Noncompaction cardiomyopathy (NCCM) is a rare primary cardiomyopathy caused by an arrest in myocardial morphogenesis. The clinical manifestations are highly variable from asymptomatic to severe heart failure, arrhythmias, sudden cardiac death, or systemic thrombo-embolic events. Association of NCCM and electric disorders has been reported as rare case reports with WPW syndrome and Brugada syndrome, but to the best of our knowledge, an association with catecholaminergic polymorphic ventricular tachycardia (CPVT) and NCCM has never been reported.

The aim of the case report is to present unique features of both NCCM and gene mutation–proven CPVT in 1 patient, raising new questions.

Case

A 39-year-old woman was referred with frequent palpitations, exercise-induced dyspnea, fatigue, and tendency to faint. Her medical and family history revealed no cardiac disease. ECG demonstrated sinus bradycardia, 50 beats per minute, and mild inferolateral repolarization abnormalities. Echocardiography and MRI showed normal left ventricular function (ejection fraction, 66%) and typical signs of NCCM, with excessive apical and midventricular trabeculations (Figures 1, 2A, and 2B). Coronary angiography revealed no abnormalities. Twenty-four–hour Holter showed frequent nonsustained ventricular tachycardias (VTs; maximal 10 runs, 180 beats per minute) and very frequent (4656/24h) and complex premature ventricular complexes. Exercise test showed moderate exercise intolerance (max. 67% predicted), with increasing numbers of complex premature ventricular complexes and bidirectional VTs (Figure 3).

Figure 1. Two-dimensional apical 4-chamber echocardiographic view showing excessive apical hypertrabeculation.

Figure 2. MRI 2-chamber (A) and apical short-axis view (B) demonstrating excessive apical to midventricular hypertrabeculation with typical 2-layer structure of the myocardium like in noncompaction cardiomyopathy.
Genetic test revealed heterozygotic mutation (c.169-198_273+823dle) in ryanodine receptor gene, confirming the diagnosis of CPVT.

β-blocker therapy was given, although an optimal dose could not be reached because of symptomatic bradycardia. She underwent a dual chamber pacemaker-defibrillator implantation with further titrating of β-blocker therapy (bisoprolol 7.5 mg); under these treatments she was doing a little bit better, with New York Heart Association functional class II. One year later, she showed up because of more frequent palpitations, dyspnea, and dizziness. Twenty-four-hour Holter and ECG showed frequent monomorphic premature ventricular complexes. Exercise testing showed again moderate decreased exercise tolerance (maximal 102 Watt, 67% of predicted) and frequent premature ventricular complexes and a supraventricular tachycardia during rest. Flecainid was given without efficacy. Finally, an ablation was performed in the left ventricular outflow tract by magnetic navigation. After 6 months of follow-up she was doing well with minimal symptoms.

Discussion

In this report we present a unique case with presenting with both classic CPVT with ryanodine receptor mutation and classic morphological features of NCCM. CPVT is considered an inherited arrhythmia syndrome, characterized by bidirectional or polymorphic VT induced by physical or emotional stress. Mutation in ryanodine receptor gene cause about half of all cases of CPVT. Structural heart disease is usually absent and the baseline ECG is normal, although sinus bradycardia is common like in our case. This raises the question whether this is a coincidence or a real association between these 2 rare disorders. In other words, is there a common link during the development of the heart that can explain this phenomenon?

NCCM is a relatively rare primary cardiomyopathy that may lead to heart failure, (malignant) arrhythmias, thromboembolic events, and sudden cardiac death. The abnormal structures of NCCM are characterized by excessively prominent trabecular meshwork and deep intertrabecular recesses, as seen early in human embryogenesis. Therefore, the primary patho-physiological hypothesis is that NCCM is most likely caused by an arrest of myocardial morphogenesis (or immatures myocardium) between the 32nd and 70th day of fetal life. The development of the conduction system occurs, importantly, exactly during this period. The atrioventricular node as a nodal structure becomes gradually identifiable from about 5 weeks of development onward. The ventricular conduction system develops between the 5th to 7th weeks of fetal life. Epicardium-derived cells migrate into the myocardium and differentiate into interstitial, subendocardial, and coronary adventitial fibroblasts, as well as coronary smooth muscle cells. These epicardium-derived cells are essential for formation of the compact myocardium and promote Purkinje fiber differentiation as well. A disorder in this period (immature conduction system?) can cause both structural and electrical disease, as it was presented in this unique case. Therefore, this raises not only a new hypothesis needing further research, but emphasizes also the need of appropriate evaluation of cardiac morphology in patients with a presumed primary electric disorder.

Disclosures

None.

References

Primary Electrical Disorder or Primary Cardiomyopathy?: A Case With a Unique Association of Noncompaction Cardiomyopathy and Cathecolaminergic Polymorphic Ventricular Tachycardia Caused by Ryanodine Receptor Mutation
Zsófia Szentpáli, Tamas Szili-Torok and Kadir Caliskan

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