomyopathy

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Abstract

Description

Left ventricular non-compaction cardiomyopathy is an uncommon type of cardiomyopathy caused by malformation of the myocardium during embryogenesis. This results in trabeculations within the ventricular wall that can affect the left and, less commonly, right ventricles. Presentation ranges from clinically asymptomatic to life-threatening arrhythmias. It is a rare and relatively unknown form of cardiomyopathy, though thought to be underdiagnosed. Prevalence is increasing due to improvements in imaging and awareness. Management is similar to that of other cardiomyopathies including angiotensin-converting-enzyme inhibitors or angiotensin receptor blockers, beta-blockers, diuretics, automatic implantable cardioverter defibrillator placement and cardiac transplantation. We present a case of a 38-year-old, otherwise healthy, Indian male who presented with flash pulmonary edema and was found to have left ventricular non-compaction cardiomyopathy. This report includes a review of left ventricular non-compaction cardiomyopathy.

Keywords

cardiomyopathies/physiology/etiology/genetics; arrhythmia; pulmonary edema/etiology; echocardiography; spongiform cardiomyopathy; LVNC; inborn genetic diseases

Introduction

Left ventricular non-compaction cardiomyopathy (LVNC), also known as non-compaction cardiomyopathy or spongiform cardiomyopathy, is a rare phenotype of cardiomyopathy. Sporadic and inherited forms have been described. Bellet and Gouley first described characteristics of LVNC in 1932 after a newborn autopsy.¹ Dusek et al. later described the post-natal persistence of intertrabecular spaces and sinusoids seen in LVNC in histologic sections of postmortem analysis of stillborns, newborns and infants.² In 1984, echocardiographic features of LVNC were described by Engberding and Bender.^{1,3} Diagnosis remains challenging, with no universal criteria established. Here we report a case of LVNC presenting as flash pulmonary edema and heart failure, review common diagnostic criteria and discuss principles of management.

Case Description

A 38-year-old Indian male with no significant medical history presented to a freestanding emergency room complaining of shortness of breath and a cough productive of pink, frothy sputum. Upon initial examination, he was found to have two-word dyspnea, elevated blood pressure and tachycardia. A chest x-ray was significant for bilateral airspace disease. He was placed on non-invasive positive pressure ventilation and given intravenous furosemide and ceftriaxone. His respiratory status continued to decline, and he was intubated prior to transfer to our hospital. He was admitted to the intensive care unit where vasopressor support and broad-spectrum intravenous antibiotics were initiated.

Laboratory studies were significant for elevated lactic acid (3.7 mmol/L), leukocytosis (26.6/ μ L), elevated troponin (0.093 ng/ml, peaked at



Figure 1. Apical 4-chamber view demonstrating classic non-compaction cardiomyopathy appearance with prominent trabeculations and intertrabecular recesses.

0.471 ng/ml), and a pro-BNP of 1090 pg/ml. An electrocardiogram revealed sinus tachycardia. Initial echocardiogram showed mild concentric left ventricular hypertrophy, left ventricular ejection fraction of 28%, diffuse left ventricular hypokinesia and grade 3 diastolic dysfunction. Increased trabeculations and blood flow through intertrabecular recesses within the apex of the left ventricle were also noted. **(Figure 1)** Non-compaction to compaction (NC/C) ratio of 2.1 was consistent with non-compaction cardiomyopathy by Zurich criteria. **(Figure 2)**

Discussion

Left ventricular non-compaction cardiomyopathy (LVNC) results from abnormal embryogenesis of the myocardium. Development of the heart in utero begins with a meshwork of

muscle fibers and trabeculations that allow blood flow to the ventricle before coronary vasculature develops. Once coronary vessels form, the trabeculated myocardium compacts into a smooth endocardial surface.⁴ LVNC results from failure of this transition, which normally occurs in the 12th to 18th week of embryogenesis. This results in the formation of a thickened endomyocardial layer with deep recesses, trabeculae that are continuous with the left ventricular cavity and a thin compacted epicardial layer.^{1,3-5} Similar sinusoidal phenotypes can be seen in association with other inherited heart defects, such as pulmonary atresia. In isolated LVNC, sinusoids do not communicate with the epicardial circulation and are present primarily in the apex and lateral walls of the heart.⁶⁻⁷

Sporadic and inherited forms of LVNC have been described. LVNC is inherited in 15-20% of



Figure 2. Parasternal short axis view showing >2:1 ratio of non-compacted to compacted myocardium. End-systole. (Zurich criteria)

cases and more commonly identified in childhood.⁵⁻⁶ Patients diagnosed at infancy are often more severely affected.⁵ Among the inherited forms, X-linked, autosomal dominant, autosomal recessive and mitochondrial inheritance have been reported. Implicated genes code sarcomeric, cytoskeletal and ion channel proteins.⁴ Sarcomeric gene mutations MYH7, MYBPC3, ACTC1, LDB3, TNNT2, and TPM1 are known to cause LVNC.⁸ Cytoskeletal genes implicated include DTNA and LMNA. HCN4 and SCN5A are the known LVNC-causing ion-channel gene mutations. Additionally, associated genes include MIB1, PRDM16 and TAZ.⁸ Familial LVNC often co-exists with neuromuscular disorders, such as Barth syndrome and myotonic dystrophies.³⁻⁵

Cases of LVNC have been identified in utero to the 10th decade of life, and males appear to be predominantly affected.⁹ Prevalence is estimated to range from 0.014% to 0.24% and up to 3–4% in all patients with heart failure.⁹⁻¹¹ Increase in incident cases is potentially related to improved clinical recognition and diagnosis due to higher resolution in imaging modalities, such as cardiac magnetic resonance imaging (CMR) and widespread awareness of the clinical entity.¹¹

LVNC presentation can vary from clinically asymptomatic to fatal arrhythmias. Findings at presentation can include systolic or diastolic heart failure, arrhythmia and systemic thromboemboli.^{4,12} Asymptomatic patients are identified incidentally upon cardiac imaging or after referral for genetic testing.¹¹ Presence of ventricular arrhythmia is estimated at 2–62% and roughly 40% in children.^{4,13} The incidence of sudden cardiac death varies between 6–23%.^{2,14} Systemic thromboemboli are more common in LVNC than other cardiomyopathies, affecting between 5–38% of patients with an event rate of 1–2% per year.³⁻⁵

Diagnosis of LVNC is made through echocardiography, CMR or cardiac computed tomography (CT). Electrocardiogram findings support this diagnosis but are not confirmatory.¹³ There are currently no universal criteria for diagnosis. Echocardiography is historically the imaging modality of choice.^{13,15} The two most widely used sets of diagnostic tools are the California and the Zurich criteria. Both require the

absence of coexisting cardiac anomalies and the presence of a bilayered endomyocardium with a thickened, non-compacted layer and a thin compacted layer.^{10,12,16} The California criteria focuses on posterior wall thickness to depth of recesses at end-diastole while the Zurich criteria measures non-compaction to compaction (NC/C) ratio at end-systole.⁹⁻¹¹ The Vienna criteria requires images at both end-systole and end-diastole.¹⁷ The Milwaukee criteria compares the NC/C layer in various windows and cardiac cycles.¹⁸ These criteria are illustrated in **Table 1**. CMR provides added information in patients with technically difficult or limited ultrasound studies and allows better visualization of the left ventricular apex and detection of myocardial fibrosis using late gadolinium enhancement.¹³ A proposed CMR criteria for the diagnosis of LVNC is a NC/C ratio of greater than 2.3 in diastole.¹⁹ Cardiac CT can be used to assess concurrent coronary artery disease (CAD) in low-risk CAD patients.³

Management is based on the pathologic symptomatology of the disease. In asymptomatic patients, clinical follow-up may be the only management necessary.¹ Heart failure and arrhythmias are treated according to existing evidence-based guidelines, which include cardiac transplantation in appropriate patients with disease that is refractory to medical therapy. Anticoagulation in LVNC is a debated topic. Anticoagulation should be considered in patients thought to be at elevated risk for thromboembolism, such as those with LV dysfunction or prior embolic events. Anticoagulation should be initiated for those in whom an atrial or ventricular thrombus is identified.¹ While management is unchanged when an LVNC-causing mutation is found in an index patient, cascade genetic testing is recommended and first-degree relatives should be evaluated.⁵

Our patient was treated with intravenous diuretics and guideline-directed medical therapy for dilated cardiomyopathy, including sacubitril/valsartan. Cardiac catheterization was performed after the patient's volume status stabilized, which revealed angiographically normal coronary arteries and diffuse left ventricular hypokinesis. An automatic implantable cardioverter defibrillator was recommended, which the patient declined. Genetic testing and

Table 1. Echocardiographic criteria for non-compaction cardiomyopathy.

	Chin et al.^{12,16,18} (California criteria)	Jenni et al.^{10,18} (Zurich criteria)	Stöllberger et al.¹⁸ (Vienna criteria)	Paterick et al.^{17,18} (Milwaukee criteria)
Echocardiogram view	Parasternal short-axis and apical views	Short-axis views	End-systolic and end-diastolic images must be viewed	Bilayered myocardium should be seen in the following views: •Short-axis view at mid and apical areas •Apical 2- and 4-chamber views •Apical long-axis views
Criteria	Ratio X/Y ≤ 0.5, calculated at end-diastole Where: •X = distance from the epicardial surface to the trough of the trabecular recesses •Y = distance from the epicardial surface to the peak of the trabeculation	•Multiple prominent trabeculations (primarily in the apex, mid-lateral, and mid-inferior areas of the left ventricular wall) •Non-compaction to compaction (NC/C) > 2.0 at end-systole measured at maximal wall thickness •Color Doppler imaging that shows multiple deep intertrabecular recesses communicating with the ventricular cavity	All 4 criteria must be met: •More than 3 prominent trabeculations along the left ventricular wall seen in end-diastole •Trabeculations should move with the compacted myocardium •Trabeculations are best seen in end-systole •Color Doppler imaging that shows perfusion of intertrabecular spaces at end-diastole	•NC/C > 2.0 at end-diastole; preferably measured in the short-axis views •Abnormal ventricular function and myocardial mechanics

repeat imaging were recommended as well but, the patient was lost to follow-up before these procedures could be completed.

Conclusion

LVNC is a rare phenotype of cardiomyopathy and must be considered when patients present with symptoms of heart failure. Both sporadic and inherited forms have been described. LVNC presentation can vary from clinically asymptomatic to end-stage heart failure with sequelae causing sudden cardiac death. Increase in cases are likely due to improved clinical recognition. LVNC diagnosis remains challenging, and no universal criteria have been established. The

two most widely used sets of diagnostic tools are the California and Zurich criteria. Management is dependent upon the clinical presentation.

Conflicts of Interest

The authors declare they have no conflicts of interest.

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