






Biventricular non-compaction cardiomyopathy with pulmonary stenosis, interatrial septal aneurysm, atrial septal defect, bradycardia, and mental retardation in a single case: A case report

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Introduction

Non-compaction cardiomyopathy is a rare myocardial disease that belongs to the non-classified congenital cardiomyopathies (1). Although the left ventricle is mainly affected, biventricular involvement has also been described in recent years (2). The clinical features of non-compaction cardiomyopathy are non-specific and can range from being asymptomatic to symptoms of arrhythmia, thromboembolism, and congestive heart failure (2). Non-compaction cardiomyopathy is a complicated disease that can be isolated or be associated with other anomalies, and these patients can present with concomitant pathological findings, including obstructive ventricular anomalies (3, 4), mitral cleft (5), ventricular septal defect (6), and atrial septal defect (7). In 2008, Wessels et al. (8) described a three generation family with nine patients affected by a combination of cardiac abnormalities and left isomerism. The cardiac anomalies included ventricular non-compaction (mostly biventricular), secundum atrial septal defect, pulmonary valve stenosis, and conduction defects. The laterality sequence anomalies included left bronchial isomerism, azygous continuation of the inferior vena cava, polysplenia, and intestinal malrotation, all compatible with left isomerism (8). The authors described these individuals as a member of a new syndrome, which is inherited in an autosomal dominant pattern. A genome-wide linkage analysis suggested a linkage to chromosome 6p24.3–21.2 with a maximum LOD score of 2.7 at the marker D6S276. The linkage interval was located between the markers D6S470 (telomeric side) and D6S1610 (centromeric side) and overlapped with the linkage interval in another family with heterotaxy (8). Herein, we report a 45-year-old woman who had moderate mental retardation and biventricular non-compaction cardiomyopathy in association with other congenital heart malformations.

Case Report

A 45-year-old woman with moderate mental retardation presented to the hospital with dyspnea and cyanosis as the first man-

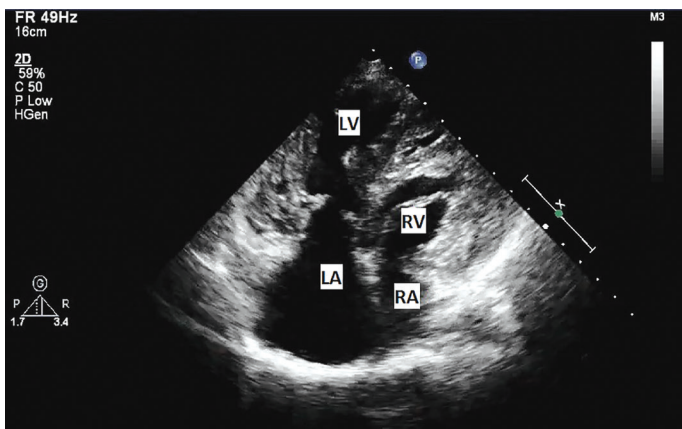


Figure 1. Trabeculated and spongiform appearance of both ventricles in a transthoracic echocardiogram

LA- left atrium; LV- left ventricle; RA- right atrium; RV- right ventricle

ifestation of a heart disease. She had a 6-month history of lower leg extremity edema managed with furosemide by her primary care doctor and presented with worsening lower leg edema and dyspnea on exertion with a decreased exercise tolerance. She had no other significant medical history apart from a history of cognitive impairment from an early age. She was a non-smoker. She had no history of sudden cardiac death or heart failure in her family. Initial vital signs were within normal limits. Cardiovascular examination was remarkable for a systolic murmur of grade 3/6 over the left second intercostal area without radiation to the carotids and a pansystolic murmur of grade 3/6 at the apex with a radiation to the mid-axillary line. The neck examination showed a jugular venous distention of about 7 cm. The chest examination demonstrated reduced breath sounds over both lung bases with basal crackles.

Bilateral pitting pedal edema of grade 1 was noted. She had similar signs and symptoms in the past and was treated for obstructive pulmonary disease with β_2 -agonist drugs. The laboratory workup was unremarkable, except for an elevated brain natriuretic peptide of 1452 pg/mL. Electrocardiography revealed sinus bradycardia, right bundle branch block, and peaked P-waves in DII. A transthoracic echocardiogram (Fig. 1, Video 1) showed a trabeculated and spongiform appearance of the both ventricles, a globally dilated heart with a systolic dysfunction (left ventricle ejection fraction, 35%), moderate mitral and tricuspid regurgitation, and severe pulmonary stenosis (peak systolic velocity, 5.26 m/s) (Fig. 2). The ratio of non-compacted/compacted myocardium in both ventricles was >2 in endsystole, a characteristic of the non-compaction myocardium. Cardiac magnetic resonance imaging confirmed the diagnosis of biventricular non-compaction (Fig. 3, Video 2). Transesophageal echocardiography (Fig. 4, Video 3) revealed interatrial septal aneurysm, which was a localized "saccular" deformity at the level of the fossa ovalis protruded to the right and left atrium and secundum atrial septal defect in addition to biventricular non-compaction and pulmonary stenosis. The patient and her relatives did not accept any further investigation or treatment.

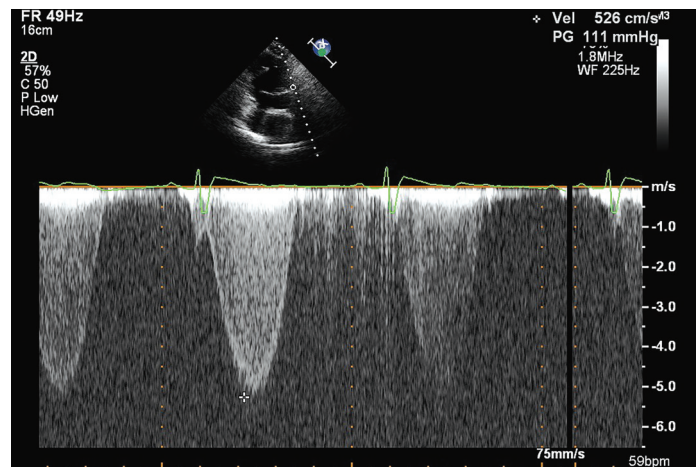


Figure 2. Transthoracic Doppler echocardiogram demonstrating pulmonary peak systolic velocity

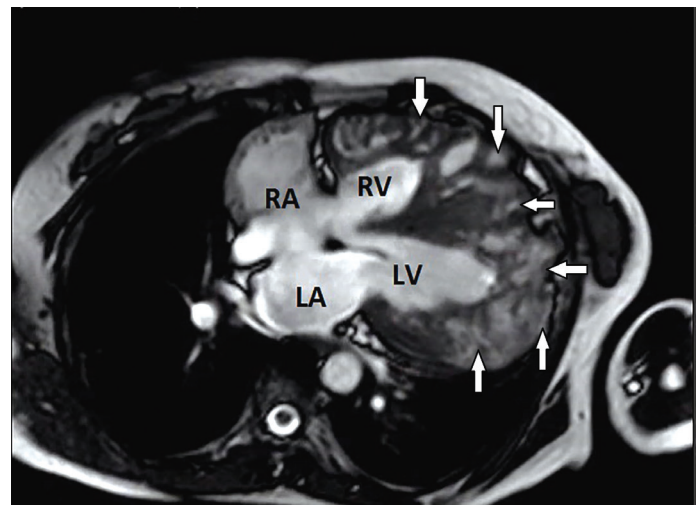


Figure 3. Cardiac magnetic resonance imaging of biventricular non-compaction cardiomyopathy

LA- left atrium; LV- left ventricle; RA- right atrium; RV- right ventricle

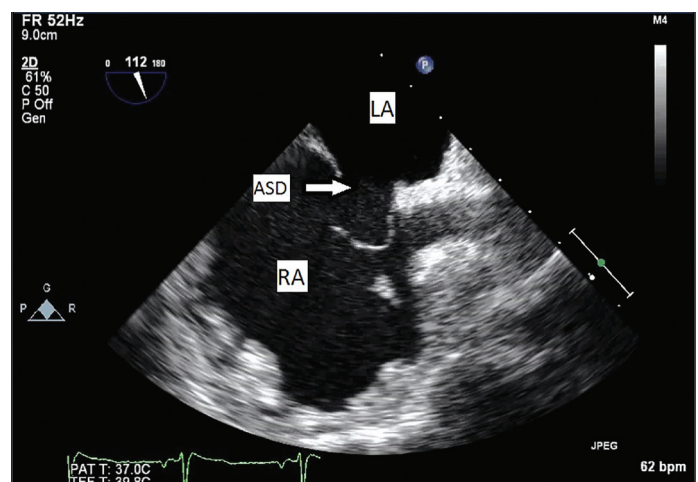


Figure 4. Transesophageal echocardiography demonstrating interatrial septal aneurysm and secundum atrial septal defect

ASD- atrial septal defect; LA- left atrium; RA- right atrium

Discussion

Non-compaction cardiomyopathy is most commonly a genetic disease with autosomal dominant inheritance; however, it can also be sporadic (9). The most frequent source is a mutation in genes encoding proteins in the sarcomeres, especially tropomyosin, actin, myosin binding protein C, and troponin (9). Non-compaction cardiomyopathy may be seen isolated or may occur with congenital malformations, such as Wolf-Parkinson-White syndrome, bicuspid aortic valve, pulmonary atresia, atrial and ventricular septal defects, coarctation, Ebstein anomaly, and other conditions (10). Associated non-cardiac disorders have also been found with Hirschsprung's disease (11), neuromuscular disorders, and metabolic diseases, such as the Marfan syndrome (12).

Non-compaction cardiomyopathy is usually diagnosed at the early stages of life; however, a few cases diagnosed at an older age have been reported (13). The clinical presentation has a wide spectrum ranging from asymptomatic to symptoms of heart failure, arrhythmia, and systemic embolism. Thromboembolic events associated with non-compaction cardiomyopathy can be due to atrial fibrillation, decreased ventricular function, and trabeculated ventricle. If non-compaction cardiomyopathy is not recognized and treated, the events can subsequently lead to pulmonary embolism, systemic emboli, mesenteric infarction, and stroke (14). Because of its variable phenotypical and clinical presentation, it is often unrecognized or misdiagnosed as another disease. The diagnosis requires genetic testing combined with various cardiac imaging modalities (15). Our patient was a middle aged female presenting with dyspnea, cyanosis, and lower leg extremity edema, treated as an obstructive pulmonary disease but diagnosed with non-compaction cardiomyopathy and heart failure after an echocardiographic and CMR evaluation.

Non-compaction cardiomyopathy is often associated with conduction defects. Wessels et al. (8) previously described nine patients affected by a combination of cardiac abnormalities. Eight of these patients also had cardiac arrhythmia, with sinus bradycardia in most cases, similar to our patient. Apart from non-compaction of the ventricular myocardium, situs abnormalities were typical for the patients who were defined by Wessels et al. (8). Six of the nine patients had anomalies, including theazygous continuation of the inferior vena cava, polysplenia, left bronchial isomerism, and intestinal malrotation in this family. We planned to investigate situs abnormalities and genome-wide linkage analysis for our patient.

Because of the high risk of thrombus formation within the intratrabecular recesses, chronic anticoagulant therapy is suggested in non-compaction cardiomyopathy patients with atrial fibrillation, a history of thromboembolism, and/or a reduced ejection fraction (14). However, we could not investigate situs abnormalities or genetic analysis and prescribe anticoagulant therapy in our patient, as the patient and her relatives refused further investigation and therapy.

Conclusion

Non-compaction cardiomyopathy has a genetic origin that can be found in isolated form or in association with other cardiac or non-cardiac manifestations. Although it is still unclear whether the presentation of this unique disease in adulthood represents a long-standing condition or delayed manifestation of molecular pathology a better understanding of its genetics and the novel gene mutations may further delineate the natural course of this disease.

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Video 1. Trabeculated and spongiform appearance of both ventricles and a globally dilated heart with systolic dysfunction in the transthoracic echocardiogram.

Video 2. Cardiac magnetic resonance imaging of biventricular non-compaction cardiomyopathy.

Video 3. Transesophageal echocardiography demonstrating interatrial septal aneurysm and secundum atrial septal defect.

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