Accidentally discovered non-compaction cardiomyopathy in patient with initial diagnosis of acute coronary syndrome (RCD code: III-5A)

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Abstract

Isolated non-compaction cardiomyopathy is a rare congenital developmental disorder, which belongs to the group of unclassified cardiomyopathies by the ESC Position Statement. Typical echocardiographic findings include multiple trabeculations of the left ventricular muscle, separated by deep lacunae which communicate with left ventricular lumen. We present a case of accidentally discovered non-compaction cardiomyopathy in a 46-year-old male, who was initially diagnosed with an acute coronary syndrome. The diagnosis of the left ventricular non-compaction was confirmed by transthoracic echocardiography and cardiac magnetic resonance. Occupational contribution (lead and zinc exposure and repeated electric shocks) to the onset of the heart failure was additionally evaluated. JRCD 2013; 1 (3): 103–108

Key words: cardiomyopathy non-compaction, congenital heart defects, heart failure

Case presentation

46-year-old patient working in mining and steel, chronic tobacco smoker, with no previous history of cardiovascular diseases, was referred to our Centre for cardiological evaluation with suspicion of an acute coronary syndrome. Initial electrocardiogram (ECG) showed left bundle branch block (LBBB) and the emergency echocardiography revealed impaired left ventricular muscle contractility. He had two episodes of loss of consciousness on the prior to admission. Two days before hospitalization he had suffered an electric shock at work. His past medical history disclosed repeated exposure to electrical shocks as well as hazardous working environment including toxic zinc and lead compounds. In 2006 LBBB was diagnosed during periodic medical check-up. There were no abnormalities of the heart and valves indicated in previous echocardiography examinations. At admission to our hospital he presented no ailments. He was haemodynamically stable with no signs of neurological impairment. His heart rate (HR) was 80 beats per minute (bpm) and the blood pressure (BP) – 119/79 mm Hg. Laboratory work-up

showed normal levels of myocardial necrotic markers (peak high sensitive troponin T < 0.003 ng/mL [<0.014 ng/mL], peak creatine kinase-MB isoenzyme of 12 U/L [<24 U/L], peak creatine kinase of 52 U/L [<190 U/L]), abnormalities in lipid profile (total cholesterol of 5.6 mmol/L [3,10 – 5,0 mmol/L], triglycerides of 2,05 mmol/L [<1,70 mmol/L], cholesterol LDL of 3,74 mmol/L [<3,00 mmol/L], cholesterol HDL of 0.92 mmol/L [> 1,00 mmol/L], normal renal function parameters (Creatinine – 76 umol/L [<106], GFR > 90 [>60], K+ of 4.7 mmol/L [3.3–5,1 mmol/L], Na+ of 141 mmol/L [129–145]). ECG revealed sinus rhythm, 88 bpm with LBBB and single premature ventricular beats (VES) (Figure 1).

Coronary angiography unveiled a muscular bridge in middle segment of anterior descending branch (LAD) that causing systolic 70% lumen stenosis; no atheromatous lesions in coronary vessels were found (Figure 2).

Echocardiography showed enlarged left ventricle (LV) with sphere-like remodelling and significant global dysfunction with the ejection fraction (EF) of 20%. Significant intraventricular and interventricular asynchrony was also observed. Thick trabeculation of the posterior and lateral walls and the apex was noticed, suggesting

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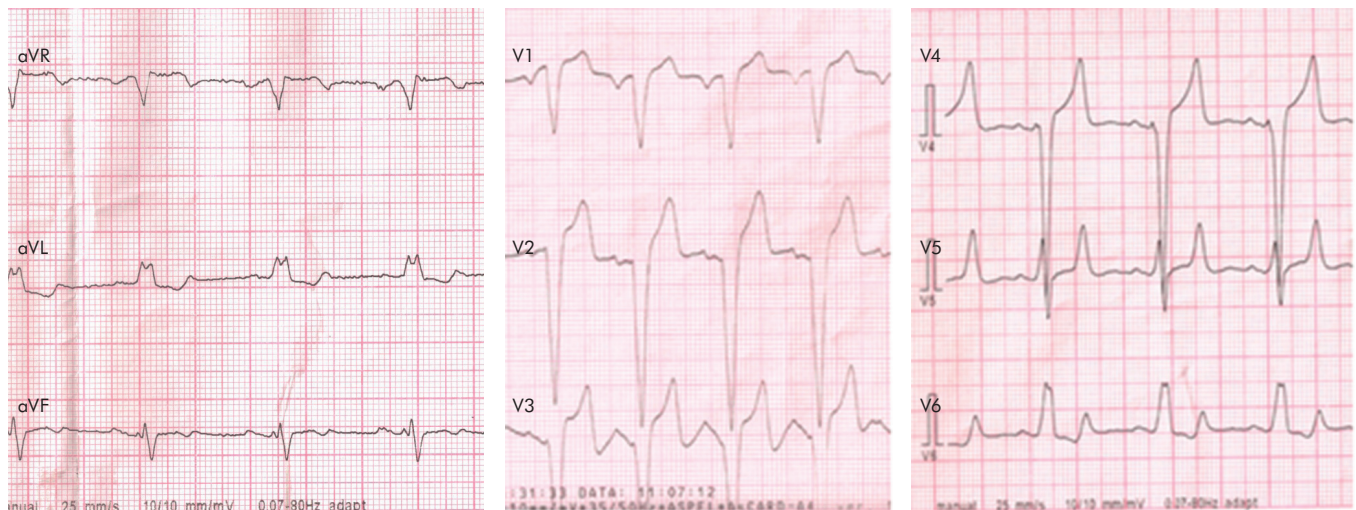
Figure 1. Electrocardiogram. Sinus rhythm, regular with ventricular frequency 88 beats per minute, left axis deviation, LBBB, Complex QS in leads V1-V3. PQ interval 160 ms, QRS complex duration 160ms, QTc 329 ms

ventricular non-compaction. Thickness of the non-compacted myocardium was 15 mm, while the compacted layer thickness was 6–7 mm. No valvular dysfunction was found. Pseudonormal mitral inflow was detected with the E/E' ratio of 10, and moderate left atrium (LA) enlargement – left atrial volume index (LAVI) was 36ml/m^2. Right ventricular systolic pressure (RVSP) was found to be normal. A spontaneous contrasting of the blood in the LV cavity was seen on the echo study (Figure 3).

Due to suspicion of the occupational factors contribution to the LV non-compaction (toxic effects of zinc and lead compounds), cardiac magnetic resonance (CMR) was performed. It revealed significant enlargement of the LA (29.6 cm^2; 6.7×4.6 cm) and the LV (7.6/7.1 cm), as well as thinning of the apical wall (0.4 cm). Thickness of the remaining left ventricular walls was normal. Thick trabeculation of the apex, inferior, posterior, lateral, anterior walls and the anterior part of the interventricular septum (IVS) was confirmed. Maximum diastolic ratio of the trabeculated part to the LV wall at the apex was 2.8/0.4 = 7. The pattern fulfilled the morphological criteria of LV non-compaction [19, 20]. The scan confirmed severe global LV systolic dysfunction (EF 18%). No signs of inflammatory process or ischemic myocardial damage was seen on the CMR study (Figure 4, 5).

Pharmacological therapy including angiotensin converting enzyme inhibitor (ACEi), beta-blocker, aldosterone receptor blocker and acetylsalicylic acid (ASA), as well as a statin for lipid disorders was initiated. In addition, low molecular weight heparin (LMWH) was used due to risk of thrombosis related to the spontaneous LV contrasting on echo.

Cardiopulmonary exercise test (CPET) was performed, and was discontinued in the 10th minute due to general fatigue. Maximum minute oxygen absorption (VO_{2max}) was 15.2 ml/kg/min. There were two runs of non-sustained ventricular tachycardia (nsVT) in 24-hour holter ECG monitoring. Cardiac resynchronizing device with defibrillator function (CRT-D) was implanted (Figure 6).

The patient had a follow-up visit after 4 months. Rest ECG and echo results were comparable to the previous examinations.
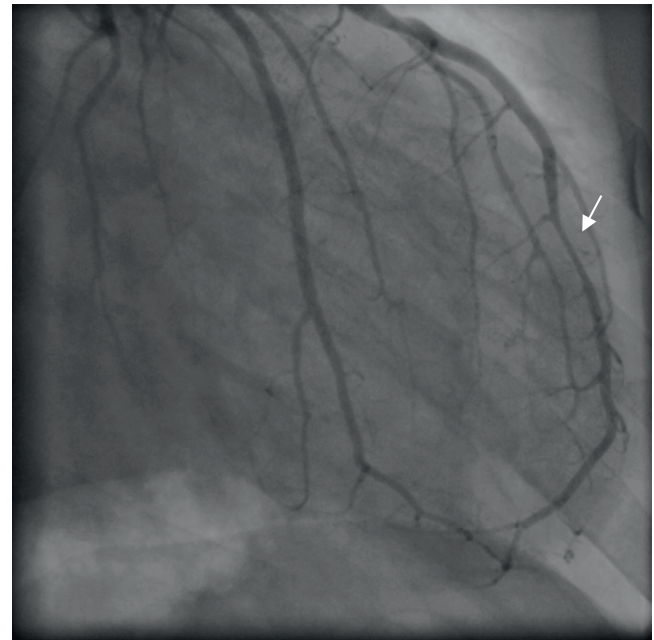

Figure 2. Coronary angiography. Left coronary artery – muscular bridge (arrow) in middle segment of left anterior descending artery causing systolic 70% lumen stenosis

Patient reported no chest pain (CCS I) or exertional dyspnea. Good tolerance of physical effort was reported (NYHA I).

Conclusion

This case of non-compaction cardiomyopathy was presented on the Centre for Rare Cardiovascular consultation meetings 5 months after discharge. The experts recommended clinical and genetic screening of the patient's relatives. They also suggested CRT-D stimulation parameters optimization according to QRS width and echocardiography findings. They advised to perform
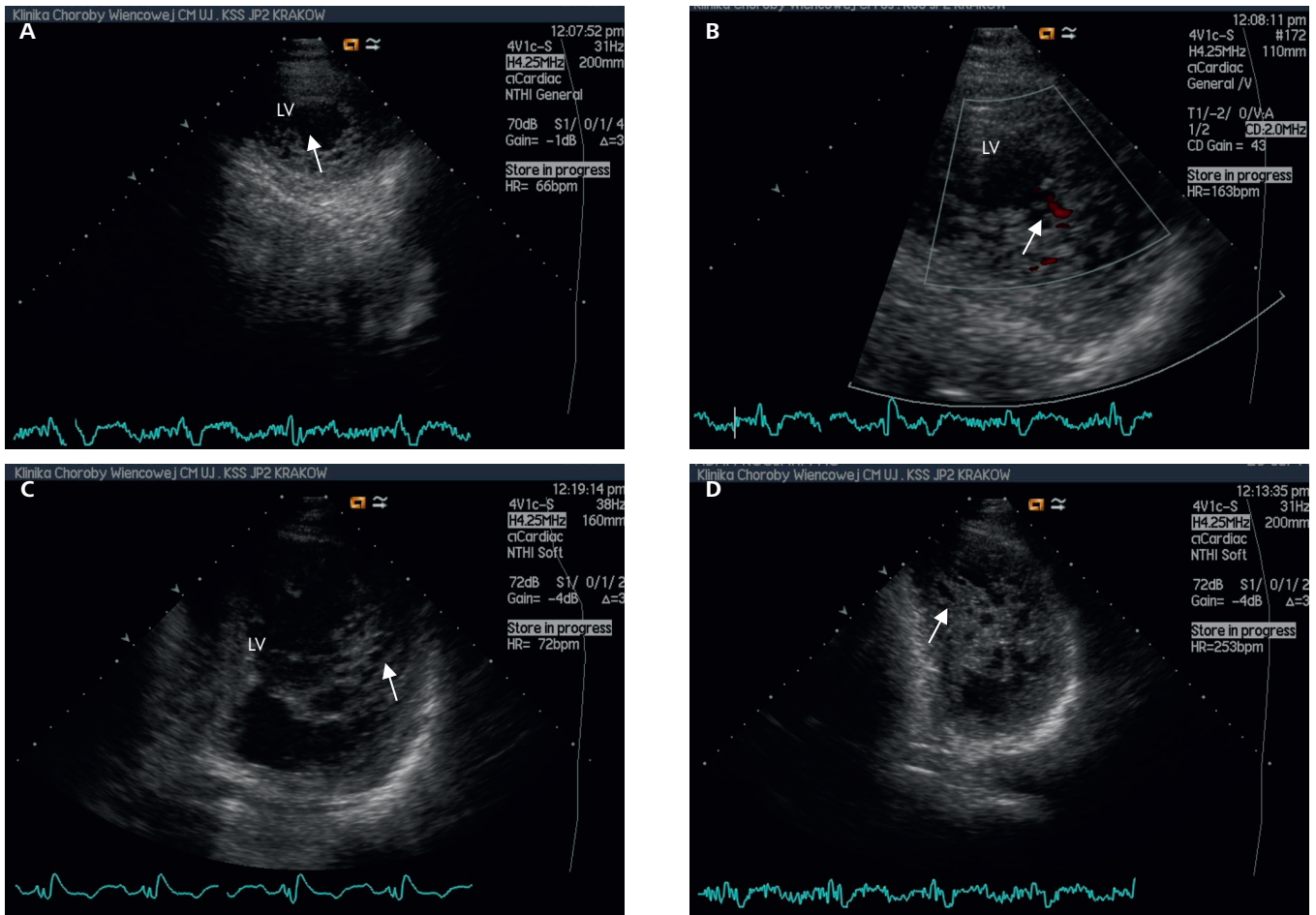
Figure 3. Transthoracic echocardiography. A. Short axis view of the LV apex. Heavy trabeculation of the LV muscle (arrow). B. Zoomed image. C–D. Modified apical four and two chamber views. Cross-sections of the non-compacted LV myocardium (arrow). LV – left ventricle
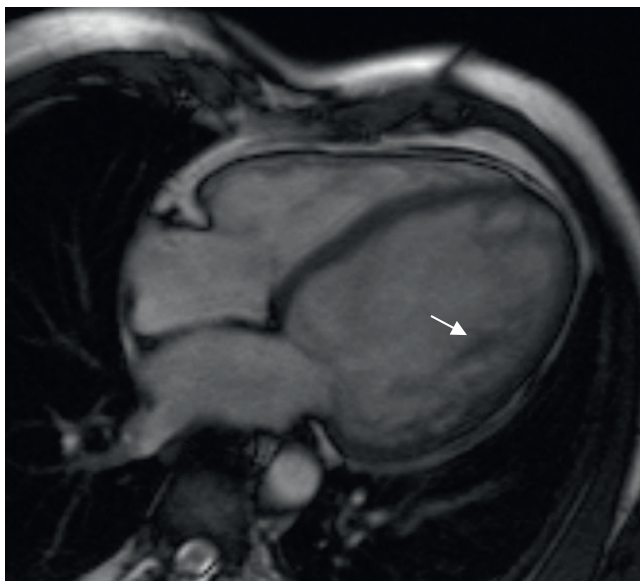

Figure 4. Cardiac magnetic resonance. Four chamber projection showing the cross-section of the non-compacted part of the left ventricle (arrow)
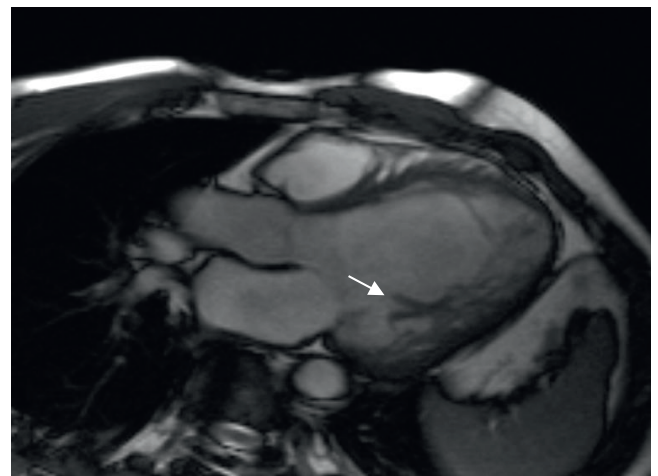

Figure 5. Cardiac magnetic resonance. Three chamber projection showing the cross-section of the non-compacted part of the left ventricle (arrow)
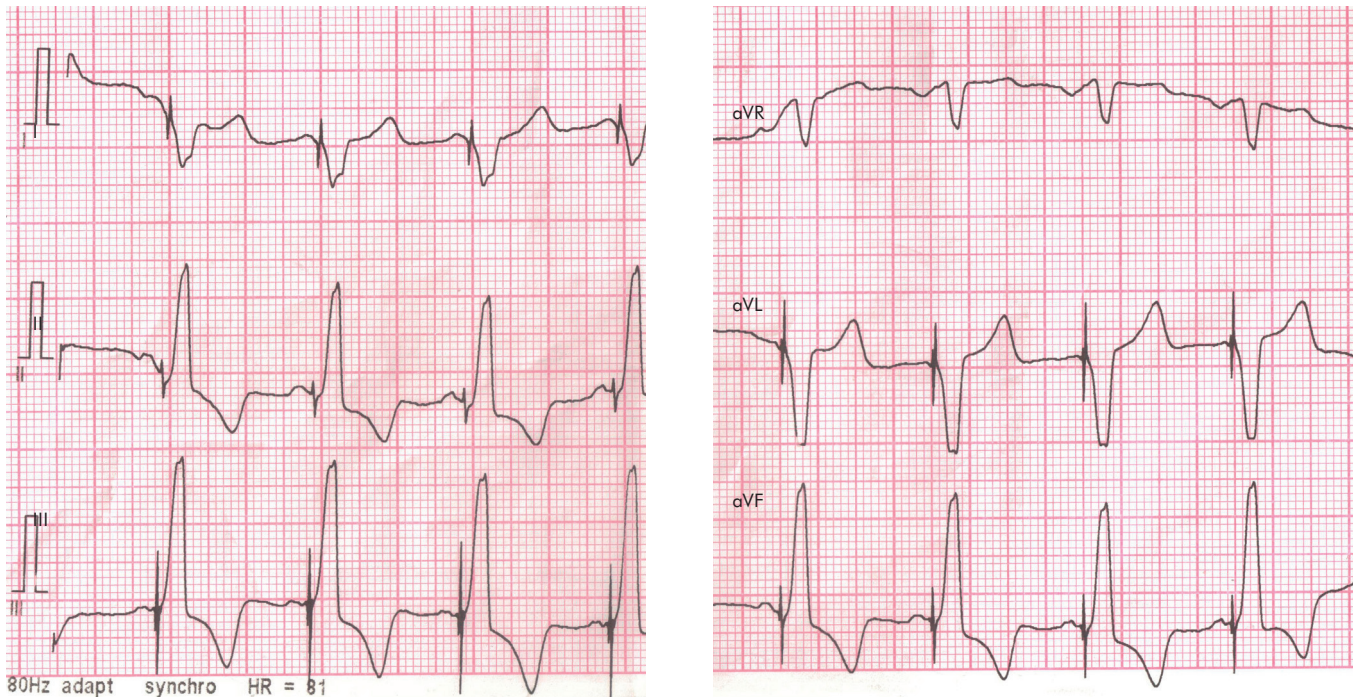
Figure 6. Electrocardiogram. Normal pacing. QRS complex duration 140 ms

right heart catheterization in the future to prepare the patient for potential heart transplantation.

In CRT-D interrogation after 6 months no shocks were recorded. There was a single VT episode, which subsided spontaneously, without CRT-D intervention. VT detection and therapy parameters were modified. Due to numerous ventricular beats (approx. 1500/24h VPBs, with including R/T phenomenon), amiodarone was initiated. Patient remains stable in the follow-up.

Review of literature

Isolated left ventricular non-compaction (ILVNC) is a rare, congenital developmental anomaly, included in the unclassified cardiomyopathies by the ESC Position Statement. The disease is characterized by heavy trabeculation of the muscle of LV or both ventricles, separated by deep sinuses communicating with LV cavity [1]. LVNC is supposed to be the result of an arrest or failure of the muscle compaction process during endomyocardial embryogenesis.

Epidemiology

The incidence of this pathology in the general population is estimated at 0,014–1.3%. [2, 3, 4, 5]. IVLNC has been described in children as well as adults, including the elderly [4]. The prevalence is low, probably 0.05%, but may actually be higher because of underdiagnosing or misdiagnosing as hypertrophic cardiomyopathy [6]. Men appear to be affected more often than women, with males accounting for 56% to 82% of cases in the 4 largest reported series of LVNC [2, 7, 8, 9]. A retrospective cohort study of cardiomy-opathy in Australia identified 314 of pediatric cases, of which 29 (9.2%) had a diagnosis of LVNC [10]. The frequency (incidence, prevalence) is not well known and there has been a scarcity of population-based studies of LVNC.

Genetics

A new era of medical genomics has created opportunities to carry out genetic research, that improves diagnosis and treatment of cardiovascular diseases. LVNC is a genetically heterogeneous disorder with a sporadic and familial form. Multiple gene mutations, including LIM domain binding protein 3 (LDB3), α-dystrobrevin (DTNA) on chromosome 18q12, G 4,5 on chromosome Xq28 (TAZ), β-heavy chains of myosin (MYH7), α-filaments hearts (ACTC), Lamins A/C, SCN5A and gen ZASP [11, 12, 13] have been reported. The search for genes associated with LVNC is ongoing, and there is evidence for a role of mutations of the following genes [14]. G4.5 mutations have been identified repeatedly in some of the larger series of LVNC but accounts for a small proportion of cases [4]. G4.5: this gene is located on Xq28 and was initially described in patients with Barth syndrome, some of whom were found to have LVNC. The gene products, called taffazins, are expressed mainly in heart and muscle cells and their action is thought to take place mainly in the mitochondria. To date mutations of G4.5 have been reported in young boys rather than adults. Alpha-dystrobrevin: this autosomal gene was identified in a Japanese family with six members affected by LVNC [11]. It is not yet possible to know the quantitative contribution of these genes to LVNC and such assessment awaits the publication of large systematic screens. Such studies would help compare the genetic

contribution among children vs. adults, in apparently isolated vs. familial cases, and by severity and clinical phenotype.

Clinical manifestations

Clinical manifestations are highly variable, ranging from no symptoms to disabling congestive heart failure, arrhythmias, and systemic thromboembolic complications. In the reported patient, LBBB could have been the first discernible sign. Less frequently it is supraventricular arrhythmias, atrial fibrillation, occasionally Wolff Parkinson White syndrome and other non-specific conduction disturbances. The main symptoms of the LVNC is probably due to disturbed blood supply to both layers of endocardium and epicardium with interstitial fibrosis, which induce disorder of systolic and diastolic ventricular function (more than 2/3 of patients) and ventricular arrhythmias [16].

Diagnosis of LVNC

The diagnosis of this cardiomyopathy is established mainly by echocardiography or magnetic resonance. Chin et al. and Jenni et al. presented echocardiographic changes typical for ILVNC [7, 17, 18]. According to him, the thickened myocardium with a two-layered structure consisting of a thin compacted epicardial layer/band (C) and a much thicker, non-compacted endocardial layer (N) or trabecular meshwork with deep endomyocardial spaces; N/C ratio > 2.0 determined LVNC. Predominant location of the pathology is mid-lateral, mid-inferior, and apex. Colour Doppler investigation evidences deep intertrabecular recesses filled with blood from the left ventricular cavity. Consideration of this value allows for differentiation of ILVNC and excessive meshwork in the case of left ventricular hypertrophy or dilated cardiomyopathy [17]. China et al. uses in the diagnosis of ILVNC two-layered structure of the myocardium (epicardial compacted, endocardial non-compacted layer) and distance ratio between the epicardial surface through the intertrabecular recess (X) to the distance between epicardial surface and peak of trabeculation (Y). Typical the ratio X/Y < 0,5 recognizes ILVNC. The measurements of the X-to-Y ratio shall be made at end-diastole, using parasternal short-axis view [7]. The current diagnostic criteria of ILVNC according to CMR findings are presented by Petersen et al. and Jacquier et al. [19, 20]. According to them the ratio between the non-compacted and compacted layer is > 2.3 in end-diastole [19]. In turn, Jacquier et al. states that the trabeculated left ventricular mass should be more than 20% of the global left ventricular mass [20]. In differential diagnosing, following pathologies should also be taken into account: apical hypertrophic cardiomyopathy, arrhytmogenic right ventricular cardiomyopathy, endocardial fibroelastosis, cardiac metastases. Non-compacted cardiomyopathy can be associated with neuromuscular diseases, such as mitochondrial myopathy, muscular dystrophy, myotonic dystrophy, Pompe disease, or Becker, ataxia Friedrich'a, syndrom Barth'a or Charcot-Marie-Tooth disease [8, 15, 21]. If suspicion of skeletal/mitochondrial myopathy, the neurological assessment should be performed.

Prognosis

The prognosis for patients with ILVNC is not fully known. ILVNC is recognized postmortem, after sudden cardiac death without prior symptoms. Prominent left ventricular trabeculations were observed in 323 (68%) of the 474 specimens [22]. Rapid progression of heart failure can be expected in patients with enlarged left ventricular (diastolic dimension > 60 mm) with left bundle branch block or atrial fibrillation [4, 21]. In these patients, the prognosis is worse. In 86 patients with left ventricular hypertrabeculation/noncompaction, during a 51-month follow-up the mortality rate was 5.3%/year. Advanced age, associated neuromuscular disorders, heart failure with dilated LV, and decreased ejection fraction were all associated with higher mortality [23]. Incidence of New York Heart Association (NYHA) class I/II heart failure in 65% and class III/IV in 35% has been reported by Oechslin et al. in their 34 patients [2]. Lofiego et al. [24] reported heart failure in 83% (40 of 48) and NYHA class III/IV heart failure in 44% (21 of 48) of their patients. Higher incidence of heart failure has been reported in adults compared with pediatric population [25].

Management

Main strategy of treatment includes typical heart failure drug treatment together with primary prevention of sudden cardiac arrest (cardioverter defibrillator implantation [ICD]) [26] or heart transplantation. In patients with widen QRS complexes there might be an indications for implantation of the cardiac resynchronization therapy with defibrillator (CRT-D), which improves LV contractility. [27]. Prevention of embolic complications is also an important management issue, and several authors have recommended long-term prophylactic anticoagulation for all patients with ventricular noncompaction whether or not thrombus has been found [2, 8]. Aspirin therapy has been recommended for all patients to decrease the risk for systemic embolism. Current data suggest that ILVNC is more a condition than previously thought. Use of the proposed diagnostic echocardiographic and CMR criteria along with clinical picture allow accurate diagnosis to be made, which is very important with regard to sudden death risk.

Conclusions

Non-compaction cardiomyopathy occurs as a diagnostic and therapeutic challenge for physicians. Despite established diagnostic criteria, diagnosis is difficult, and requires experience and echocardiographic equipment of good quality. Echocardiography is a standard diagnostic tool. It is recommended to perform echocardiography for first- degree relatives of patients with LVNC [28]. Diagnosis of ILVNC requires diagnostic tests on family members and perhaps genetic counseling. Due to coexistence of numerous neuromuscular disorders, it is recommended to assess the neurological and musculoskeletal status of LVNC patients [29]. The coexistence of symptomatic arrhythmias and syncope indicates execution of electrophysiology studies [3]. The prognosis

for patients with this condition requires further research. Mortality of patients with ILVNC is akin to patients with no-ischemic dilated cardiomyopathy (3 years survival rate of 85% vs 83%) [30]. Isolated ventricular non-compaction is a rare congenital cardiomyopathy, presenting with heart failure, arrhythmia, or cardioembolic events, which requires optimal treatment. An important issue is to regulate the use of anticoagulation for prevention of systemic embolism.

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