Clinical Characterization of Left Ventricular Noncompaction: A Case Series of Patients

Feridoun Noohi MD, FACC, Maryam Esmaeilzadeh MD, FCAPSC, Maryam Moshkani Farahani, MD, Anita Sadeghpour MD, FASE, S. Zahra Ojaghi MD, Niloofar Samiei MD

Abstract

Background-Non-compaction of ventricular myocardium (LVNC), also known as LVHT (left ventricular hypertrabeculation), is a rare embryonic cardiomyopathy that is thought to be a consequence of intrauterine arrest of compaction. It is characterized by an excessively prominent trabecular meshwork, which is accompanied by depressed ventricular function, systemic embolism and ventricular arrhythmia. This study was conducted to clarify the clinical features of patients with left ventricular noncompaction (LVNC) who were diagnosed in Shahid Rajaei Cardiovascular Medical Center.

Methods and Results- We retrospectively reviewed patients with LVNC between December 2004 and December 2005. A total of twenty-four patients were identified. In 4 patients there were associated cardiac lesions. They consisted of 6 females and 18 males with a mean age of 38.2 years (age range: 13-62 years). The average ejection fraction was 23.3%.The extension of noncompacted myocardium that was observed on 2-D echocardiography, was predominantly at the apex. There were two patients with systemic emboli, one with nonsustained ventricular tachycardia (VT), and one with Wolf-Parkinson-White sydnrome. The most common abnormality in the the electrocardiogram was left bundle branch block.

Conclusions- LVNC is most frequently diagnosed primarily by echocardiography and its prevalence seems to be increased with the improvement of cardiac imaging; so echocardiographers should be aware and trained to recognize this abnormality ***(Iranian Heart Journal 2007; 8 (4): 35-42).***

Key words: Non-compaction ■ left ventricle ■ cardiomyopathy ■ heart failure

Noncompaction of the ventricular myocardium is an embryonic cardiomyopathy that is thought to be a consequence of intrauterine arrest of compaction.[1] It is characterized by multiple, myocardial cotyledon-like protrusions and interwoven strings, all lined by endocardium. The definition of non-compaction includes thickened myocardium with a two layered structure consisting of compaction epicardial and noncompaction endocardial myocardium (maximum end-systolic ratio noncompaction to compaction >2) with a meshwork of perfused intertrabeculation recesses and regional hypokinesia.[2-6] It may occur without other cardiac abnormalities (isolated ventricular noncompaction) or may be associated with congenital cardiac malformations. In three quarters of cases, LVHT is associated with neuromuscular disorders.[6] Usually LVHT is congenital, but it was found to develop later in life (acquired LVHT).[7, 8]

Received March 22, 2006; Accepted for publication July. 5, 2007.
From the Department of Echocardiography, General Cardiology and Cardiac Surgery, Shaheed Rajaie Cardiovascular Medical Center, Iran University of Medical Sciences, Tehran, Iran.
Corresponding author: Maryam Esmaeilzadeh, MD, Shaheed Rajaie Cardiovascular Medical Center, Vali Asr Ave, Mellat Park, Tehran, Iran.

Noncompaction of LV myocardium, right ventricular myocardium, or both can occur in isolation, in congenital heart diseases, in valvular heart diseases, in neuromuscular disorders, skeletal abnormalities and in endocrinologic abnormalities.[3-5] Clinical presentation is similar to other cardiomyopathies and includes depressed systolic and diastolic function, systemic embolism and tachyarrhythmias.[2] ECG findings include signs of marked biventricular hypertrophy, with extreme QRS voltages; isolated or diffuse T-wave inversions; and arrhythmias, including Wolf-Parkinson-White syndrome with or without supraventricular tachycardia, ventricular arrhythmias, or conduction abnormalities, including heart block.[9-13]

Methods

We conducted a case series study in our institution between December 2004 and December 2005 in patients who were diagnosed with LVNC. They were referred to our echocardiography laboratory for evaluation of cardiac asynchrony, source of emboli, infective endocarditis and arrhythmias. We focused on ejection fraction, ventricular dimensions and features of congenital heart disease. The posterior wall myocardial thickness in the parasternal short-axis view was obtained in end-systole. Myocardial thickness was also determined at the site of the most prominent trabecular meshwork. The distribution of prominent trabeculations in the ventricle was assessed using parasternal, apical and subxiphoid imaging planes. Echocardiography videotapes were reviewed and interpreted by two authors to confirm the diagnosis. Twelve-lead ECG was also examined for identifying any abnormalities and arrhythmias, based on normal ECG standards. Wolf-Parkinson-White (WPW) syndrome was diagnosed based on documented spontaneous ventricular pre-excitation; individuals with a PR interval <100 ms.

Diagnostic criteria

LVNC was diagnosed when 3 criteria were established:

1) The characteristic appearance of multiple, excessively prominent trabeculations

2) Multiple deep intertrabecular recesses communicating with the ventricular cavity, as demonstrated by color Doppler imaging and the recesses demonstrated in the apical or middle portion of the ventricle.

3) A two-layered structure of the endocardium with a noncompacted to compacted ratio>1.4 in children and >2 in adults[6] (Fig. 1).

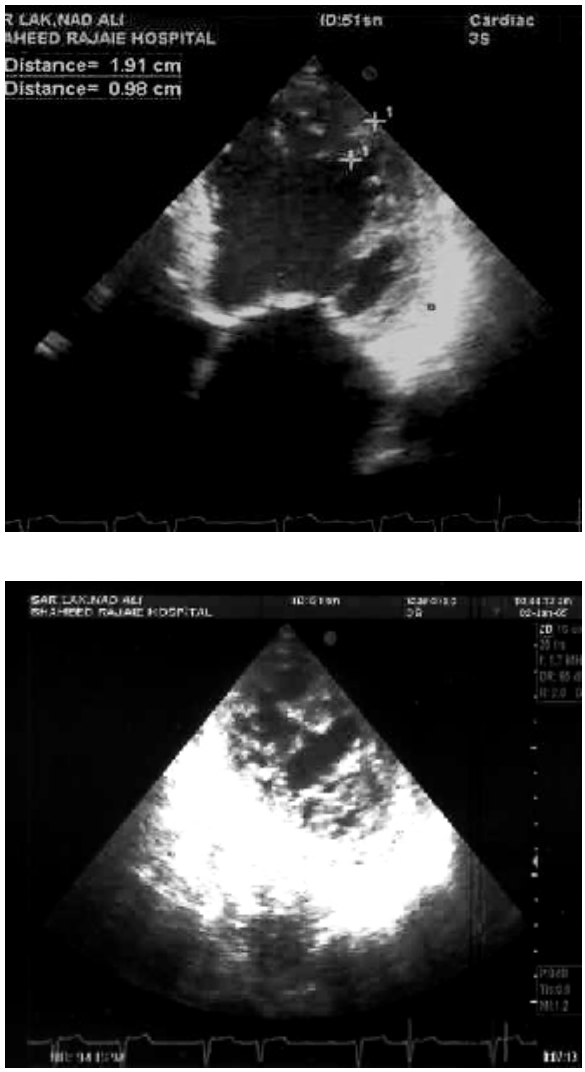


Fig. 1. Apical 4-chamber and parasternal short axis views show a two layered myocardium with

noncompacted to compacted ratio more than 2, and trabecular meshwork in apical area.

Results

Patients Population and Demographics

Twenty-four cases were identified from transthoracic echocardiography during a period of one year. They consist of 6 females and 18 males. The median age at presentation was 38.2 years (range, 13-62 years). Table 1 shows the demographic features of the patients.

Table I: Clinical and demographic characteristics of patients

Patient	age	sex	CHD	LV/RV	EF%	arrhythmia	emboli	CAD
1	42	M	NO	LV	12	NO	NO	NO
2	35	M	NO	LV	12	NO	NO	NO
3	13	M	NO	LV	11	NO	NO	NO
4	19	M	NO	LV	10	NO	NO	NO
5	50	M	NO	LV	27	NO	NO	YES
6	49	M	NO	LV	10	NO	NO	NO
7	50	M	NO	LV	7	NO	NO	NO
8	25	M	NO	LV	30	YES	NO	NO
9	59	M	NO	LV	17	NO	NO	NO
10	60	M	NO	RV	30	NO	NO	YES
11	35	M	NO,AI	LV	25	NO	NO	NO
12	39	M	NO	LV	20	NO	YES	NO
13	28	M	NO	LV	8	NO	NO	NO
14	20	M	NO	LV	55	NO	NO	NO
15	50	M	NO,AI	LV	30	NO	NO	NO
16	45	F	NO	LV	15	NO	NO	NO
17	13	F	NO	LV	25	WPW	NO	NO
18	21	F	PDA	LV	40	NO	NO	NO
19	44	F	NO	LV	50	NO	YES	NO
20	53	F	NO	LV	23	NO	NO	NO
21	62	F	NO	LV	20	NO	NO	YES
22	32	M	NO,IE	LV	35	NO	NO	NO
23	50	M	NO,MR	LV	30	NO	NO	NO
24	24	M	PDA,PS,VSD	LV	20	NO	NO	NO

Clinical Presentation

No dysmorphic features was found in our patients. The underlying reasons for initial referral and subsequent diagnosis of LVNC are outlined in Table II. The most common presenting symptom was dyspnea secondary to low cardiac output / congestive heart failure (CHF), which was noted in 12 patients (50%).

Three patients were referred for evaluation of wall motion abnormality due to CAD, 2 patients presented with arrhythmia, 3 patients with embolic events, 2 patients for evaluation of AI severity, 1 patient for evaluation of MR severity, 1 patient with infective endocarditis, and 1 patient was diagnosed incidentally. Four patients had associated congenital cardiac anomalies. Two patients with ascending aortic aneurysm and severe AI, a case with multiple congenital anomalies including muscular VSD, double-chambered RV, bicuspid pulmonic valve with severe PS, ASD, mitral valve involvement with severe MR, another patient had PDA with large highly mobile masses on main PA and pulmonic valve suggestive of vegetation.

Table II. Clinical presentation in patients with LVNC

Reason for presentation	number of patients
Low cardiac output/CHF	12
CAD	3
Source of emboli	3
Arrhythmia	2
Severity of AI	1
Severity of MR	1
IE	1
Routine echocardiography	1

Electrocardiographic Findings

A high prevalence of ECG abnormalities in affected subjects was noted (84%). The most prominent feature was ventricular conduction defects (LBBB) in 44% of patients.

Other patterns included LVH with extreme QRS voltage (Fig. 2), diffuse T-wave inversion, biventricular hypertrophy with RBBB in the patient with multiple congenital anomalies and WPW syndrome with supraventricular arrhythmia in a patient with a history of aborted sudden cardiac death last year (Fig. 3).

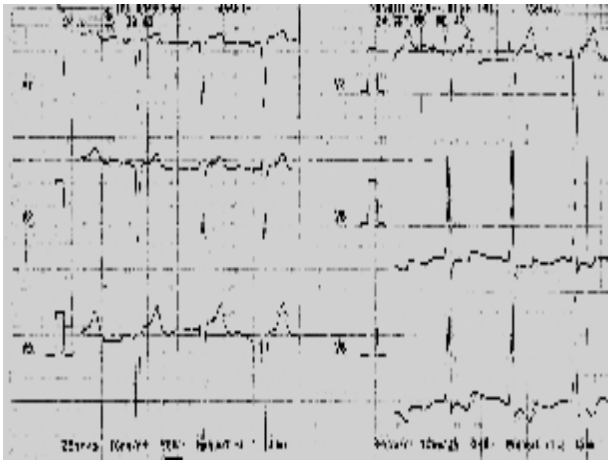


Fig. 2. 12-lead ECG in patient with LVNC revealed LVH with extreme QRS voltage.

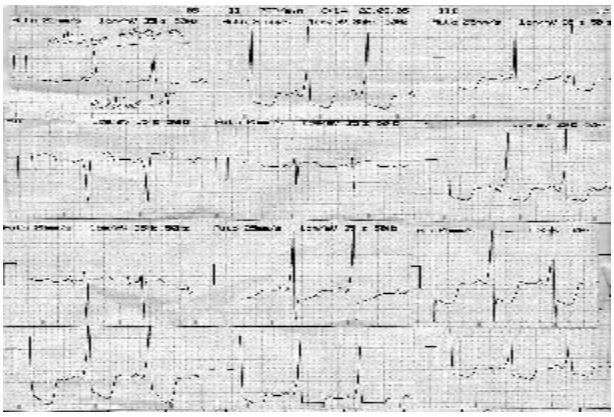


Fig. 3. 12-lead ECG in patient with WPW syndrome showed short PR interval, delta wave, LVH with strain pattern.

Echocardiographic Findings

Characteristic noncompaction morphology was found in the left ventricle in all 24 patients and isolated RV involvement in 1 patient. Use of color Doppler with typical forward and reversed flow between prominent trabeculations during cardiac cycles in the parasternal short-axis and apical 4-chamber views improved visualization of the trabeculations within the left ventricular endocardium (Fig.1). The median noncompacted to compacted left ventricular ratio was 2.1 (range 2 to 3.2).

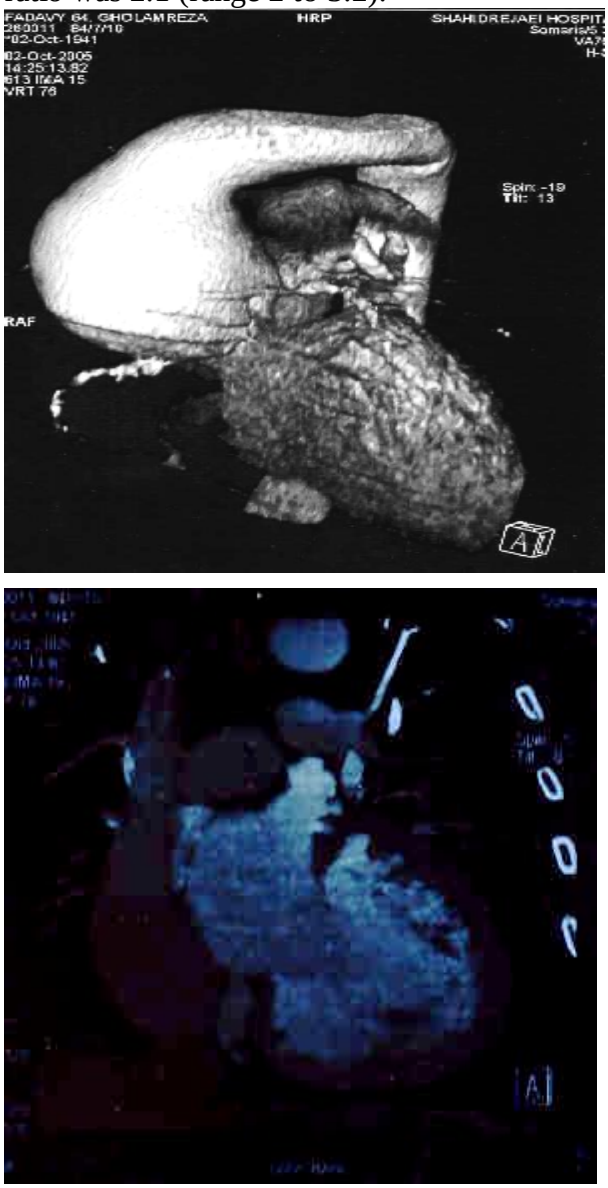
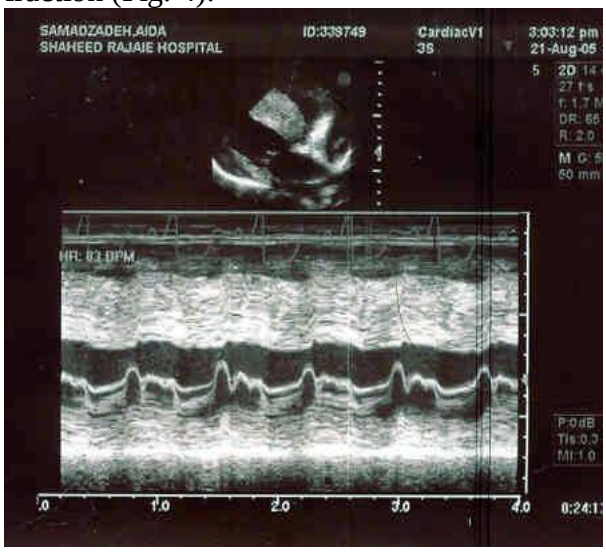


Fig.4. Cardiac CT showed aneurysmal dilation of ascending aorta with multiple trabeculations and deep intertrabecular recesses suggestive of LVNC.

Left ventricular systolic function was depressed in 23 patients and it was normal in 2 patients with median ejection fraction 23.3%. Ascending aortic aneurysm with severe AI (Fig. 4) was detected in 2 patients, one of them had Marfan's syndrome. Left ventricular thrombus was found in 1 patient. In one patient these multiple trabeculations and thick layer of noncompacted myocardium was initially misdiagnosed as hypertrophic cardiomyopathy with reduced ejection

fraction (Fig. 4).



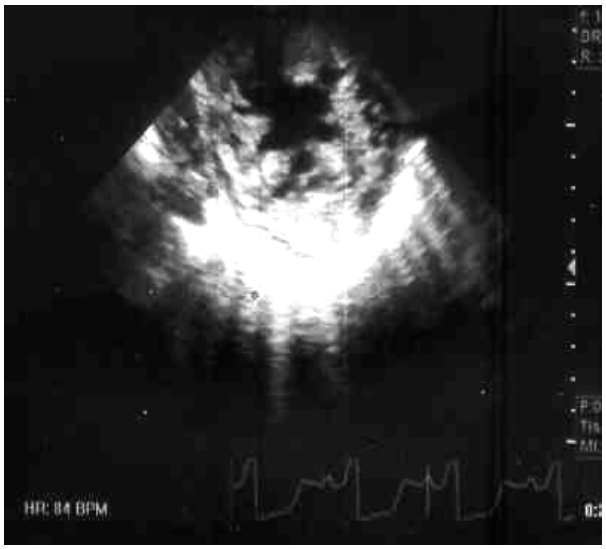


Fig. 5. M-mode parasternal long axis view showed severe asymmetrical septal hypertrophy which mimics HCM, but in 2D parasternal short axis view a two layered myocardium with multiple prominent trabeculations and deep intertrabecular recesses is noted .

Cardiac catheterization

Cardiac catheterization with selective coronary angiography was done in 3 patients with high probability of coronary artery disease.

CT Angiography

In one patient with ascending aortic aneurysm and severe aortic insufficiency, CT angiography was done to evaluate coronary artery disease.

Medical Therapy

Treatment of CHF consisted of diuretics, cardiac glycosides, and afterload reducers in all patients. Anticoagulant therapy was given in 8 patients, those with systemic embolism and those with severe LV dysfunction. Implantation of ICD was performed in 2 patients, and radiofrequency ablation in one with WPW syndrome and accessory pathway.

Surgical Therapy

In patients with ascending aortic aneurysm and severe AI, Bentall operation with CABG was done in one case, the other patient refused surgery.

Discussion

Pathogenesis

During a period of normal embryonic development the myocardium exists as a loose meshwork of interwoven myocardial fibers that form trabeculae with deep inter-trabecular recesses through a process of compaction of myocardium[14,15], the inter-trabecular recesses are transformed into the coronary circulation.

Embryonic arrest of this process (normally in the first month of the fetal life) leads to the persistence of prominent myocardial trabeculations with deep recesses that communicate to the LV cavity in the absence of co-existing congenital heart abnormalities. The condition is termed isolated ventricular non-compaction. LVNC may be associated with congenital cardiac malformations, thickening of the left ventricular (LV) myocardium, cardiac emboli, atrial septal aneurysm, valve abnormalities, LV dilatation, decreased LV systolic function or sudden cardiac death[16]

The apical region of the LV myocardium, the lateral wall and the posterior wall are the predominant sites of LVNC. This may be due to the LV ejection force.[17] Intraventricular

pressure during systole in these regions is highest within the ventricle. Several pathogenic concepts have been proposed for LV non-compaction.[2,18]

1) LVNC is hypothesized to represent persistence of embryonic sinusoids and results from an arrest in the compaction process of the myocardium.[2,17]

2) LVNC might result from an attempt of an impaired myocardium to grow and, thus, trying to overcome an inborn error.

3) LVNC might be the result of an adaptation to special hemodynamic conditions.

4) LVNC might be the consequence of an impaired adhesion of cardiac myocytes as a result of malfunction of gap junctions.[18]

5) LVNC might be a result of a cardiac neuropathy, a disturbance associated with the cardiac conduction system comprising his and Purkinje fibers.[19]

The cause of LVNC has not absolutely detected, (probably mutations in the gene G4.5 on the Xq28 chromosomal region are responsible)[7,15,20,21] and both sporadic and familial causes have been described for this disease state.[14,19] LVNC is a morphologic abnormality with genetic heterogeneity. Today it is categorized as an unclassified cardiomyopathy.[21]

Clinical Manifestations

Isolated ventricular non-compaction may affect both sexes although there is a male preponderance.[14] Patients may be asymptomatic or present with congestive heart failure, sudden cardiac death, arrhythmia and embolic events.[2] Congestive heart failure is the most common presenting condition.[2,3,4,5] CHF can be a result of either systolic or diastolic ventricular dysfunction. Diastolic dysfunction is probably a result of the abnormal ventricular trabecular structure causing impaired relaxation and filling.[2] The cause of systolic dysfunction is less clear, chronic myocardial ischemia due to coronary micro-circulatory dysfunction has been recently suggested as a possible mechanism.[20] Mechanisms of arrhythmogenic in LVNC include sympathetic nerve dysfunction and abnormalities in cardiac conduction system.[19]

Among the noncardiac abnormalities associated with LVNC, neurologic abnormalities are the most frequent (29% reported in one study).

If patients with LVNC are systematically referred to the neurologist the rate of neurologic abnormalities (particularly neuromuscular) are increased to 81-100%. [2-6]

Diagnosis

Echocardiographic findings are often diagnostic. Presence of more than three trabeculations within one image plane, apical from the insertion of the papillary muscles are a practically useful criterion.[14,15,20,22] The affected myocardium shows a thick non-compacted endocardial layer and a thinner compact epicardial layer (Fig. 1). LV mass was estimated both with and without the incorporation of trabeculations from the short axis view. A maximal end systolic ratio of non-compacted layer to compacted layer of 2 or more considered diagnostic or trabecular mass/total mass>20% may be a useful index in diagnostic measures. Presence of deep inter-trabecular recesses with direct blood flow from the ventricular cavity into the recesses demonstrable in color Doppler imaging is also diagnostic.[23] The diagnosis of LVNC can be made in the presence of these echocardiographic features. In the absence of co-existing congenital abnormalities the LV is affected primarily, the apical, lateral and inferior segments are commonly involved, (involvement of the midventricular anterior wall and septum and the basal segments is much less frequent).[23] The RV may also be affected but differentiation from normal trabeculations may be difficult. LV systolic and diastolic dysfunction are commonly present. The morphological appearance of LVNC has also been described on angiography, computed tomographic and magnetic resonance imaging .ECG findings

are abnormal in 74% of the patients and showed most frequently ST-T changes and signs of LVH.

Treatment and Prognosis

There is no specific treatment. The treatment is directed at the patients' symptoms and complications and include all that is available for the treatment of heart failure. A more aggressive approach to diagnosis and treatment of ventricular arrhythmias is considered. Because of the higher risk of thrombus formation within the intra-trabecular recesses, patient with LVNC and AF should receive oral anticoagulation. LVNC associated with rhythm disorder is primarily treated with antiarrhythmic drugs and in some patients, implantation of an ICD is necessary.[13]

In some cases heart transplantation may be considered. Therapy in patients with LVNC and neuromuscular disorder is limited to physiotherapy use of orthoses and symptomatic therapy of pain from muscle cramps, sensorimotor polyneuropathy and noncardiac non-neurologic disorders comprise the established therapy used for specific disorder.[2,6]

The prognosis of patients with LVNC is assessed controversially.[2,5,24] In earlier reports, LVNC was reported to be associated with high mortalities as a result of heart failure and SCD. According to a Mayo clinic report,[7] 59% of patients with isolated ventricular noncompaction had died or had a heart transplant within 6 years of diagnosis. The most common cause of death in these patients was sudden cardiac collapse. Many patients suffered from transient ischemic attacks, pulmonary embolisms, heart failure events, pulmonary edema episodes, cardiogenic shock and sustained ventricular tachycardia.[7] In the meantime, many cases of LVNC have been published with a better prognosis; this difference in prognosis can be explained with improvement in medical and surgical therapy for heart failure as a result of β blocker agents,[4,20,24] ACE inhibitors, implantation of cardioversion / defibrillators and heart transplantations. All symptomatic patients have a high risk of mortality and morbidity.[14,15,20] For patients diagnosed at the asymptomatic stage, the short term to medium term prognosis is favorable but progressive ventricular dysfunction is common.[20]

Conclusions

In conclusion LVNC most frequently diagnosed primarily by echocardiography and its prevalence seems to be increased with the improvement of cardiac imaging, so echocardiographers should be aware and trained to recognize this abnormality.

References

1. Varnava AM. Isolated non-compaction: a distinct cardiomyopathy? Heart 2001; 86: 599-600.

2. Strollberger C, Finstere J. Left ventricular hyperterabeculation / noncompaction. J of ASE Jan 2004; 17 (1): 91-100.

3. Stollbeger C, Finstere J, Valentin A, Blazek, Tscholakoff D. Isolated left ventricular abnormal trabeculation in adult is associated with neuromuscular disorder. Clin Cardiol 1999; 22: 119-23.

4. Oechslin EN, Attennofer C, Jost CH, Rojas JR, Kaufmann PA, Jenni R. Long term follow up of 34 adults with isolated LVNC: A distinct cardiomyopathy with poor prognosis. J Am Coll Cardiol 2000; 36: 493-500.

5. Frischknecht BS, Attenhofer CH, Erwin N, et al. Validation of LVNC criteria in dilated cardiomyopathy, and valvular and hypertensive heart disease . J Am Soc Echocardiography Aug 2005; 18 (8): 865-872.

6. Jenni R, Oechslin E, Schneider J, Jenni, E Oechslin, J Schneider, C Attenhofer Jost, and P A Kaufmann. Echocardiographic and pathoanatomical characteristics of isolated noncompaction: a step towards classification as a distinct cardiomyopathy. Heart 2001; 86: 666-671.

7. Riter M, Oechslin E, Sutsch G, Attenhofer C, Scheider J, Jenni R. Isolated noncompaction

of the ventricular myocardium in adults. Mayo Clin Proc 1997; 72: 26-31.

8. Dusk J, Ostadal B, Duskova M: Postnatal persistence of spongy myocardium with embryonic blood supply. Arch Pathol 1975, 99: 312-317.

9. Maile S, Kunz M, Oechslin E, Zund G, Rahn M, Lachat ML, Turina MI. Intractable tachycardia and bridging to heart transplantation with a non-pulsatile flow assist device in a patient with isolated left ventricular noncompaction. J Heart Lung Transplant 2004; 23 (1): 147-9.

10. Nihei K, Shinomiya N, Kabayama H, Ikeda C, Hosono T, Aoki T, Matsu N. Wolf Parkinson White (WPW) syndrome in isolated noncompaction of the ventricular myocardium (INVM). Circ J 2004; 68 (1): 82-4.

11. Stollberger C, Finsterer J. Left ventricular hypertrabeculation/noncompaction. J Am Soc Echo 2004; 17(1): 91-100.

12. Taniguchi M, Hioka T, Maekawa K, Takagagi K, Shoji K, Yoshida K. Adult case of isolated ventricular noncompaction discovered by complete atrioventricular block. Circ J 2004; 68 (9): 873-5.

13. Weiford BC, Subbarao VD, Mulhern KM. Noncompaction of the ventricular myocardium. Circulation 2004; 109 (24): 2965-71.

14. 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.

15. Jenni R, Oechslin E, Schneider J, Jost CA, Kaufmann PA. Echocadiographic and pathoanatomical characteristics of isolated left ventricular non-compaction; a step towards classification as a distinct cardiomyopathy. Heart 2001; 36: 493-500.

16. Dagdeviren B, Eren M, Oguz E: Noncompaction of ventricular myocardium, complete atrioventricular block and minor congenital abnormalities: Case report of an unusual coexistence. Acta Cardiol 2002; 57: 221-224.

17. Bogaert J, Rademakers FE: Regional nonuniformity of normal adult human left ventricle. Am J Physiol Heart Circ Physiol 2001; 280: H610-H620.

18. Peters NS, Severes NJ NS Peters, NJ Severs, SM Rothery, C Lincoln, MH Yacoub, and CR Green spatiotemporal relation between gap junctions and fascia adberens junctions during postnatal development of human ventricular myocardium. Circulation 1994; 90: 713-25.

19. Ansart A, Ho SY, Anderson RH. Distribution of the Purkinje fibers in the sheep heart. Anat Rec 1999, 254: 92-7.

20. Ichida F, Hamamichi Y, Miyawaki T. Clinical features of isolated noncompaction of the ventricular myocardium.J Am Coll Cardiol 1999; 34: 233-40.

21. Bleyl SB, Mumford BR, Brown-Harrison M-C, Pagotto LT, Carey JC, Pysher TJ. Xq28-linked noncompaction of the left ventricular myocardium: prenatal diagnosis and pathologic analysis of affected individuals. Am J Med Genet 1997; 72: 257-65.

22. Richardson P, McKenna W, Bristow M. Report of the 1995 World Health Organisation /International Society and Federation of Cardiology Task Force on the definition and classification of cardiomyopathies. Circulation 1996; 93: 841-2.

23. Maltagliati A, Pepi M. Isolatded noncompaction of the myocardium: multiplane transesophageal echocardiography diagnosis in an adult. J Am Soc Echo 2000;13: 1047-9.

24. Corrado G. Isolated noncompaction of the ventricular myocardium: A study in on adult move and literature review Ital Heart J 2000; 1: 372-5.