Isolated noncompaction of the ventricular myocardium. A study in an adult male and literature review

Giovanni Corrado, Mauro Santarone, Emilio Miglierina, Sandro Beretta*, Tiziano Frattini**, Giorgio Tadeo, Giovanni Foglia Manzillo, Luca M. Tagliagambe

*Department of Cardiology, *Department of Neurology, **Department of Radiology, Valduce Hospital, Como, Italy*

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Noncompaction of the ventricular myocardium is a rare congenital disorder characterized by the presence of numerous prominent trabeculations and deep intertrabecular recesses which communicate with the left ventricular cavity. The disease uniformly affects the left ventricle, sometimes also affecting the right ventricle. Noncompaction of the ventricular myocardium is believed to be a disorder of endomyocardial embryogenesis. Familial occurrence has been observed. It may be accompanied by depressed ventricular function, cardiac arrhythmia and systemic embolism. Although noncompaction of the ventricular myocardium is a congenital myocardial disorder, the onset of symptoms is frequently delayed until adulthood. We describe a case of noncompaction of the ventricular myocardium in a 33-year-old male with the typical echocardiographic and cardiac magnetic resonance imaging features of this disease.

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Address:

Dr. Giovanni Corrado

Unità Operativa di Cardiologia Ospedale Generale Valduce Via Dante, 11 22100 Como E-mail: cardiologia@valduce.it

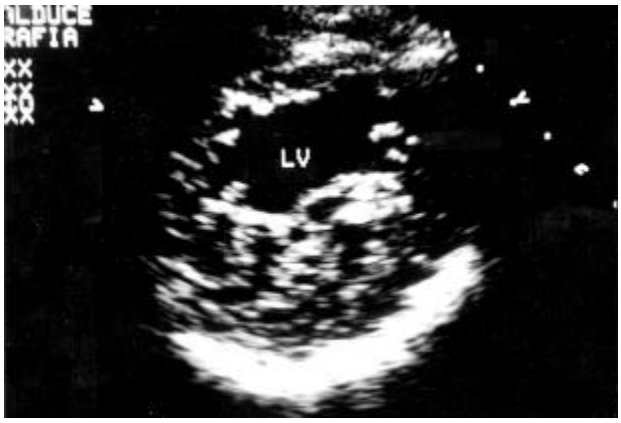
Noncompaction of the ventricular myocardium (NVM), also referred to as "spongy myocardium", is a rare congenital disorder. Noncompaction refers to the arrest of compaction of the loosely interwoven meshwork of myocardial fibers during embryogenesis[1]. We report a case of isolated NVM in an adult male.

Case report

A 33-year-old outpatient was referred by his primary physician to our Cardiology Department because of palpitations and presyncope induced by exercise. Since 1988 multiple echocardiographic examinations performed elsewhere have been interpreted as apical hypertrophic cardiomyopathy. For this reason the patient was given beta-blockers, which were subsequently withdrawn. There was a family history of cardiomyopathy involving seven relatives.

The patient's vital signs were normal. On cardiac auscultation the first and the second heart sounds were normal; a precordial ejection functional murmur was present. The remainder of the examination findings was unremarkable. Electrocardiography demonstrated sinus rhythm with non-specific repolarization abnormalities; QRS duration was 90 ms.

We repeated a complete echocardiographic and Doppler examination. Cross-sectional echocardiography disclosed numerous prominent trabeculations (with the same echogenicity of the surrounding myocardium) and deep intertrabecular recesses involving the left ventricular apical region and the adjacent posterior and inferior mid ventricular free walls (Figs. 1A and B). Color flow imaging disclosed forward and reverse flow between prominent trabeculations during the cardiac cycle (Fig. 1C). Echocardiographic contrast-enhanced study was performed after infusion of Levovist® (Schering AG, Berlin, Germany), a suspension of galactose microparticles; 8 ml of sterile water was added to 4 g of Levovist® such as to obtain a 400-mg microparticle/ml concentration. The contrast agent was injected at a rate of 240 ml/hour through a 20-gauge cannula positioned in an antecubital vein. Echocardiographic examination was carried out using second harmonic imaging and triggered end-systolic power harmonic imaging. We observed opacification of the intertrabecular spaces, confirming the



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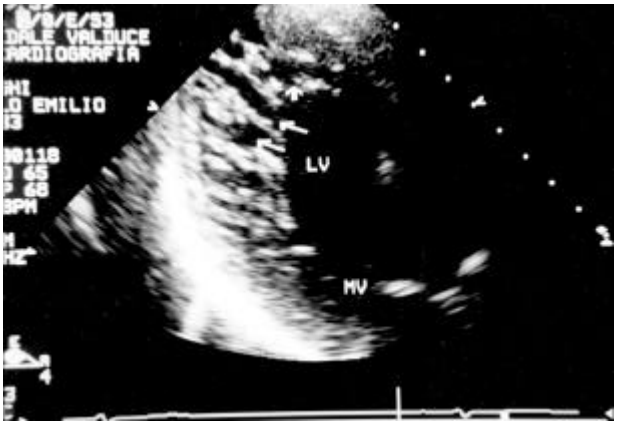

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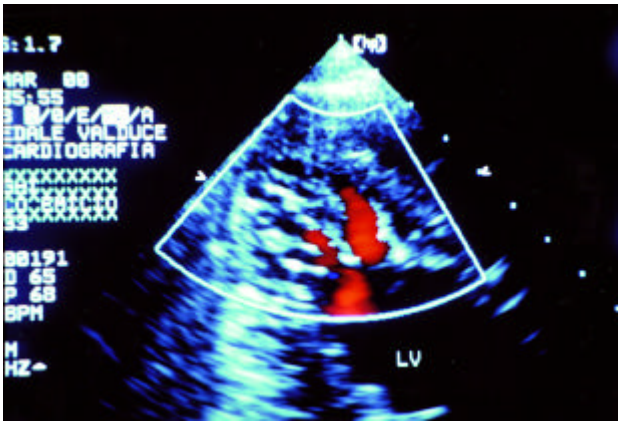

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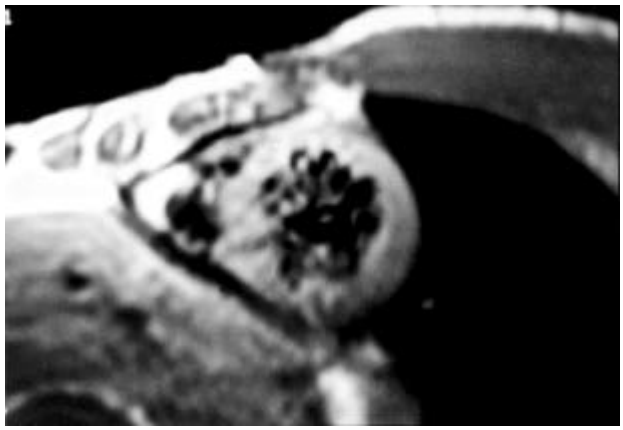
Figure 1. *Transthoracic cross-sectional echocardiography.* A: *parasternal short-axis view at the level of the papillary muscles. Note the honeycomb myocardium appearance resulting from multiple trabeculations involving the posterior wall of the left ventricle.* B: *apical long-axis view. Note the multiple trabeculations and intertrabecular recesses in the mid and apical left ventricular posterior wall* (arrows). C: *apical long-axis expanded view at the same level as in* B. *Note the color Doppler imaging demonstrating the presence of forward* (red color) *flow from the left ventricular cavity to the intertrabecular recesses. LV = left ventricle; MV = mitral valve.*

communication between intertrabecular recesses and the left ventricular cavity. Overall left ventricular systolic function was normal. Doppler interrogation of mitral inflow and pulmonary venous flow did not disclose any signs of left ventricular diastolic dysfunction. Echocardiographic abnormalities of the atrial chambers and of the right ventricle were not detected.

Magnetic resonance imaging of the heart confirmed the existence of abnormal inner zones of noncompacted myocardium, which were mainly located in the left ventricular apex and posterior wall (Fig. 2). Due to a history of palpitations we performed a 24-hour ambulatory ECG which showed sporadic premature ventricular beats. Signal-averaged electrocardiography did not detect ventricular late potentials. Good exercise capacity (workload 16 METS) was demonstrated on treadmill exercise testing; no significant ventricular arrhythmia was observed during stress testing.

Clinical neurological examination and upper and lower limb muscle electromyography were normal. Serum lactate at rest and creatine phosphokinase levels were also normal. Brain magnetic resonance imaging was negative for focal lesions.

The patient refused invasive procedures, i.e. muscular biopsy and invasive electrophysiological study.



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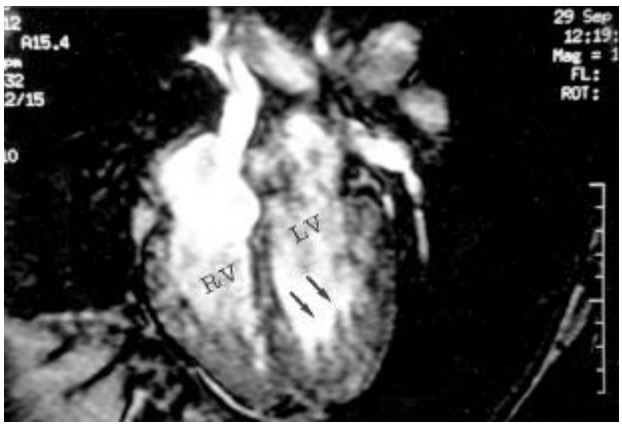

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Figure 2. *Magnetic resonance imaging.* A: *short-axis view of T1-weighted imaging of the heart (apical level). The image reveals abnormal trabeculations within the left ventricular cavity.* B: *fast cardiac imaging (coronal plane) showing an inner zone of noncompacted myocardium* (arrows) *in the apical region of the left ventricle. LV = left ventricle; RV = right ventricle.*

We interpreted the abnormal structures within the left ventricle as abnormal trabeculations also named "left ventricular noncompaction" or "spongy myocardium".

Discussion

NVM is a rare congenital cardiomyopathy that results from an arrest in normal endomyocardial morphogenesis. In the early embryo, before the development of the coronary circulation, the heart consists of a spongy meshwork of interwoven muscle fibers[2]. These fibers form trabeculae with deep intertrabecular recesses which communicate with the left ventricular cavity. The blood is supplied to the myocardium through the intertrabecular spaces, resembling the blood supply of nonmammalian vertebrates such as fishes and reptiles. In the normal development during the fifth to eighth week of intrauterine life the honeycomb structure of the ventricular myocardium is transformed into compact myocardium. The intertrabecular spaces change into capillaries with parallel development of the coronary circulation. Generally the process of compaction proceeds from the epicardium to the endocardium and from the basal parts of the ventricles to the apex. NVM represents an arrest in the compaction process of the myocardium resulting in the persistence of multiple abnormal ventricular trabeculations with deep intertrabecular spaces. Relatively rare in any case, NVM has been associated with other congenital cardiac malformations including anomalous origin of the left coronary artery from the pulmonary artery[3], complex cyanotic heart disease[4], and obstruction to the right or left ventricular outflow[3,5,6]. Furthermore, NVM may be associated with various neuromuscular disorders such as Becker's muscular dystrophy, mitochondrial myopathy and polyneuropathy[7]. Facial dysmorphism, characterized by a prominent forehead, strabismus, low-seat ears, high-arched palate and micrognathia, has been observed in some children with NVM[8,9]. Nevertheless, NVM may occur as an isolated cardiac disease[8-10]. Familial recurrence[8,9,11] has been reported.

The cardiac clinical manifestations of isolated NVM may include: 1) depressed systolic function of the noncompacted left ventricle resulting in heart failure; 2) cardiac arrhythmia and conduction defects including atrial fibrillation, ventricular arrhythmia, sometimes fatal, conduction defects (either atrioventricular or bundle branch blocks) and Wolff-Parkinson-White syndrome[8-10]; 3) cardioembolic complications[8,10] resulting from either atrial fibrillation or clot formation within the myopathic left ventricle. This latter mechanism is supported by necropsy reports of mural thrombi within the deep intertrabecular recesses[8]. Although NVM is a congenital cardiomyopathy, the clinical manifestations and age at onset of symptoms are highly variable. The clinical picture may range from the absence of any symptom to severe heart failure, leading to heart transplantation or death[8-10,12]. Due to the high incidence of family recurrence, not infrequently this cardiomyopathy is discovered during familial screening of patients affected by NVM. In our patient, clinical neurological examination and central nervous system magnetic resonance imaging were negative for focal ischemic lesions; furthermore, no ventricular thrombus was seen on transthoracic echocardiogram. Thus we decided to avoid either anticoagulant treatment or antiplatelet agents. No clinical signs of neuromuscular disease were found. Nevertheless, the patient refused a muscular biopsy; thus, subtle muscular abnormalities cannot be excluded. Noninvasive diagnostic tests did not disclose meaningful arrhythmia; invasive electrophysiological study was not performed because of the patient's refusal.

Various imaging techniques have been employed in the diagnosis of NVM including ventriculography[1,4,9,13,14], ultrafast computed tomography[9], and magnetic resonance[9]. Nevertheless, echocardiography is the imaging modality of choice for NVM[7-10,12].

Echocardiographic diagnosis of NVM is based on the finding of multiple prominent ventricular trabeculations with intertrabecular spaces communicating with the ventricular cavity, as demonstrated by color Doppler or by contrast-enhanced imaging. To quantify the depth of penetration of the intertrabecular recesses Chin et al.[8] suggested an X-to-Y ratio, where X represents the distance between the epicardial surface through to the trabecular recesses and Y the distance between the epicardial surface and the peak of trabeculations. The left ventricle is always involved in cases of NVM; biventricular involvement occurs in less than 50% of cases[10].

Our patient was initially diagnosed as affected by an apical form of hypertrophic cardiomyopathy. As a matter of fact the primary diagnosis of NVM is missed in most cases[9,12]. This is probably due to unfamiliarity with the NVM diagnostic pattern and to similarities between NVM and other more common cardiomyopathies. In hypertrophic cardiomyopathy trabeculae and deep intertrabecular recesses are typically absent. Furthermore, dilated cardiomyopathy may be accompanied by prominent myocardial trabeculations, but to a lesser extent than in NVM[10]. Finally, differential diagnosis includes prominent normal myocardial trabeculations, false tendons and aberrant bands, cardiac tumors and left ventricular apical thrombus. Prominent left ventricular trabeculations are always three or less in number, are rarely located in the apical region[15], and thus differ from the multiple apical trabeculations present in NVM. False tendons and aberrant bands typically cross the left ventricular cavity[16]. Left ventricular thrombi may be falsely diagnosed when noncompaction is confined to the left ventricular apex; however, apical thrombi exhibit a different echogenicity from the surrounding myocardium[17].

The ultimate outcome of patients remains unclear. The prognosis may range from a prolonged asymptomatic course to a rapid deterioration of left ventricular systolic

function leading to heart transplantation or death[8-10]. In general, both in adults and in the pediatric population the prognosis was better in asymptomatic patients[9,10].

The diagnosis of NVM often appears to be delayed because of similarities with more frequent conditions and the examiner's unfamiliarity with its specific diagnostic pattern[9-12]. Correct diagnosis of this rare congenital cardiomyopathy is mandatory for appropriate management and follow-up. Moreover, due to possible association with neuromuscular disorders, cardiologists should consider a neurological referral in patients with NVM. Finally, because of the high incidence of family recurrence, echocardiographic evaluation of family members is recommended to identify unrecognized cases of NVM.

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