Case reports

Isolated noncompaction of the myocardium: an exceedingly rare cardiomyopathy. A case report

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Isolated noncompaction of the left ventricular myocardium is a rare cardiac disorder due to an arrest in myocardial morphogenesis. It is characterized by prominent and excessive trabeculation in a ventricular wall segment, with deep intertrabecular spaces perfused from the ventricular cavity. Echocardiographic findings are important clues for the diagnosis. Clinical symptoms include signs of left ventricular systolic dysfunction even to the point of heart failure, ventricular arrhythmias, and embolic events.

We describe an adult case in whom the only clinical symptoms were life-threatening ventricular arrhythmias. Transthoracic echocardiography did not contribute to the diagnosis, which was made thanks to left ventricular contrast angiography. Electrophysiological testing induced a fast monomorphic sustained ventricular tachycardia, with hemodynamic impairment, that was refractory to pharmacological treatment, and for this reason a permanent cardioverter-defibrillator was implanted.

A subsequently performed transesophageal echocardiographic examination showed a localized, regional increase in left ventricular wall thickness and degree of trabeculation.

The causes and electrophysiological mechanisms of arrhythmias in noncompaction are still unknown: grossly irregular branching and connecting of myocardial fascicles in the noncompacted segments, isometric contraction with increased wall stress, and localized coronary perfusion impairment can all induce disorganized or delayed activation and increase the potential for arrhythmias.

This is the first reported case of noncompaction in which an implantable defibrillator was used to control life-threatening arrhythmias.

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The heart of the early embryo is composed of a loosely interwoven mesh of muscle fibers. As the developing myocardium condenses, from the subepicardial layers toward the subendocardium, the loosely arranged meshwork of fascicles becomes progressively more compact. The interfascicular spaces evolve into sinusoids and then capillaries; the large recesses within the trabecular network communicating with the ventricular cavity flatten out or disappear[1,2].

In the developed heart, trabecular compaction is more complete in the left ventricular myocardium: discrete muscle bundles may be observed, but are few in number[3].

Noncompaction of the ventricular myocardium is believed to be due to an arrest in myocardial morphogenesis, almost invariably associated with congenital malformations with severe left or right ventricular outflow tract obstruction.

Isolated ventricular noncompaction, i.e. noncompaction without associated anomalies, is extremely rare, with only a few cases[4-10] or small series[11-13] reported. The gross anatomical appearance is characterized by exceedingly prominent regional trabeculation, with deep intertrabecular recesses.

The clinical aspects of this anomaly have not been completely defined: we describe a case, in which arrhythmias were the main feature of clinical presentation.

Case report

M.R. was a healthy 41-year-old man, non smoker, with no family history of heart disease, and an amateur sportsman. A past episode of transient dyslalia was reported. In July 1997, while riding uphill during a bicycle race, he felt fast palpitations, fol-

lowed by complete loss of consciousness. He fell to the ground, sustaining a head injury. He was rapidly brought to the Hospital Emergency Room, and an ECG was recorded, which showed premature ventricular contraction and a short episode of complete atrioventricular block.

On physical examination, blood pressure was 130/85 mmHg, heart rate 70 b/min, while no significant cardiac murmurs or abnormal heart sounds could be detected.

The ECG at rest showed regular sinus rhythm, slight delay of right bundle branch conduction, and occasional premature ventricular contractions (Fig. 1). On a first echocardiographic examination, the dimensions of cardiac chambers were normal (aorta 32 mm, left atrium 35 mm, left ventricular diameter: diastolic 54 mm, systolic 33 mm, fractional shortening 38%, wall thickness: posterior 8 mm, septal 9 mm); left ventricular function was considered to be normal, with no wall motion abnormalities.

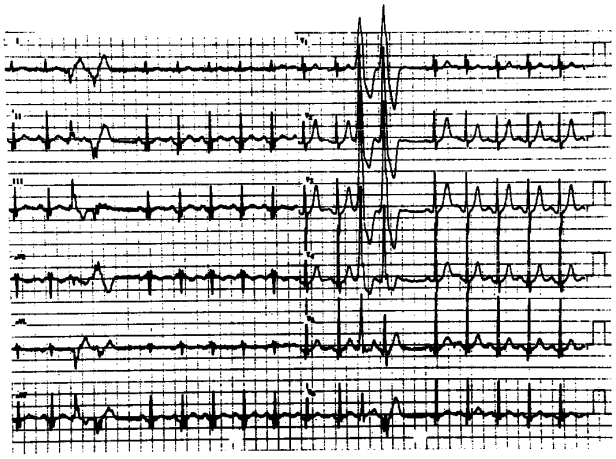

Figure 1. *Rest ECG: regular sinus rhythm, heart rate 105 b/min, P wave 110 ms, PR interval 160 ms, QRS axis +80 , QRS duration 110 ms, RSR morphology in V_1, normal repolarization, QT/QTc 280/378 ms. Two couples of premature ventricular contractions of different morphology.*

On admission to our S ervice, a second two-dimensional and Doppler echocardiographic examination was performed, by which hypokinesia of the inferior left ventricular wall could be documented. Global contractile function was at the lower limits of normal; left atrial filling contribution was increased.

The bicycle ergometer exercise test (20 min, 250 W, 95% of maximal predicted heart rate) was negative for symptoms or ST segment displacement. Frequent premature ventricular contractions (two forms, with right bundle branch block morphology) were recorded during exercise, and two couplets in the recovery phase.

A 24-hour Holter monitoring showed normal heart rate variations (min 54, max 115, mean 71), and a total of 1443 ventricular events, 113 couplets and 1 triplet. No atrioventricular conduction anomalies or ST segment changes were recorded.

The signal-averaged ECG study was negative for late potentials (40-250 Hz band-pass filtering: QRS duration 117 ms, RMS 22.2 uV, LAS 32.0 ms).

At cardiac catheterization and angiography, left ventricular pressure was normal (110/1-13 mmHg). Right and left coronary arteries were normal in origin and distribution. The left ventricular cavity was normal in volume (end-diastolic volume 81 ml/m^2). An area of localized hypokinesia was documented along the diaphragmatic and infero-lateral regions, in which the ventricular wall appeared grossly trabeculated, with deep intertrabecular recesses (Fig. 2). Systolic excursion was increased in the remaining regions, with global contractile function mildly depressed (ejection fraction 44%).

An inductive diagnosis of localized left ventricular cardiomyopathy was proposed, and the patient scheduled for intracavitary electrophysiological study. At a first electrophysiological study, sinus node and atrioventricular node function were normal. Paired ventricular stimulation induced a monomorphic sustained ventricular tachycardia with a 210 ms cycle, and right bundle branch block morphology (Fig. 3). The arrhythmia caused he-

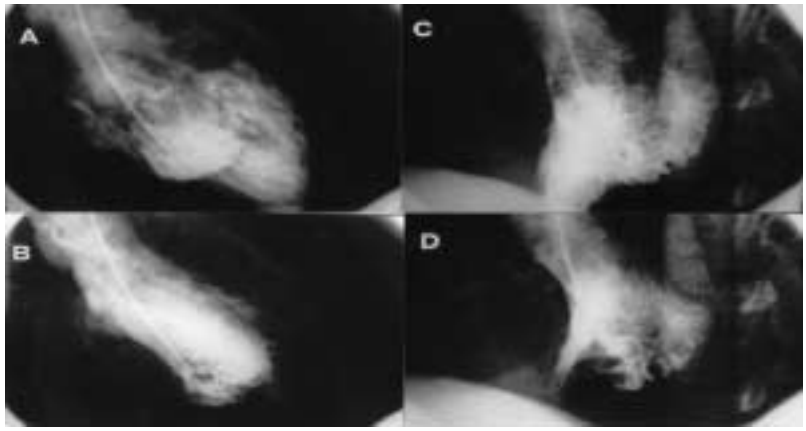

Figure 2. *Left ventricular contrast angiography.* A *and* B: *diastole and systole in the right anterior oblique projection.* C *and* D: *diastole and systole in the left anterior oblique projection. The hypokinetic segment along the inferior profile seen in* B *corresponds to the grossly and irregularly trabeculated segment along the infero-lateral region of the left anterior oblique projection. Wall excursion is increased at the apex and remaining segments.*

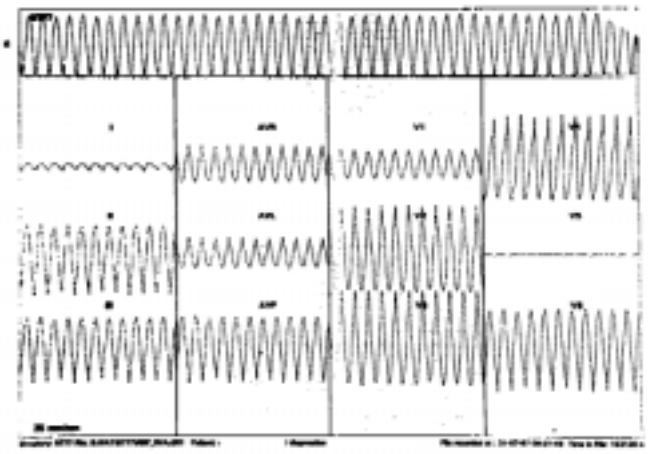

Figure 3. *Electrophysiological testing inducing sustained ventricular tachycardia, with a 210 ms cycle, and right bundle branch block configuration.*

modynamic impairment, preventing endocavitary mapping, and DC shock was required to terminate it.

Two more electrophysiological studies were performed in the following months, after full dose sotalol and amiodarone treatment schedules. On both occasions the paired stimulation induced sustained ventricular tachycardia, with a slightly longer cycle of 260 ms, but still requiring DC shock.

Four months after the initial symptoms an implantable cardioverter-defibrillator was inserted.

A transesophageal echocardiographic examination was eventually performed, which showed a hypokinetic-akinetic area localized at the mid portion of the inferior and postero-lateral left ventricular wall, in proximity to the papillary muscle insertion. This area was overlaid by thick, prominent trabeculation protruding into the left ventricular cavity. Blood flow from the inner ventricle to the intertrabecular spaces was documented by color flow Doppler interrogation.

After a 28-month follow-up the patient is well, with no recurrence of syncopal episodes. The cardioverter-defibrillator has discharged properly 4 times.

Discussion

Isolated noncompaction of ventricular myocardium is an exceedingly rare congenital disorder, due to an incomplete coalescence of the loosely interwoven meshwork of myocardial fibers during cardiac morphogenesis. The disease is anatomically characterized by an excessively prominent trabeculation of the inner myocardial wall, with deep intertrabecular recesses.

In its isolated form, that is not associated with other congenital anomalies, noncompaction has been categorized as unclassified cardiomyopathy by the Task Force of the World Health Organization/International Society and Federation of Cardiology[14].

To date, only a few cases and three small series have been reported in the literature. A pediatric series reported by Chin et al.[11] from the University of Los Angeles (CA, USA) included 8 cases (5 clinical and 3 necropsy); the age ranged from 11 months to 22.5 years. In 3 children a peculiar facial dysmorphism was present, in 4 cases a familial recurrence. The necropsy findings ranged from moderately abnormal trabeculation to a profoundly abnormal, loosely compacted ventricular wall. The echocardiographic images reflected the morphological appearance at necropsy. An echocardiographic index was proposed, based on the ratio of the prominence of trabeculations to the trough of intertrabecular recesses. Using the characteristic morphological features identified by echocardiography, Ritter et al.[12] from the University Hospital in Zurich (Switzerland), reviewed a 10-year experience of 37 555 echocardiographic examinations, and were able to identify 17 cases of isolated ventricular noncompaction in adults (14 men, 3 women, 18 to 71 years of age). On the basis of echocardiographic criteria the disease prevalence was therefore 0.05%. The measured ventricular wall thickness in the noncompacted regions proved to be 2.5 times that of non-diseased portions of the septum or posterior free wall.

By a 30 – 28 month follow-up, the authors were able to define the rather poor prognosis of this cardiac disorder: within 6 years of the diagnosis 59% of patients were dead or had undergone heart transplantation. Survival was even lower (30%) in the presence of clinical symptoms.

In all the pathological anatomical examinations (3 in the pediatric group, 6 patients and 2 explanted hearts in the adult series) excessive trabeculation and deep recesses were found at the apex, as well as at the inferior or infero-lateral wall of the left ventricle. The apical region of the right ventricle was often involved by the disease process. The thickened ventricular wall showed labyrinthine intertrabecular spaces communicating with the ventricular cavity, legitimating the alternative denomination of spongy myocardium [15,16]. On histologic examination, these deep recesses were found to be lined with endocardial endothelium spreading close to the epicardial surface, reflecting continuity with the ventricular cavity, and thus indicating that the recesses are not persisting sinusoids.

The most common clinical findings in both the pediatric and adult series[11,12] were those deriving from systolic dysfunction, with clinical signs of overt heart failure in more than half of the cases. The very high incidence of ventricular arrhythmias, and the increased risk of systemic embolization were other major causes of severe, often fatal complications.

Our case was unlike the previously reported cases in some ways. No clinical signs of left ventricular systolic dysfunction were present: our patient showed good physical fitness, was actively practicing sports, with a

completely normal working capacity at the exercise stress test.

The two-dimensional echocardiographic findings were completely nonspecific, revealing only localized hypokinesia along the inferior wall of the left ventricle, and slight depression of overall systolic function. The gross trabeculation and deep recesses described in the literature could not be detected, even *a posteriori*. Poor echogenicity might partially account for the missed diagnosis, but this might also imply that transthoracic echocardiography is not sufficiently sensitive for this examination to constitute a screening procedure for isolated ventricular noncompaction.

The previously described echocardiographic findings of a localized increase in ventricular wall thickness due to a prominent and excessive trabeculation, with deep intertrabecular recesses, could be documented only by a subsequent transesophageal echocardiographic examination. The diseased segment appeared to be quite limited in extent, localized to the inferior and postero-lateral regions of the left ventricular wall.

The reported transient episode of dyslalia might possibly have been caused by a small embolic episode[3], as in the Zurich adult series, in which 4 patients (24%) had had a systemic embolic event, with three transient ischemic attacks and one stroke[12].

The main clinical feature of our patient was represented by ventricular arrhythmias, the opening scenario presumably being a fast tachycardia with syncope. Frequent premature ventricular contractions were recorded on hospital admission, as well as during the exercise stress test and Holter monitoring, which led to coronary angiography to rule out an ischemic etiology.

The coronary arteries were normal, but left ventricular angiography was instrumental in identifying isolated ventricular noncompaction of the left ventricular myocardium. As in a case documented by magnetic resonance[17] and another recently reported by the same Zurich group[18], the left ventricular angiogram showed an abnormally prominent trabecular zone and deep intertrabecular recesses in the hypokinetic infero-lateral wall, giving a honeycomb-like contour to the cavity profile. The increased systolic excursion in the other ventricular segments accounted for the preservation of global left ventricular function, with only slightly depressed ejection fraction.

Recesses in the left ventricular wall can sometimes be observed at angiography, most often at the apical level: they are diverticular in aspect, and their systolic squeezing demonstrates the muscular nature of the wall. But these recesses never occupy an extended segment of the ventricular profile.

On three electrophysiological studies the arrhythmia was a fast, sustained, monomorphic ventricular tachycardia, easily induced by paired electrical stimulation even after drug treatment, which led to hemodynamic impairment and required DC shock for termination.

In 2 cases in the pediatric series[11] and 7 in the adult series[12] ventricular tachycardia was documented, demonstrating the highly arrhythmogenic potential of isolated ventricular noncompaction. Two cases in the Zurich series somewhat resembled our patient: an 18-year-old male who collapsed, and a 71-year-old male with palpitation, no overt signs of systolic dysfunction, who had ventricular tachycardia as a complication, and sudden cardiac death.

The high incidence of ventricular arrhythmias in isolated ventricular noncompaction has not yet been explained by a well-defined morphological substrate. We do not agree with the assumption[12] that severe depression of systolic function and impairment of left ventricular performance is in itself the major cause of the increased incidence of life-threatening arrhythmias. An appealing hypothesis is that the arrhythmogenic substrate lies in the grossly irregular arrangement of myocardial fascicles in the noncompacted segments, the branching and connecting trabeculation with bizarre labyrinthine intertrabecular spaces representing a rich substrate for reentry phenomena.

In the more recent series of 5 pediatric cases reported in Zurich[13], electrophysiological tests revealed abnormalities (late potentials or prolonged QT dispersion) only in the more extensive forms of left or right noncompaction. By means of positron emission tomography perfusion studies were conducted at rest and after dipyridamole: flow values and coronary flow reserve demonstrated decreased myocardial perfusion at rest and after vasodilator stress in the noncompacted segments, as compared with nonaffected areas. Localized subendocardial ischemia, and isometric contraction of the grossly hypertrophic trabeculation with increased wall stress, might be responsible for areas of subendocardial fibrosis, with the occurrence of delayed or disorganized ventricular activation. For the present, however, the cause and mechanisms of the increased arrhythmogenesis in isolated ventricular noncompaction remain unknown.

The case we have presented suggests that in the presence of life-threatening arrhythmias, when echocardiographic findings are nonspecific, left ventricular angiography may be necessary to rule out the diagnosis of isolated ventricular noncompaction. Electrophysiological intracavitary testing seems mandatory in this rare disease, to assess the nature and characteristics of arrhythmias.

To our knowledge, this is the first case reported of a patient with an angiocardiographically documented diagnosis of isolated ventricular noncompaction, in whom an electrophysiological study was performed, and in whom an automatic implantable cardioverter-defibrillator was successfully used for the treatment of the arrhythmic complications.

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