CASE REPORTS

Ventricular Non-Compaction Cardiomyopathy

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Non-compaction of the left ventricle is an extremely rare cardiomyopathy resulting from a defective morphogenesis of the endomyocardium. It results in an architecturally aberrant ventricular wall consisting of two layers: a compacted layer and a loose interwoven meshwork with prominent trabeculae and deep intertrabecular recesses that communicate with the left ventricular cavity. This report describes the case of a 25-year-old man with dilated cardiomyopathy, due to non-compaction of the left ventricle, presenting with a transient ischemic attack.

Key words: Non-compaction, Cardiomyopathy, Hypertrabeculation

A 25-year-old man presented to the emergency room because of sudden onset of dizziness, slurred speech, and weakness of the right-sided extremities. Diagnosis of dilated cardiomyopathy had been established five months prior to this incident, when he developed signs and symptoms compatible with congestive heart failure. Conventional treatment for heart failure was instituted.

Physical examination revealed mild dysarthria, 0/5 strength in the right upper extremity, and 2/5 strength in the right lower extremity. A grade 2/6 pansystolic murmur at the left lower sternal border was also appreciated. The remainder of the examination was within normal limits.

Head computed tomography (CT) scan failed to reveal evidence of acute intracranial pathology and within the next 24 hours, neurologic symptoms had resolved, for which a diagnosis of Transient Ischemic Attack (TIA) was established.

A transthoracic echocardiogram with contrast media demonstrated a hypokinetic and markedly dilated left ventricle with a double-layer arrangement consisting of a thin epicardial muscle layer and a thick endocardium (Figure 1) consisting of multiple trabeculae and deep recesses (Figure 2), suggestive of Left Ventricular Non-Compaction (LVNC).

Over the following six months, the patient had multiple hospitalizations due to recurrent thromboembolic events and decompensated heart failure. The patient was referred to an electrophysiologist for placement of an implantable cardioverter-defibrillator (ICD). During the procedure, the patient developed an intractable ventricular arrhythmia and subsequently died in spite of appropriate resuscitation measures.

Autopsy confirmed a grossly enlarged heart, weighing 980g. The left ventricular (LV) wall demonstrated segmental thickening with a two-layer arrangement consisting of a thin compacted epicardial layer and a thick, non-compact endocardial layer with prominent trabeculations and deep recesses comprising over 50% of the LV wall (Figure 3), consistent with LVNC. Microscopic examination of the tissue revealed focal fibrosis (Figure 4).

First-line relatives of this patient were submitted to echocardiographic studies, but no abnormalities have been reported so far.
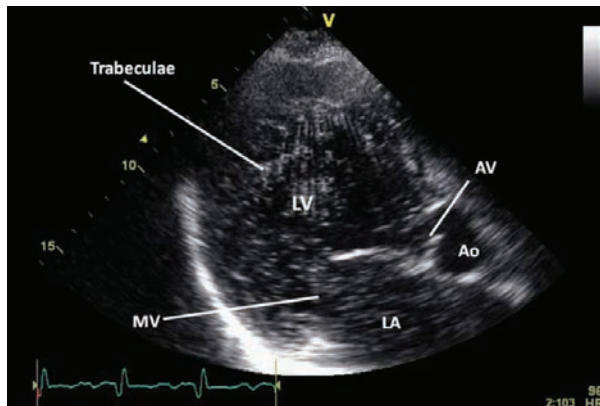
Discussion

Noncompaction of the left ventricle (LVNC) is an extremely rare cardiomyopathy resulting from defective morphogenesis of the endomyocardium. The architecturally aberrant ventricular wall consists of two layers: a compacted layer, and a loose interwoven meshwork with prominent trabeculae and deep intertrabecular recesses that communicate with the left ventricular cavity (1-4). As a result, the myocardium is thickened and may be easily confused with other –albeit more common– cardiomyopathies. This probably explains why even though occasional reports corresponding to LVNC had been published during the second half of the twentieth century (5), the condition remained unrecognized until 1984, and it is still included under "unclassified" cardiomyopathies by the World Health Organization [WHO] (6).

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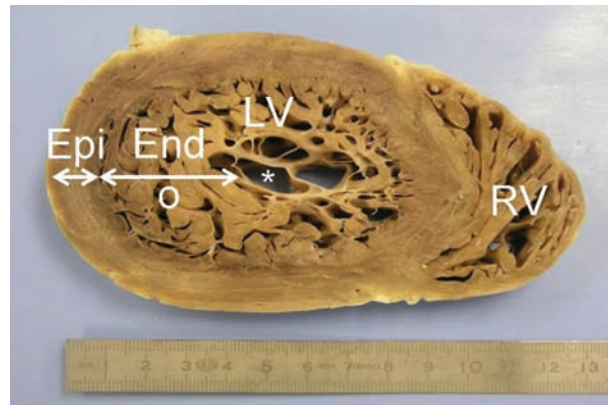
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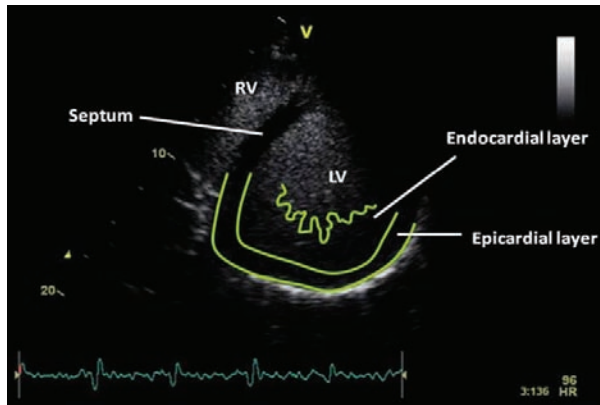
Figure 1. Transthoracic echocardiogram, parasternal short axis view. This view clearly demonstrates the characteristic two-layer arrangement of LVNC, consisting of a thin epicardial layer and a thick endocardial layer. LV = Left ventricle; RV = Right ventricle

Figure 3. Autopsy Heart, Transverse View. Segmental thickening of both ventricular walls demonstrating the two-layer arrangement with a thin compacted epicardial layer and a thick endocardial layer with prominent trabeculations and deep recesses. Endo = endocardium; Epi = epicardium; LV = left ventricle; RV = right ventricle; * = LV cavity

Figure 2. Transthoracic echocardiogram, apical view. In this apical view, multiple apical trabeculae with deep recesses, as well as the double-layer arrangement of LVNC are appreciated. Ao = aorta; AV = aortic valve; MV = mitral valve; LA = left atrium; LV = Left ventricle
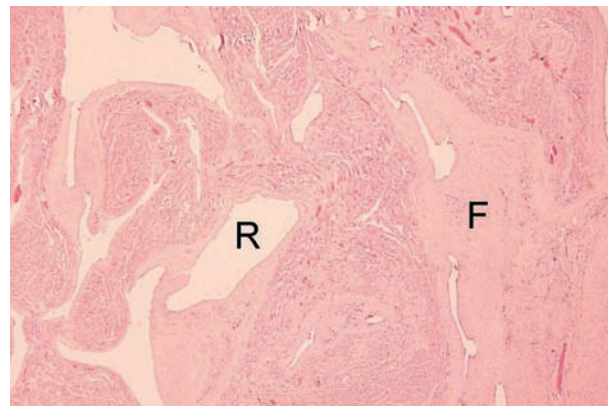
Figure 4. Myocardium, Microscopic View (40x). Segmental fibrosis of the endocardium. F = fibrosis; R = recess

Noncompaction of the ventricular myocardium results from an intrauterine arrest of the cardiac embryogenesis. During the first eight weeks of gestation, trabeculations emerge in the luminal myocardial layers of the ventricles, providing myocardial perfusion in the absence of epicardial coronary circulation by means of intracavitary perfusion, increasing surface area to provide adequate oxygenation (7). As the epicardial coronary vessels develop, the myocardium undergoes compaction through a process of remodeling and resorption; the trabeculae solidify or condensate, adding thickness to the epicardial compact layer. This process is believed to

be abruptly interrupted in LVNC patients (3-4, 8). This pathophysiologic model was challenged by Stollberger and Finisterer (9), who argue in favor of other etiologies for the adult population, as serial echocardiographic observations of apparently originally normal adult hearts documented the development of "acquired" LVNC. Ventricular non-compaction has been documented associated with cardiac abnormalities that promote high intracavitary ventricular pressures, suggesting that these changes might represent hypertrophic and ischemic consequences of the hemodynamic challenge rather than a primary anomaly.

The differential diagnosis includes enlarged trabeculae that may occur with left ventricular hypertrophy and dilated cardiomyopathy, although usually less than three prominent trabeculae may be observed. Endomyocardial fibroelastosis, infiltrative cardiomyopathy, eosinophilic endomyocardial disease, cords, and false tendons are often present in normal hearts, and should also be considered (8). This condition may be isolated, or may be associated with a variety of other abnormalities, such as congenital left or right ventricular outflow tract abnormalities (10), Barth's syndrome, Ebstein's anomaly, and bicuspid aortic valves (11). Left ventricular hypertrabeculation, which is considered a completely separate entity from LVNC (12), may occur in patients with neuromuscular disorders, resembling but not fulfilling LVNC diagnostic criteria (13). For the sake of simplicity, this discussion is limited to isolated LVNC.

The exact prevalence of LVNC is unknown, though it must be emphasized that this entity is easily mistaken for other cardiomyopathies and extensive research in the subject is lacking. In 2000, Oechslin and colleagues (14) published a series of 34 cases of LVNC within a period of 15 years, representing 0.014% of echocardiograms that were performed. Another two retrospective echocardiographic studies on pediatric patients report a prevalence of LVNC of approximately 0.12%, accounting for nearly 10% of diagnosed cardiomyopathies in this population (15-16).

The clinical presentation of LVNC will depend upon the extent of non-compacted cardiac segments, but heart failure, atrial and ventricular arrhythmias, and thromboembolic events constitute the cornerstones of this condition (3, 14, 17-18). Severe systolic dysfunction is reported in the majority of patients, although increased end-diastolic pressure with diastolic dysfunction and restrictive pattern may be present in up to 50% of patients (18). The 34-patient series presented by Oechslin and colleagues (14) established a 79% frequency of dyspnea consistent with New York Heart Association (NYHA) class III or IV heart failure at diagnosis. The architecturally abnormal myocardium also serves as an ideal substrate for development of atrial and ventricular arrhythmias (17), sudden cardiac death being a common occurrence in patients with LVNC. Noncompacted segments are usually hypokinetic with Color Doppler evidence of flow deep within the intertrabecular recesses (14, 19-20), which predisposes to formation of thrombi, leading to thromboembolic events such as cerebrovascular accidents in 20 to 40% of patients.

Diagnosis of LVNC may be established by echocardiography; cardiac magnetic resonance imaging; computed tomography; or ventriculography. In 2001, a group led by Jenni and Oeschlin (2), published four morphologic criteria for echocardiographic diagnosis of LVNC: (a) absence of coexisting cardiac abnormalities; (b) segmental thickening of the ventricular wall demonstrating a two-layer arrangement with a thin compacted epicardial layer and a thick endocardial layer with prominent trabeculations and deep recesses with a ratio of noncompated to compacted myocardium of at least 2:1 at end-systole; (c) predominant localization of the pathology to the mid-lateral, apical, and mid-inferior areas; and (d) Color Doppler evidence of deep perfused intertrabecular recesses (1-2, 13). A prospective study demonstrated the characteristic two-layered structure and wall thickening to be present in 100% of patients with LVNC, whereas hypokinetic segments and perfused recesses were present in 89% and 95% of patients, respectively (1), thus validating these criteria. Burke and colleagues (21) also published a detailed pathologic review including 14 cases, correlating these criteria to anatomical specimens.

The parasternal short axis view best depicts the delineation between the two layers (20). The left ventricle is preferentially involved, with predominant localization of the pathology in the apical mid-lateral, and mid-inferior walls. The right ventricle may be affected in nearly half of cases, as it is in our case, while the interventricular septum is usually spared (8). Other echocardiographic findings include reduced left ventricular ejection fraction, diastolic dysfunction, left ventricular thrombi, and abnormal papillary muscle structure (14). The use of contrast echocardiography may help establish the diagnosis among patients with suggestive but non-diagnostic findings (22). The use of cardiovascular magnetic resonance for diagnosis of LVNC has also been evaluated with positive results (23).

A familial association has been observed in multiple case series. In the 34-patient series published by Oechslin, et al. (14), 18% of patients had a familial history of LVNC. This genetic association is most often autosomal dominant and several gene mutations have been implicated in the development of this condition (24). The G4.5 gene in the Xq28 region, which encodes for tafazzins (15, 25-26), proteins thought to be involved in metabolism of phospholipids has been reported in LVNC patients. This mutation is also responsible for Barth's syndrome and endocardial fibroelastosis. Mutations of the genes coding for alpha-dystrobrevin (4, 26) and Cypher/ZASP (27), proteins involved in linking the extracellular matrix of the myocardial cell to the cytoskeleton, have also been found in familial cases. Though genetic studies are not generally recommended, echocardiographic screening of relatives of patients with LVNC is appropriate, as in one study 8 out of 32 asymptomatic family members had evidence of LVNC, left ventricular dysfunction with or without LVNC, and other cardiac anomalies (18).

Published series demonstrate high rates of morbidity and mortality among patients with LVNC (14). There is no specific therapy for LVNC, and therapeutic goals strive at management of heart failure symptoms, arrhythmias, and prevention of embolic events. Early identification of these patients is important for adequate treatment and prevention of possible complications. Anticoagulation, especially when the fractional shortening falls below 25%, should be considered (28). Heart transplantation is the treatment of choice for patients with end-stage heart failure (5, 14).

Conclusions

This is the first case of left ventricular non-compaction cardiomyopathy reported in Puerto Rico. This condition is rare at the very least. However, its prevalence is probably underestimated, but improvements in echocardiographic imaging, such as the use of contrast media, and increasing awareness of LVNC as a genetic condition, will probably lead to enhanced recognition of previously missed cases.

Resumen

La cardiomiopatía no compacta del ventrículo izquierdo es sumamente rara y resulta de una morfogénesis aberrante del miocardio. Esto resulta en una pared ventricular de arquitectura anormal, que consiste en un arreglo de doble capa: una capa compacta y una capa gruesa en forma de maya con trabécula prominentes y recesos profundos. En este caso presentamos un hombre de 25 años de edad con esta cardiomiopatía.

Acknowledgments

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