Isolated Ventricular Noncompaction: A Rare Type of Hereditary Cardiomyopathy with Poor Prognosis

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Isolated ventricular noncompaction is a very rare form of cardiomyopathy. It is characterised by the presence of multiple recesses in the ventricular myocardium that are perfused directly from the ventricles. We describe the case of a male infant who at the age of 8 months presented with symptoms of heart failure. The two-dimensional and Doppler echocardiogram showed significant hypertrophy with multiple, prominent trabeculations and deep intertrabecular recesses with blood flow within them in the myocardium of the left ventricle. There was no anatomical cardiac anomaly. The patient had a syncopal episode at the age of 10 months. Holter monitoring recorded multiple supraventricular extrasystoles, as well as salvoes of tachycardia, and diltiazem was added to the treatment regimen. The patient suffered recurrent episodes of pulmonary oedema and died at the age of 12 months from non-compensated heart failure.

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Isolated ventricular noncompaction is a rare anomaly. It is characterised by the persistence of multiple recesses in the ventricular myocardium, which are perfused directly from the ventricles, while the remaining cardiac anatomy is physiological.[1] The particular morphological characteristics of the disease may be recognised on the two-dimensional echocardiogram,[1-3] while a series of diagnostic criteria have recently been proposed.[4] The disease in adults has a poor prognosis with manifestations of heart failure, thromboembolic episodes and sudden death.[5] The prognosis in paediatric patients is similar.[6]

We describe the case of an infant who exhibited symptoms of heart failure at the age of 8 months. The transthoracic echocardiogram confirmed the presence of noncompacted myocardium. The patient died at the age of 12 months from non-compensated heart failure.

Case presentation

A male infant aged 8 months was brought to the outpatients' department with symptoms of heart failure during progression of a viral infection of the respiratory system. He was the only child of phenotypically healthy parents. Gestation, birth, perinatal and subsequent history were negative. Auscultation of a 2/6 musical systolic murmur was reported by the personal paediatrician at the age of 3 months, but no further investigation was recommended. The family history included two males who died at the ages of 2 and 16 years from sudden death.

The infant's general condition was severe, with extreme pallor and grumbling. He had tachypnoea, used accessory respiratory muscles and had crackles at the bases of both lungs. He had a galloping rhythm and a 2/6 systolic murmur at the level of the mitral valve. The liver was palpable 4 cm below the right subcostal. Chest X-ray (Figure 1) showed a greatly enlarged cardiac index (70%) and pulmonary congestion. The electrocardiogram showed sinus rhythm, an inferior axis and negative T on the left precordial leads.

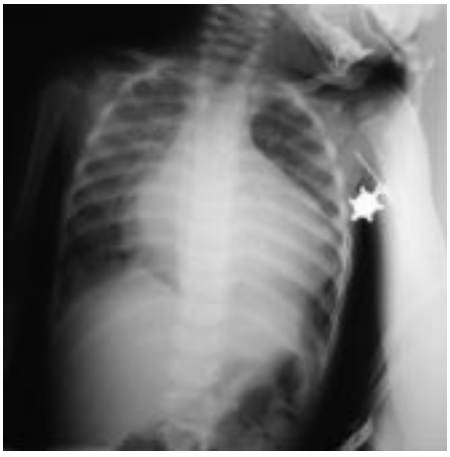

Figure 1. Chest X-ray. Situs solitus, left aortic arch. Exaggerated cardiomegaly with pulmonary congestion.

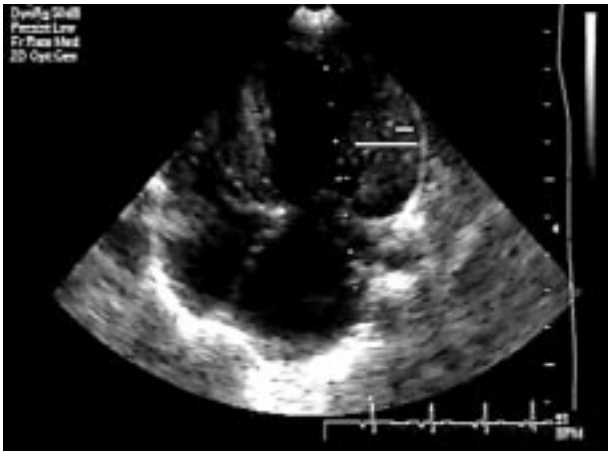

Figure 2. Two-dimensional echocardiogram, four-chamber apical view. Significant left ventricular hypertrophy. Two sections of myocardium can be clearly seen in the left ventricular free wall. One is compacted (short white line), while the other is non-compacted with trabeculae that create deep recesses (long white line). The ratio between the thickness of the compacted and the noncompacted myocardium is <0.5.

The two-dimensional and Doppler echocardiogram showed physiological systematic and pulmonary return, physiological atrioventricular and ventriculoarterial connections, intact interatrial and interventricular septum and physiological structure of the atrioventricular and semilunar valves, without stenosis at the subvalvular, valvular or supravalvular level. The aortic isthmus was physiological and there was no patent ductus arteriosus. There was, however, concentric left ventricular hypertrophy (13 mm) with multiple, prominent trabeculations and deep intertrabecular recesses, which separated the ventricular myocardium into a compacted exterior and a trabecular (noncompacted) interior section (Figure 2). The thickness ratio of the compacted to the noncompacted section at end-systole was <0.5. Colour Doppler mapping showed blood flow within and outside the recesses. There was severe distension of the left ventricle with overall reduction in myocardial contractility (fractional shortening 16%). There was also mild tricuspid regurgitation and moderate functional mitral regurgitation. The estimated right ventricular systolic pressure was 50 mmHg. The infant was started on treatment with digoxin, captopril and furosemide which achieved temporary clinical stabilisation of his heart failure. Successive echocardiograms showed no improvement in left ventricular fractional shortening, but the right ventricular systolic pressure decreased (30 mmHg). Serological tests for Coxsackie and Echo were negative, while EBV and adenovirus checks gave findings indicative of past infection. The parents' echocardiographic examinations were physiological.

At the age of 10 months the infant had a syncopal episode. The electroencephalogram and computed tomography scan of the brain were physiological. Holter monitoring recorded multiple supraventricular extrasystoles as well as salvoes of rhythmic supraventricular tachycardia up to 250 bpm (Figure 3); diltiazem was added to the treatment regimen. The heart rate was controlled and the tachycardia episodes were reduced in number and duration on successive Holter recordings. Nevertheless, the patient suffered recurrent episodes of pulmonary oedema in spite of the medication. The parents refused permission for investigation of the possibility of recruitment into a transplant programme and the infant died at the age of 12 months because of non-compensated heart failure.

Discussion

Isolated ventricular noncompaction is a rare form of unclassified cardiomyopathy[7] that is characterised by the presence of multiple, prominent trabeculations in the ventricular myocardium with deep intertrabecular recesses between the muscular trabeculae.[1-7] It has been described as an isolated cardiac anomaly in fewer than 100 infants and children up to the present,[6] while reports in adults are much rarer.[2,4]

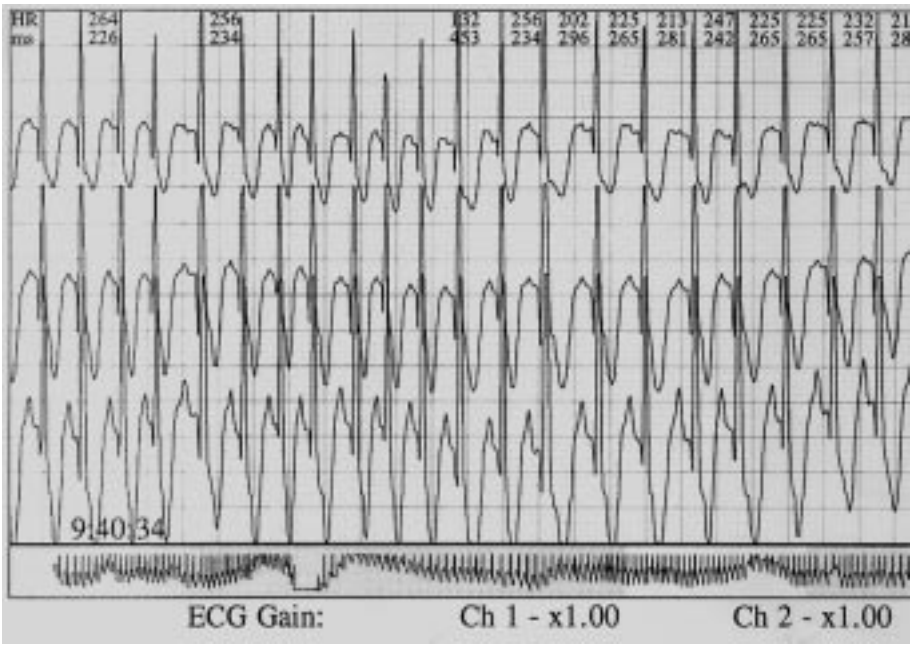

Figure 3. Holter recording of rhythmic supraventricular tachycardia up to 250 bpm.

The disorder extends to the left and, to a lesser degree, the right ventricle and to the interventricular septum.[1-6] The recesses are covered by endocardium, while the coexistence of endocardial fibroelasticity is a common finding on pathological examination.[8] The transthoracic echocardiogram is the diagnostic method of choice.[4,6] The multiple, prominent trabeculations in the ventricular myocardium are apparent on the two-dimensional echogram. The endocardium shows two distinct layers: an endocardial, noncompacted layer and an epicardial, compacted layer where the thickness of the former compared to the latter is in a ratio >1.4:1. The free flow of blood within and around the recesses can be verified with colour Doppler.[4,6] The infant we describe satisfied all the above criteria for isolated ventricular noncompaction.[4,6]

It has been hypothesised that isolated ventricular noncompaction is the result of inhibition of the physiological endomyocardial morphogenesis. At the embryonic stage of development, the myocardium consists of a loose network of muscle fibres in the form of a honeycomb, because of the presence of large numbers of recesses, through which the myocardium receives a direct blood supply.[9] Subsequently, the myocardium gradually becomes compacted, beginning with the epicardial surface and proceeding towards the endocardium, upon which the recesses involute and are transformed into capillary vessels. Finally, the myocardium is converted into a compacted layer, as it is in adulthood, around the 7th week of embryonic life and is supplied by the coronary vessels.[9,10]

There are very few cases of antenatal diagnosis of isolated ventricular noncompaction,[12,13] whereas failure to recognise the disease on the embryonic echocardiogram is more usual.[13] The delayed diagnosis is probably due to the echocardiographer's lack of familiarity with this particular anomaly, resulting in a degree of underdiagnosis both in children and in adults.[2,3] Hypothesis aside, there is no scientific proof that noncompacted myocardium represents an anomaly in the physiological process of myocardial morphogenesis.[14] The detection of noncompacted myocardium at 27 and 30 weeks in 2 foetuses who had previously shown clearly compacted heart muscle is likely to reinforce the views of those who are sceptical about the inhibition of myocardial embryogenesis being the sole pathogenetic mechanism of the disease.[11]

According to the extent of the damage, patients may be asymptomatic or may exhibit symptoms of heart failure, systematic emboli, or various forms of arrhythmia.[1-3,6] The electrocardiogram is usually pathological in both children and adults with noncompacted myocardium and may show a right or left axis deviation, left or right bundle branch block, or even non-specific ST segment changes.[1-3,6] Various types of arrhythmia have been described in these patients, such as atrial fibrillation, paroxysmal supraventricular tachycardia in the context of Wolff-Par-

kinson-White syndrome, ventricular arrhythmias and sudden cardiac death.[1-3,6]

Some cases are isolated, although familial distribution of the disease has been described.[1-3] Inheritance may be either dominant or recessive. A severe, sex-linked form of noncompacted myocardium has also been described, caused by mutation of the G 4.5 gene in the q28 region of the X chromosome, allelic with the gene responsible for Barth syndrome.[15] Barth syndrome is hereditary, sex-linked and recessive in nature, and is characterised by the presence of dilated cardiomyopathy, skeletal myopathy, neutropenia, short stature, low carnitine levels and anomalous mitochondria.[16] The appearance of multiple trabeculae in the left ventricle has been described in an adult with Becker type muscular dystrophy, who had previously had echocardiographically confirmed compacted left ventricular myocardium.[17] In another 3 cases of sex-linked noncompacted myocardium, related to mutation of Xq28, the foetal echogram recorded between the 24th and 30th week showed distension of the left ventricle only in 1 case and was in any case non-diagnostic. Even in retrospect, it was impossible to detect the characteristic echocardiographic abnormalities of noncompacted myocardium.[18]

Some patients have a characteristically deformed visage, with a projecting forehead, low-placed ears, domed palate and micrognatheia.[1,3,6] The infant we describe had noncompacted myocardium unaccompanied by other major anomalies. He had neither a deformed visage, short stature, nor neutropenia and in consequence the possibility of noncompacted myocardium could not be clinically supported. There are some reports in the literature of noncompacted myocardium existing in combination with specific syndromes,[19,20] a fact which makes it even more difficult to inform the patients' families about the prognosis of the disease.

Finally, noncompacted myocardium has been described in infants with severe obstructive diseases of the left and right ventricle,[21,22] in cases of anomalous origin of the coronary arteries from the pulmonary artery,[21] or even in combination with more complex congenital heart disease.[20]

As far as we can determine, our case is the first to be described involving an infant of Greek origin. There is only one recent report of 2 adult siblings of Cypriot origin with isolated ventricular noncompaction. In the brother it was detected when he was 19 years old and showed neurological symptoms following a cerebrovascular episode. His sister, who exhibited mild, intermittent neurological symptoms, was found to have multiple trabeculations at the apex of the left ventricle during an echocardiographic examination of the family and was medicated with anticoagulants and atenolol.[23] Early diagnosis is extremely important for the treatment of the disease and prevention of associated complications. The familial distribution of the disease necessitates the examination of first degree relatives and genetic counselling in cases of future pregnancies, as in other forms of cardiomyopathy.

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