CASE PRESENTATION

Left ventricular noncompaction in a highly arrhythmogenic, apparently structurally normal heart

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Summary: Introduction – Premature ventricular contractions (PVCs) are relatively common clinical findings. One of the major determinants of prognosis in these patients is the presence of underlying structural heart disease. We report a notable case of highly arrhythmogenic left ventricular noncompaction (LVNC), undetected with the standard techniques used in the workup of patients with frequent PVCs. Case report – The ECG performed in a 53 year-old, asymptomatic male, without any personal cardiac history, revealed frequent, polymorphic PVCs, confirmed by ambulatory ECG monitoring. Transthoracic echocardiography failed to show any significant structural abnormalities, and coronary angiography excluded significant coronary artery disease. Complete resolution of PVCs at rest was obtained with Propafenone, but treadmill ECG testing revealed tachycardia-related reoccurrence of PVCs, suggesting the involvement of sympathetic activation in the etiology of ventricular arrhythmias. Cardiac magnetic resonance imaging revealed multiple base-to-apex trabeculae, fulfilling the criteria for LVNC over four segments. Conclusions – Electrocardiographic criteria, such as the occurrence of the arrhythmias during exercise and/or the polymorphic appearance of the arrhythmias, may prove useful in selecting candidates for additional imaging workup. It remains to be established if these subtle structural abnormalities, undetected using the standard techniques, carry the same prognosis as those revealed by echocardiography.

Keywords: ventricular tachycardia, premature ventricular beats, myocardial noncompaction, magnetic resonance imaging

INTRODUCTION

Premature ventricular contractions (PVCs) and non-sustained ventricular tachycardia (NSVT) are relatively common findings in clinical practice. The presence of these arrhythmias is often revealed during routine ECG, ambulatory ECG monitoring, or exercise stress ECG testing performed for other reasons in asymptomatic patients. The major challenge is to establish whether these ventricular arrhythmias are benign or indicative of an increased risk of sudden cardiac death (SCD). One of the major determinants of prognosis in these patients is the presence or absence of underlying structural heart disease. Standard ECG, exercise ECG testing, transthoracic echocardiography, and coronary angiography are usually used, collectively or in various combinations, to rule out structural heart disease.

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However, even in the presence of fully normal standard diagnostic techniques, novel imaging techniques have often identified structural cardiac abnormalities, particularly in patients with right ventricular outflow tract tachycardias\textsuperscript{4}. To date, it remains unclear how extensively should these patients be evaluated. Moreover, no consensus exists so far on the definition of structurally normal hearts.

We report a case of high ventricular arrhythmogenicity in the absence of any apparent cardiac structural abnormalities, as assessed using standard diagnostic techniques.

**CASE REPORT**

A 53-year-old asymptomatic Caucasian male, without any personal cardiac history or ambulatory treatment, presented to a cardiologist for routine physical examination. At that time, all blood tests were within normal ranges and physical examination didn’t find any abnormalities. Particularly, there were no signs of anemia, hypoxia, or electrolyte imbalance. The ECG revealed frequent, polymorphic PVCs, including episodes of ventricular bigeminy and couplets. PVCs displayed at least three different morphologies, suggestive of left ventricular outflow tract, left bundle branch fascicles, and inferior septal origins (Figure 1A, arrows). Ambulatory ECG monitoring confirmed the presence and the polymorphic feature of PVCs, revealing over 20,000 PVCs / 24-h, as well as the presence of multiple NSVT episodes with left bundle branch block morphology (Figure 1B), probably originating in the inferior septal area. Remarkably, QRS morphology during tachycardia was not homogeneous, suggesting multiple exit-points, probably around a restricted area. Transthoracic echocardiogram (Figure 2) failed to show any significant structural abnormalities, but the patient had poor acoustic windows. Similarly, coronary angiogram (Figure 3) excluded significant coronary artery disease.

The high ventricular arrhythmic burden prompted us to start the patient on Amiodarone. The antiarrhythmic treatment was rapidly efficient, ambulatory ECG monitoring confirming complete resolution of PVCs and NSVT episodes.

Two years later, the patient developed Amiodarone-induced thyrotoxicosis of unclear mechanism. Amiodarone was halted and the patient was started on Prednisone and antithyroid medication, allowing full normalization of the thyroid function within a few months. Shortly after cessation of Amiodarone, ventricular arrhythmias’ recurrence was noted. The patient was started on Propafenone 450 mg/day and was scheduled 48-h later for an ECG stress testing. By that time, complete resolution of PVCs was noted at rest. Treadmill stress ECG testing using the standard Bruce protocol revealed the reappearance of PVCs and NSVT at a heart rate of 114 bpm, with rapid resolution when the heart rate decreased below 100 bpm (Figure 4), suggesting the involvement of sympathetic activation in the etiology of ventricular arrhythmias. This finding prompted us to supplement the patient’s treatment with a beta-blocker.

The patient was scheduled for cardiac magnetic resonance imaging (MRI), which revealed left ventricular volumes at the upper normal range and increased left ventricular mass index, as well as moderate global hypokinesia, with mild impairment of the left ventricular ejection fraction (LVEF; 58%). Left ventricular anterior and lateral segments displayed multiple ba-
se-to-apex trabeculae, fulfilling the Petersen criteria for left ventricular noncompaction (LVNC) over four segments (Figure 5A-D). The right ventricle presented normal volumes and normal systolic function. The free wall of the right ventricle displayed crenelated appearance, but no significant kinetic abnormalities or aneurismal changes were noted. On delayed enhancement imaging, there was late gadolinium enhancement involving the basal region of the infero-lateral segment of the left ventricle, affecting the endocardial layer of the myocardium, limited to an area of noncompaction (Figure 5E and F, arrows).

Six months later, clinical and echocardiographic follow-up of the patient revealed no progression of the myocardial disease. Resting and stress ECG under combined beta-blocker and Propafenone treatment showed complete resolution of ventricular arrhythmias.

**DISCUSSION**

Non-sustained ventricular tachycardia and PVCs have been recorded in a wide range of conditions, from apparently healthy individuals to patients with significant heart disease. Although in the vast majority of patients PVCs entail a favorable benign prognosis, in patients with structural heart disease the presence of PVCs has been associated with a higher risk of SCD, particularly in patients with prior myocardial infarction.

Accordingly, current management of patients with frequent PVCs is designed to identify an underlying structural substrate of these arrhythmias. Although resting ECG, exercise ECG testing, transthoracic echocardiography, and coronary angiography are commonly used to exclude myocardial disease in some cases, particularly in patients with poor acoustic windows, other techniques may be necessary for definitive ex-
Left ventricular noncompaction using one of the modern, more sensitive imaging techniques. This allowed the diagnosis of LVNC in the absence of any apparent structural abnormalities with echocardiography.

To date, the morphological substrate and the prognostic significance of ventricular arrhythmias in patients with LVNC are far from clear. Perfusion defects in areas of noncompaction may provide a substrate for reentrant arrhythmias, explaining the often polymorphic appearance of the arrhythmias, as well as the occurrence of the arrhythmias at exercise in these patients. In the present case, the recorded QRS morphologies of PVCs and NSVTs can hardly be related to any area of noncompaction, as indicated by cardiac MRI, suggesting that other factors may also be involved in the high ventricular arrhythmogenicity observed in this population. Indeed, in the study of Shan...
et al. the frequency of SCN5A variants, encoding for the alpha-subunit of the voltage-gated sodium channel, was significantly higher in patients with LVNC that presented ventricular arrhythmias than in those who did not, suggesting that genetic factors may also represent a risk factor for arrhythmias in this population16.

In the present case, combined beta-blocker and Propafenone treatment allowed complete resolution of ventricular arrhythmias. However, suppression of arrhythmic events with antiarrhythmic drugs could not be associated with improved survival in various clinical scenarios17,18, while in studies such as CAST and CAST II, class Ic antiarrhythmics were actually associated with a significant increase in mortality in post-myocardial infarction patients, despite a significant reduction in arrhythmia burden19,20. To date, no specific data are available in LVNC patients. Accordingly, the decision of initiating antiarrhythmic treatment in this patient was driven by the high arrhythmic burden and the consequent risk of tachycardiomyopathy, and not by the rationale that this might reduce the risk of SCD. In patients with structural heart disease, Amiodarone is usually the preferred antiarrhythmic drug. The occurrence of Amiodarone-induced thyrotoxicosis prompted us to stop the treatment and to change the patient to Propafenone. However, Propafenone treatment carries a significant proarrhythmic risk in patients with heart failure, imposing regular follow-up of the patients’ left ventricular systolic function21,22, as well as the need to regularly monitor the duration of the QRS complex.

Galizio et al. recently proposed a number of criteria useful for identifying patients at increased risk of SCD23. Based on these criteria, the authors propose cardiac defibrillator implantation for the primary prevention of SCD in patients with LVNC and LVEF <30%, or at least two of the following criteria: family history of SCD, syncope or NSVT. Out of the 80 patients included in the study 28.75% benefitted of cardiac defibrillator implantation for the primary prevention of SCD. Only one of these patients benefitted of an appropriate shock during the 28 ± 22 months of follow-up; this patient was implanted based on a low LEVF. These results underline the role of decreased LVEF as main predictor of mortality in these patients. Electrophysiological studies and assessment of malignant ventricular arrhythmias induction may seem attractive for identifying patients at increased risk for SCD. However, arrhythmia induction in 24 LVNC patients could not predict the occurrence of SCD during the 61.4 ± 50 months of follow-up24. Accordingly, although the ACC/AHA/HRS 2008 Guidelines for Device-Based Therapy of Cardiac Rhythm Abnormalities recommended cardiac defibrillators implantation in all LVNC patients25, in the light of the current data, it does not seem reasonable to formulate recommendations applicable for the entire population of LVNC patients. Until additional studies are available and definitive criteria formulated, it seems reasonable to approach these patients based on parameters with established prognostic roles. Accordingly, the strongest predictor of SCD and the most widely used parameter in deciding cardiac defibrillator implantation for the primary prevention of SCD in patients with structural heart disease remains a low LVEF26.

Although cardiac MRI allowed the identification of ventricular noncompaction as substrate for arrhythmias in this patient, at present, there is little evidence to recommend the routine use of such imaging techniques in the workup of PVCs27. Moreover, it remains to be established if subtle structural abnormalities, undetected using the standard techniques, carry the same prognosis as the ‘gross’ structural abnormalities revealed by echocardiography. Further studies will have to be conducted in order to make definitive recommendations on the need and frequency of using these novel imaging techniques for the diagnosis and follow-up of these patients.

CONCLUSION

This report illustrates a case of highly arrhythmogenic LVNC undetected with the standard techniques used in the workup of patients with frequent PVCs. Additional ECG criteria, such as the occurrence of the arrhythmias during exercise and/or the polymorphic appearance of the arrhythmias, proved useful in deciding to perform further imaging workup. It remains to be established if these subtle structural abnormalities, undetected using the standard techniques, carry the same prognosis as those revealed by echocardiography.

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References


