Recurrent unexplained syncope in an adolescent girl

Stefano Di Bernado[a], Tatiana Boulos-Ksontini[a], Yvan Mivelaz[a], Niccole Sekarski[a], Etienne Pruvot[b]

[a] Paediatric cardiology unit, Department of pediatrics, University Hospital, Lausanne, Switzerland

[b] Arrhythmia unit, Service of cardiology, University Hospital, Lausanne, Switzerland

Case presentation

This fourteen year-old girl was referred to our outpatient clinic because of recurrent episodes of unexplained syncope. The episodes were of similar presentation. During endurance evaluation at school (the so-called "12-minute running test"), she repetitively developed dizziness, blurred vision and weakness after 8–10 minutes, before passing out for an unusual duration of about 6–8 minutes. After spontaneous recovery,

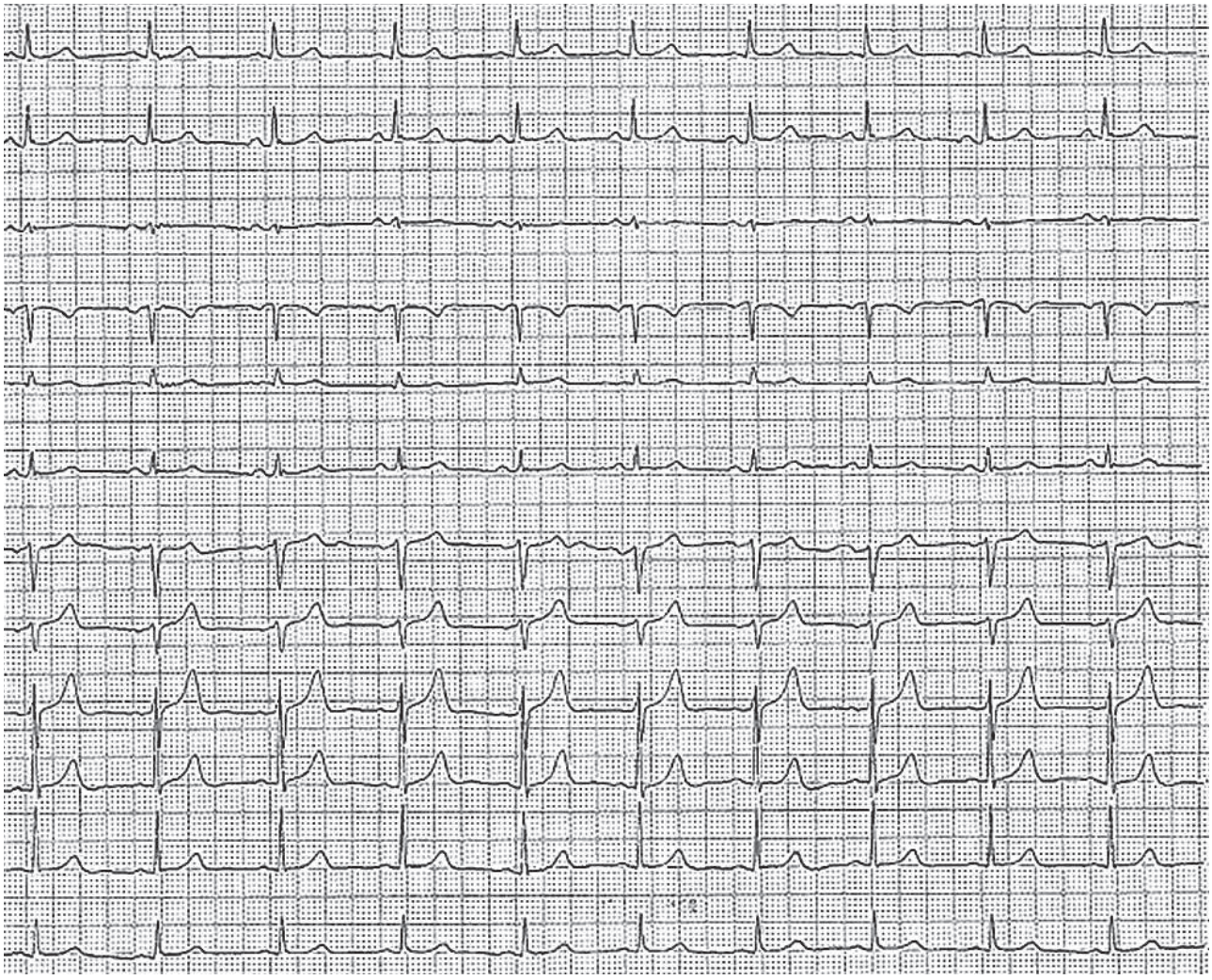

Figure 1
Surface 12-lead ECG. Normal sinus rhythm, no signs of ventricular hypertrophy, normal intervals and QRS duration.

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Correspondence:
Stefano Di Bernado, MD
University Hospital and University of Lausanne
Rue du Bugnon 46
CH-1011 Lausanne, Switzerland
stefano.di-bernardo[at]hospvd.ch

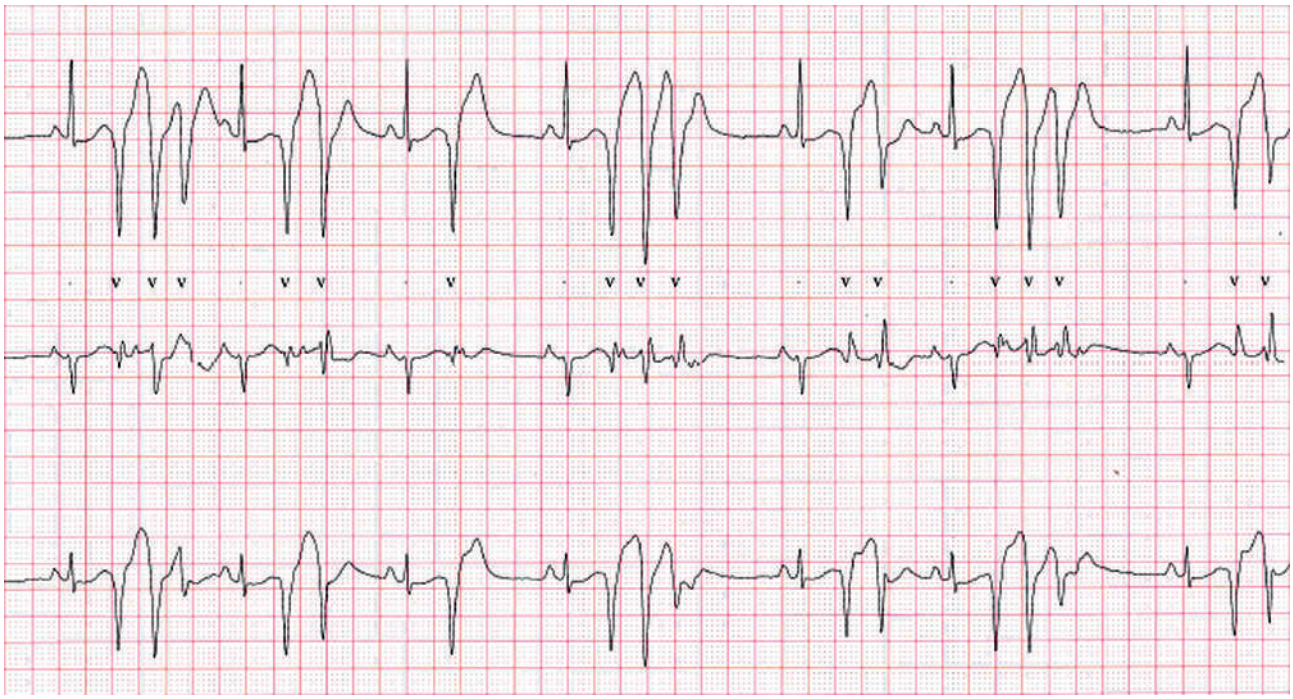

Figure 2
Three-derivation Holter recording. Short-coupled single ventricular premature beats, doublets and triplets interspaced with sinus beats during daily activity. V: ventricular beats.

she felt tired and weak for hours and reported near-death experience suggestive of severe brain hypoperfusion. Apart from these symptoms, no other signs e.g., palpitations or chest pain were noted. Witnesses described the patient as pale and sweaty during the episodes.

Figure 1 shows her ECG at rest. A normal sinus rhythm is observed at 67/min with normal PR interval (138 msec), QRS duration (85 msec), QRS axis (90), and QTc interval (420 msec), and no sign suggestive of ventricular hypertrophy or repolarisation disorder. The echocardiography demonstrated a normal heart as well with left ventricle and right ventricle dimensions and functions within limit. A cardiac MRI with late enhancement allowed us to exclude a congenital coronary anormaly, myocardial scars and signs of arrhythmogenic right ventricular dysplasia.

The 24-hour Holter recording revealed several episodes of nonsustained arrhythmia without any symptoms (fig. 2 and 3). Figure 2 shows a tree-derivation Holter recording with short-coupled single ventricular premature beats, doublets and triplets interspaced with sinus beats during daily activity. Figure 3 and 4 also shows a ventricular premature beat of a different morphology (arrow) that occasionally occurred during sinus tachycardia. Importantly, these episodes occurred only when the adolescent was involved in some physical activity or during stressful tests at school, while her rhythm was normal at night or at rest.

Question

What are the most likely diagnosis and optimal therapy?

Comments

Based on the observation of runs of nonsustained VT and premature beats of two morphologies, the diagnosis of cathecholaminergic polymorphic ventricular tachycardia (CPVT) or LQTS with normal QT interval [1] was highly suspected. Sport was prohibited and beta blocker therapy was initiated first with tapering of propranolol, followed by bisoprolol therapy because of fainting, dizziness and Rayneaud phenomenom. Based on the severity of the recurrent syncopal events and as well as persistence of runs of nonsustained VT despite prescription of beta blockers, an implantable cardioverter-defibrillator (ICD) was implanted. The patient remained asymptomatic for months under treatment. Thirteen months after the ICD implantation, a first presyncopal episode occurred during a stressful mathematical test at school. The first nonsustained polymorphic VT episode lasting 24 beats (coupling interval as short as 150 ms) was recorded by the ICD, that was suggestive of an under dosage of the beta blockers. Medication was changed for metoprolol 25 mg bid. Thirty-three months after the implantation, the patient forgot her medication one night and the next morning, while standing quietly, she presented a near

syncope that spontaneously resolved within seconds. Nonetheless, she was transferred to the hospital. Figure 5 shows the interrogation of the ICD at time of presyncope. A nonsustained polymorphic VT of 29 beats compatible with Torsades-de-Pointes is visible. Genetic analyses did not find the typical mutations associated with LQTS1-3 or CPVT.

CPVT occurs in patients without any evidence of heart disease. This disorder typically begins in childhood or adolescence. Affected patients present with

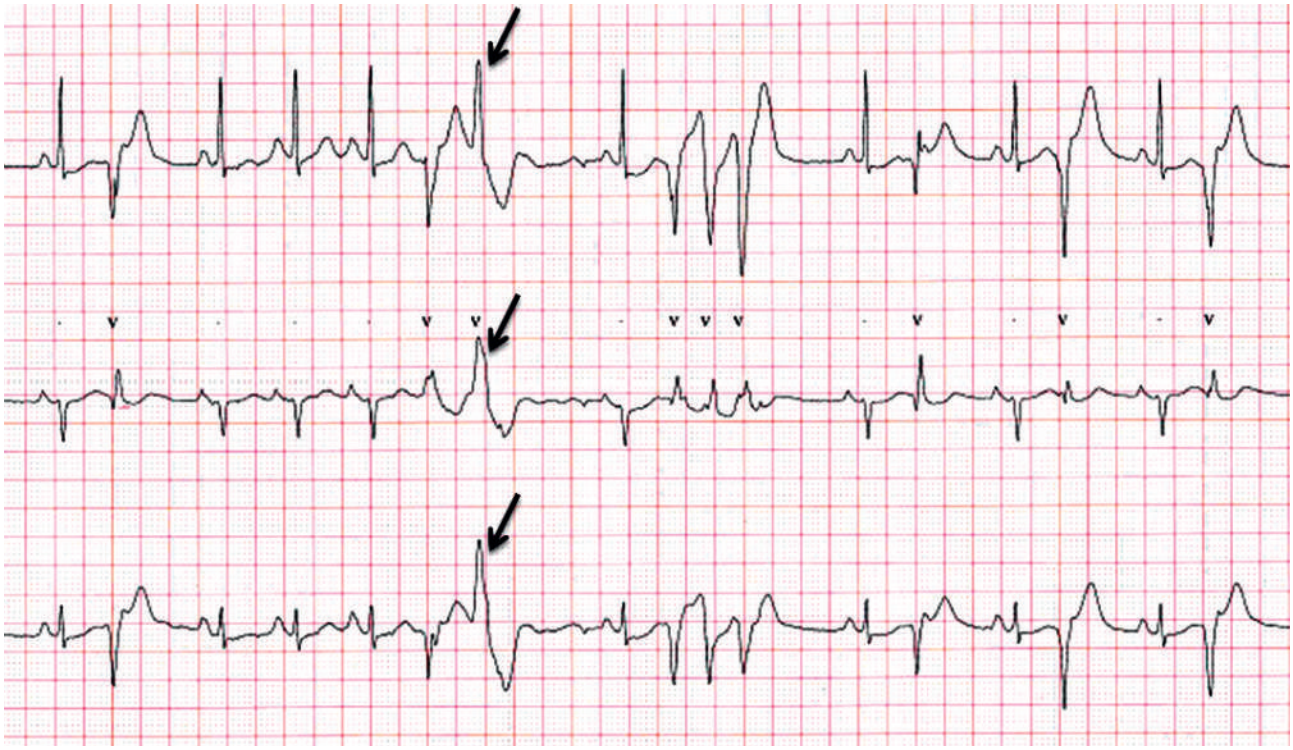

Figure 3
Three-derivation Holter recording. Short-coupled single ventricular premature beats, doublets and triplets interspaced with sinus beats during daily activity, with premature ventricular morphology varying from beat to beat (arrow). V: ventricular beats.

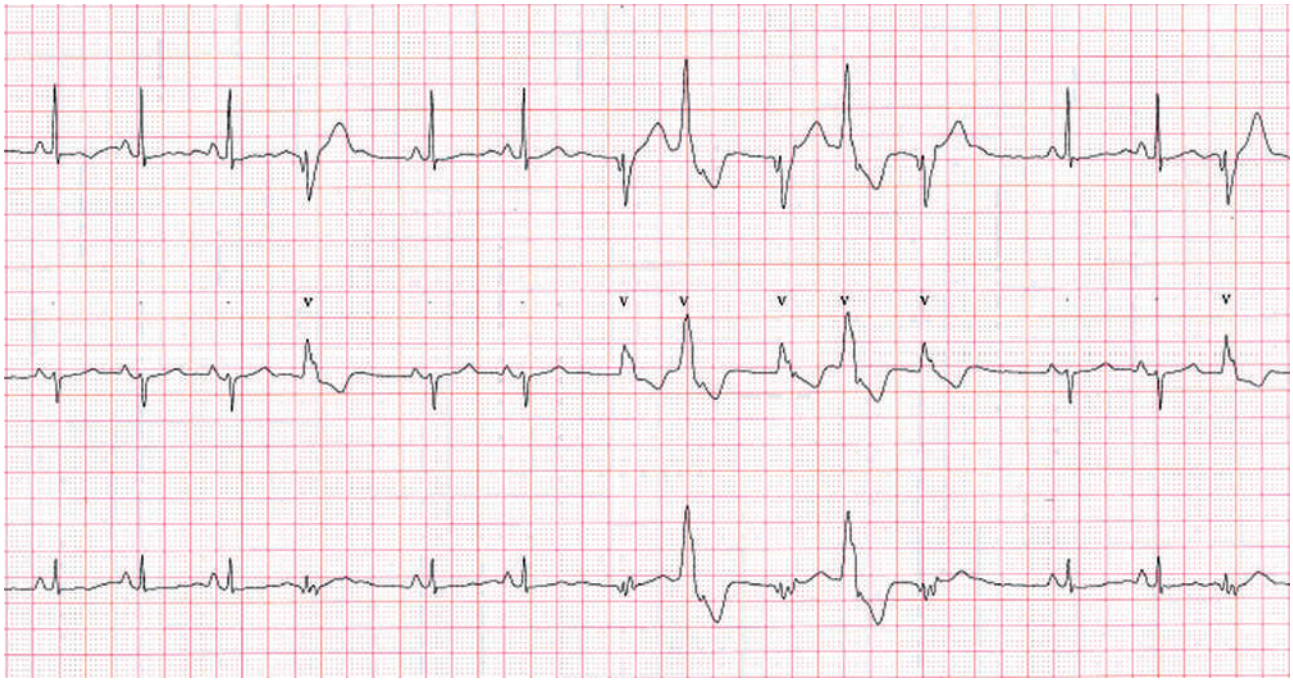

Figure 4
Three-derivation Holter recording. Nonsustained bidirectional ventricular tachycardia with QRS axis changing from beat to beat. V: ventricular.

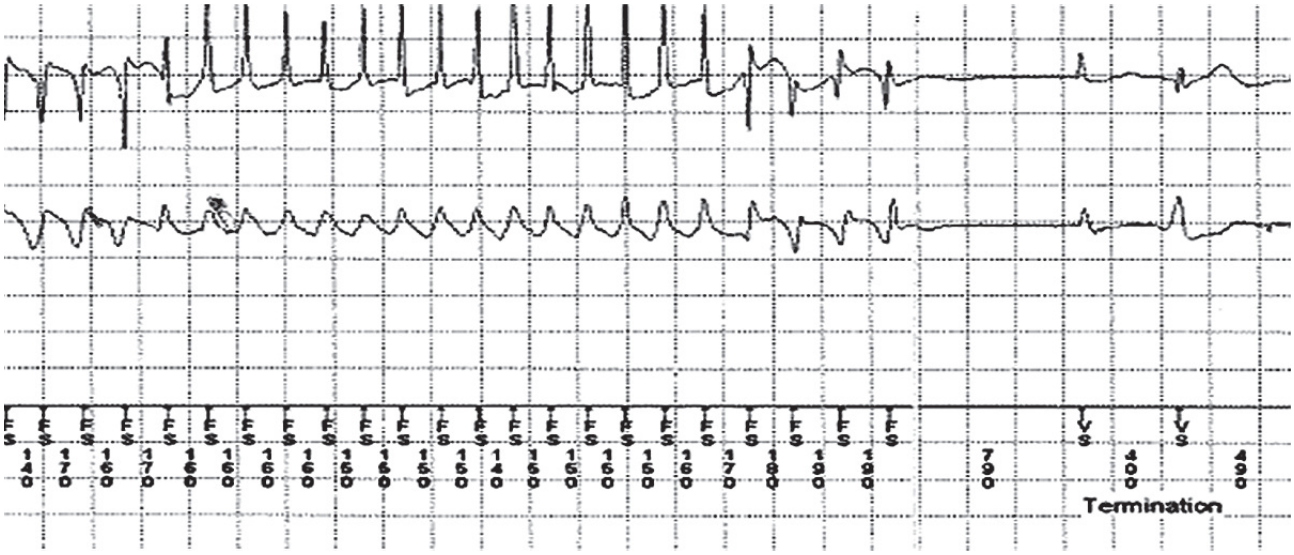

Figure 5
ICD interrogation. Nonsustained polymorphic ventricular tachycardia of 29 beats compatible with Torsades-de-Pointes with coupling intervals as short as 150 ms.

life-threatening VT or ventricular fibrillation occurring during emotional or physical stress. The VT morphology may vary continuously, from beat to beat, or may appear as a bidirectional VT [2]. Two mutations have been identified in patients with CPVT: the cardiac ryanodine receptor gene (autosomal dominant form) and the calsequestrin 2 gene (autosomal recessive inheritance) [3]. Both proteins play a major role in the regulation of cardiomyocyte's intrasarcoplasmic Ca2+. Treatments associate an ICD to terminate sustained arrhythmias and to prevent syncope and/or sudden cardiac death, and antiarrhythmic medication in order to prevent arrhythmias and minimise ICD shocks [4]. Beta blockers form the cornerstone of treatment, in patients with ongoing arrhythmias despite therapy with a beta blocker, the addition of verapamil or flecainide may be effective. In refractory cases, left sympathetic denervation can be an alternative therapeutic option [4, 5].

Syncopal episodes are usually benign in nature, in children. The evaluation of syncopal children or adolescents relies on a thorough, detailed history and physical examination. Syncopal episodes that are associated with exercise or sport have to be thoroughly evaluated for their potential danger [6, 7].

References

1 Hekkala AM, Viitasalo M, Vaananen H, Swan H, Toivonen L. Abnormal repolarization dynamics revealed in exercise test in long QT syndrome mutation carriers with normal resting QT interval. Europace: European pacing, arrhythmias, and cardiac electrophysiology: journal of the working groups on cardiac pacing, arrhythmias, and cardiac cellular electrophysiology of the European Society of Cardiology. 2010;12:1296–301.

2 Richter S, Gebauer R, Hindricks G, Brugada P. A classic electrocardiographic manifestation of catecholaminergic polymorphic ventricular tachycardia. J Cardiovasc Electrophysiol. 2012;23:560.

3 Nam GB, Burashnikov A, Antzelevitch C. Cellular mechanisms underlying the development of catecholaminergic ventricular tachycardia. Circulation. 2005;111:2727–33.

4 Van der Werf C, Zwinderman AH, Wilde AA. Therapeutic approach for patients with catecholaminergic polymorphic ventricular tachycardia: state of the art and future developments. Europace: European pacing, arrhythmias, and cardiac electrophysiology: journal of the working groups on cardiac pacing, arrhythmias, and cardiac cellular electrophysiology of the European Society of Cardiology. 2012;14:175–83.

5 Swan H, Laitinen P, Kontula K, Toivonen L. Calcium channel antagonism reduces exercise-induced ventricular arrhythmias in catecholaminergic polymorphic ventricular tachycardia patients with RyR2 mutations. J Cardiovas Electrophysiol. 2005;16:162–6.

6 Massin MM, Bourguignont A, Coremans C, Comte L, Lepage P, Gerard P. Syncope in pediatric patients presenting to an emergency department. J Pediatr. 2004;145:223–8.

7 Lewis DA, Dhala A. Syncope in the pediatric patient. The cardiologist's perspective. Pediatr Clin North Am. 1999;46:205–19.