European Journal of Echocardiography (2009) **10**, 713–715
doi:10.1093/ejechocard/jep040

ELECTRONIC PAPERS

Cardiac re-synchronization therapy in a patient with isolated ventricular non-compaction: a case report

Antoine Garnier* and Grégoire Girod

Department of Cardiology, Hôpital de Sion, 1950 Sion, Switzerland

Received 19 November 2008; accepted after revision 2 April 2009; online publish-ahead-of-print 30 April 2009

KEYWORDS
Isolated ventricular non-compaction;
Cardiac re-synchronization therapy;
Heart failure;
Arrhythmia

Isolated ventricular non-compaction (IVNC) is a rare, congenital, unclassified cardiomyopathy characterized by prominent trabecular meshwork and deep recesses. Major clinical manifestations of IVNC are heart failure, atrial and ventricular arrhythmias, and thrombo-embolic events. We describe a case of a 69-year-old woman in whom the diagnosis of IVNC was discovered late, whereas former echocardiographic examinations were considered normal. She was known for systolic left ventricular dysfunction for 3 years and then became symptomatic (NYHA III). In the past, she suffered from multiple episodes of deep vein thrombosis and pulmonary embolism. Electrocardiogram revealed a wide QRS complex, and transthoracic echocardiography showed typical apical thickening of the left and right ventricular myocardial wall with two distinct layers. The ratio of non-compacted to compacted myocardium was >2:1. Cardiac MRI confirmed the echocardiographic images. Cerebral MRI revealed multiple ischaemic sequellae. In view of the persistent refractory, heart failure in medical treatment of patients with classical criteria for cardiac re-synchronization therapy, as well as the ventricular arrhythmias, a biventricular automatic intracardiac defibrillator (biventricular ICD) was implanted. The 2-year follow-up period was characterized by improvement of NYHA functional class from III to I and increasing in left ventricular function. We hereby present a case of IVNC with favourable outcome after biventricular ICD implantation. Cardiac re-synchronization therapy could be considered in the management of this pathology.

Introduction

Isolated ventricular non-compaction (IVNC) is a rare, embryonic, developmental anomaly characterized by the persistence of numerous prominent trabeculations with interlaced recesses that deeply penetrate the myocardium. In early embryogenesis, the myocardium is composed of a loose meshwork of individual fibres. Normally, these fibres undergo progressive compaction.[1] This disorder is probably caused by an arrest in the normal development.

Isolated ventricular non-compaction is usually diagnosed using Doppler echocardiography with the presence of numerous prominent hypertrabeculations and multiple intertrabecular recesses perfused from the ventricular cavity. A valid diagnosis can be made when the non-compacted to the compacted layer ratio is higher than 2, as observed by *Chin et al.*[2] at the end of the diastole or by *Jenni et al.*[3] at the end of the systole.

Isolated ventricular non-compaction clinical manifestations are non-specific. Nevertheless, three key signs are usually observed. *Heart failure*, caused principally by severe systolic dysfunction of the left ventricle, is seen in 30–70% of cases. *Thrombo-embolic events* occur in 7–38% of cases, leading to both pulmonary embolisms and strokes.[2] *Cardiac arrhythmias* can occur including ventricular and supraventricular tachycardia as well as atrial fibrillation. These disorders can lead to syncopes and sudden death in up to 18% of patients in the observed populations.[4] Both sporadic and familial forms have been described, although the latter are less frequent.

Case report

A 69-year-old female patient consulted our emergency department in 2006, following the fourth occurrence of syncope in 6 months. Patient history included multiple episodes of deep vein thrombosis without factor V Leiden mutation or other recognized procoagulant condition. Cerebral MRI with diffusion-weighted imaging showed T2-weighted hyperintense sequelar ischaemic lesions in semioval centres and cortico-subcortical area. She suffered from heart failure. The treatment consisted of angiotensin-

* Corresponding author. Tel: +41 21 314 0565.
E-mail address: Antoine.Garnier@bluewin.ch

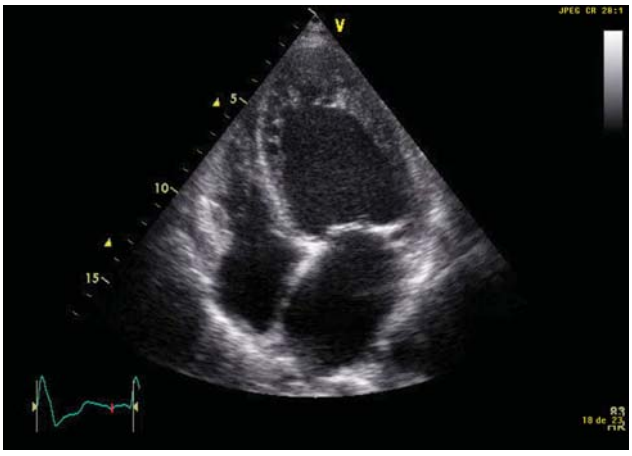

Figure 1 Apical four-chamber view. Prominent trabeculations at the apex of the left ventricle are clearly visible. The location in apical segment is typical for IVNC. A ratio of non-compacted/compacted myocardium $\geq$2 is diagnostic for IVNC.

receptor blocker and loop diuretics. Owing to side effects, neither beta blockers nor ACE inhibitors were introduced. Deep vein thrombosis risk of recurrence was treated with acenocoumarol and a platelet antiaggregant. There was no sign of neuromuscular disease.

Initial cardiopulmonary auscultation was normal. Advanced coronary disease has been ruled out by coronary arteriography. The electrocardiogram revealed sinus rhythm and left bundle branch block with QRS duration of 178 ms. Holter monitoring showed ventricular extrasystoles and bursts of ventricular tachycardia of up to five complexes. During hospitalization, she also developed one episode of supraventricular tachycardia up to 143 b.p.m., treated by medical cardioversion. Arrhythmia could be responsible for syncope. Moderate mitral valve insufficiency could also be seen by transthoracic echocardiography. The left ventricle was slightly dilated (end-diastolic volume 100 mL/m^2). Diffuse hypokinesia was present with a marked decrease in systolic function (LVEF 35%, calculated with the Simpson method). The apical region contained a hypertrabeculation with intertrabecular recesses interrupting the hypertrophic muscle bands (*Figure 1*, see Supplementary data online, *Movie S1*). These modifications extended up to the apical region of the right ventricle.

In addition, the patient showed echocardiographic criteria of intra- and inter-ventricular dyssynchrony as described in the *CARE-HF* study:[5] aortic pre-ejection delay was 175 ms and intraventricular mechanical delay was 65 ms. Furthermore, the delay between the interventricular septum and the postero-lateral wall of the left ventricle exceeded 130 ms. Based on cardiac MRI, the thinning of the compacted myocardium was measured at 4 mm and the width of trabeculations present in the apical segments reached 11 mm (ratio 2.75:1). The remainder of the left ventricular wall was measured between 15 and 18 mm. The thickness of the right ventricle ranged between 3 and 4 mm.

On the basis of these findings, the patient was diagnosed with IVNC.

In 1990, an echocardiogram performed in order to investigate a heart murmur was described as normal, without any left ventricular dysfunction or dilatation. The left ventricular walls were not thickened. Nevertheless, the quality of the images retrieved from the archives was not sufficient for exclusion of any a posteriori observation of non-compaction. Angina-like symptoms appeared in 1999, although coronary angiogram was normal. A left ventriculography performed at that time showed lower and apical hypokinesia associated with left ventricular dysfunction. Following the exclusion of common causes, the patient was diagnosed with dilated cardiomyopathy of unknown origin.

In summary, this patient had a high risk of sudden death due to underlying cardiomyopathy and moderate to severe left ventricular dysfunction. Moreover, she fulfilled the electrical and echocardiographic criteria for cardiac re-synchronization therapy.[5] Thus, she received a biventricular ICD.

Twenty-four months clinical outcome was favourable with an improvement in heart failure symptoms (from NYHA class III to class I). We did not change the medical treatment of heart failure. The LVEF increased from 35 to 50%, but oppositely to the case report of *Stöllberger et al.*[6] in similar condition, the level of non-compaction remained unchanged. The biventricular ICD did not record any new significant arrhythmia.

Discussion

The term 'non-compaction' appeared in 1990 in a echocardiographic and histological description by *Chin et al.*[2] The chosen terminology presupposes the congenital aetiology. In non-compaction associated with other cardiac or extracardiac anomalies, the physiopathological mechanism implies that during embryogenesis the left ventricle is exposed to high blood pressure.[4] Histological analysis revealed no contact—in contrast to patients with persistent sinusoids—with the coronary network.[7] The mechanism is not yet completely understood. As reminded by *Stöllberger et al.*, even the concept that non-compaction originates with an embryogenic defect is not definitively proven.[8] In fact, they also described cases of acquired non-compaction.[9] Thus, they proposed the term 'hypertrabeculation' instead of non-compaction.

Jenni et al.[3] reported a 0.014% IVNC prevalence in echocardiograms performed over 15 years. Overall, there are strong variations in the figures published in the literature.[10] IVNC prevalence in the general population is probably underestimated.

There is no specific treatment for IVNC. Heart failure should be treated. Because of the thrombo-embolic risks linked to auricular fibrillation and of the significant reduction in the left ventricular ejection volume, the administration of acenocoumarol as an anticoagulant has been proposed in many cases.[7,11,12] The occurrence of ventricular tachycardia and the high incidence of sudden death call for an in-depth assessment of arrhythmia risks and an aggressive treatment in life-threatening situations. According to *Jenni et al.* an early implantation of ICD may reduce sudden death event rate, although no specific study demonstrated definitive benefit. Recently, a positive conclusion has been reached in a retrospective study of 12 patients (mean age: 45 years), with one of two patients benefiting from ICD implantation.[13]

Conclusion

Isolated ventricular non-compaction was not detected in the patient in spite of multiple echocardiographies performed over a period of 16 years. This observation suggests that this condition may be acquired, or at the very least, that the clinical manifestations of a congenital abnormality can appear late in life. It is also possible that this diagnosis was missed in 1990—even though the first and the last examination were performed by the same sonographer—for two reasons: the low awareness to this condition and the lower echocardiographic performances. We believe that cardiac dyssynchrony should be systematically investigated, especially in case with symptoms of heart failure. As demonstrated in our patient and in other papers, biventricular ICD can be considered as a part of the management of IVNC.[6,14]

Supplementary data

Supplementary data are available at *European Journal of Echocardiography* online.

References

1. Weiford BC, Subbarao VD, Mulhern KM. Noncompaction of the ventricular myocardium. *Circulation* 2004;**109**:2965–71.
2. Chin TK, Perloff JK, Williams RG, Jue K, Mohrmann R. Isolated noncompaction of left ventricular myocardium. A study of eight cases. *Circulation* 1990;**82**:507–13.
3. Jenni R, Oechslin E, Schneider J, Attenhofer Jost C, Kaufmann PA. Echocardiographic and pathoanatomical characteristics of isolated left ventricular noncompaction: a step towards classification as a distinct cardiomyopathy. *Heart* 2001;**86**:666–71.
4. Ritter M, Oechslin E, Sütsch G, Attenhofer C, Schneider J, Jenni R. Isolated noncompaction of the myocardium in adults. *Mayo Clin Proc* 1997;**72**:26–31.
5. Cleland JG, Daubert JC, Erdmann E, Freemantle N, Gras D *et al*. The effect of cardiac resynchronization on morbidity and mortality in heart failure. *N Engl J Med* 2005;**352**:1539–49.
6. Stöllberger C, Keller H, Finsterer J. Disappearance of left ventricular hypertrabeculation/noncompaction after biventricular pacing in a patient with polyneuropathy. *J Card Fail* 2007;**13**:211–4.
7. Oechslin EN, Attenhofer Jost CH, Rojas JR, Kaufmann PA, Jenni R. Long-term follow-up of 34 adults with isolated left ventricular noncompaction: a distinct cardiomyopathy with poor prognosis. *J Am Coll Cardiol* 2000; **36**:493–500.
8. Stöllberger C, Finsterer J, Blazek G. Left ventricular hypertrabeculation/noncompaction and association with additional cardiac abnormalities and neuromuscular disorders. *Am J Cardiol* 2002;**90**:899–902.
9. Finsterer J, Stöllberger C, Gaismayer K, Janssen B. Acquired noncompaction in Duchenne muscular dystrophy. *Int J Cardiol* 2006;**106**:420–1.
10. Nugent AW, Daubeney PE, Chondros P, Carlin JB, Cheung M *et al*. The epidemiology of childhood cardiomyopathy in Australia. *N Engl J Med* 2003; **348**:1639–46.
11. Sasse-Klaassen S, Gerull B, Oechslin E, Jenni R, Thierfelder L. Isolated noncompaction of the left ventricular myocardium in the adult is an autosomal dominant disorder in the majority of patients. *Am J Med Genet A* 2003;**119**:162–7.
12. Murphy RT, Thaman R, Blanes JG, Ward D, Sevdalis E *et al*. Natural history and familial characteristics of isolated left ventricular noncompaction. *Eur Heart J* 2005;**26**:187–92.
13. Kobza R, Jenni R, Erne P, Oechslin E, Duru F. Implantable cardioverter-defibrillators in patients with left ventricular noncompaction. *Pacing Clin Electrophysiol* 2008;**31**:461–7.
14. Kubota S, Nogami A, Sugiyasu A, Kasuya K. Cardiac resynchronization therapy in a patient with isolated noncompaction of the left ventricle and a narrow QRS complex. *Heart Rhythm* 2006;**3**:619–20.