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Case Report

Polymorphic Catecholaminergic Ventricular Tachycardia as a Cause of Syncope in Pediatric Age

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Abstract

Syncope is one of the most common clinical problem in children characterized by transient, spontaneously self-terminating loss of consciousness with brief duration and complete recovery. The underlying pathophysiological mechanism is a transient and global brain hypoperfusion. In the pediatric population syncope can occur with many different etiologies. Cardiac causes of syncope in children are rare but can be life threatening and have the highest risk of morbidity and mortality. Misdiagnosis of epilepsy is common in patients presenting with syncope; therefore, the differential diagnosis between epileptic seizures and syncope is very important. Here we report the case of a girl with misdiagnosis of epilepsy and a rare arrhythmia as the cause of her recurrent syncopes.

Introduction

Syncope, classically defined as a transient, self-limited loss of consciousness and postural tone, is a common presenting complaint in the pediatric Emergency Department (ED). By definition, the recovery from syncope is spontaneous, rapid, prompt, and complete without any neurologic sequelae [1].

The underlying mechanism is a transient global cerebral hypoperfusion. Involuntary movements, often referred to as myoclonic jerks, may accompany syncope due to cardiovascular causes and create a differential diagnostic problem against seizure with important therapeutic and prognostic implications such as inadequate treatment of the underlying disease and a considerable risk of mortality for some cardiac causes of syncope [2].

The main cardiovascular mechanisms causing cerebral hypoperfusion and convulsive syncope are vasovagal reactions and brady- and tachyarrhythmias [3].

We report the case of a girl treated for epilepsy but with recurrent syncope due to a rare cardiac arrhythmia such as Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT).

Case Presentation

A 10-year-old girl was admitted to our ED for syncope during exercise (skating) followed by myoclonic jerks. She had a history of recurrent syncopes with early warning symptoms (dizziness and blurred vision) and jerking movements; all episodes were triggered by emotional or physical stress. From the age of 9 she has been treated with Antiepileptic Drugs (AEDs) without clinical benefit.

No family history of Sudden Cardiac Death (SCD) at young age or congenital heart disease; paternal aunt with childhood seizures. On physical examination, the Heart Rate (HR), orthostatic and clinostatic blood pressure, respiratory rate and cardiac auscultation were normal.

Laboratory studies including full blood count, electrolytes, blood glucose and thyroid function were performed and were normal. Electrocardiogram (ECG) and echocardiographic evaluation excluded structural heart disease or functional abnormalities.

On 24-h Holter monitoring, sinus rhythm was interrupted by 6000 premature ventricular contractions (PVCs) with occasional couplets and short runs of ectopic ventricular tachycardia (maximal HR 165 beats/minute, 7 beats). On exercise stress testing, at high workload, polymorphic ventricular tachycardia was detected with progressive worsening of the arrhythmia in proportion to the

increase in load.

The mutation of the hRyR2 gene, coding for the ryanodine type 2 receptor, was detected by genetic testing and the diagnosis of CPVT was made. EEGs, at baseline and after sleep deprivation, were also repeated and showed nonspecific abnormalities not suggestive of a diagnosis of seizures. Therefore, AEDs were suspended and treatment with high-dose beta-blockers was initiated (nadolol 1-2 mg/prokg/day).

Discussion

Syncope is one of the most common clinical problem in children. Approximately 30–50 % of children have syncope at least once in their lives till the adolescent period and this situation is usually alarming for the families of patients [4,5].

Syncopes can be classified into three major categories as neurally mediated (vasovagal, situational, carotid sinus hypersensitivity, glossopharyngeal syncope), cardiovascular (arrhythmias, functional heart, vascular problems), and non-cardiovascular ones (orthostatic hypotension, neurologic, metabolic, endocrine, psychogenic, drug associated) [6-10].

Neurocardiogenic syncope, also known as vasovagal syncope, is the most common cause of syncope and constitutes 61–80 % of all pediatric syncope cases [11].

The major challenge in the assessment of children with syncope is that most children are asymptomatic at the time of their presentation, therefore a careful and detailed history and a comprehensive physical examination are essential in all patients. Triggering factors detected in some cases are important clinical clues for the diagnosis. Prodromal symptoms such as nausea, vomiting, lightheadedness, and weakness may be seen but also short myoclonic jerks and tonic-clonic convulsion-like movements can be observed during the loss of consciousness [5].

Hypoxia resulting from syncope may trigger a real epileptic convulsion and this is called as anoxic epileptic seizure [12]. Convulsive movements may lead to a misdiagnosis of seizure by the physician in the 31.8 % of cases and it was reported that 20 % of patients admitted with syncope had medications for epilepsy [13-15].

On EEG recordings, generalised high amplitude brain wave slowing and flattening, without cortical discharges, was observed during generalised cerebral anoxia [16] and distinctly different from epileptic activity. The convulsive activity has tentatively been ascribed to activation (or loss of suppression) of the medullar reticular formation [3].

Some studies, involving a total of 101 patients, focused on cohorts of patients with presumed seizure disorders and reassessed. One hundred of them were treated with, but did not respond, to AEDs therapy. These studies have confirmed that vasovagal syncope can be accompanied by myoclonus, as well as carotid sinus hypersensitivity and primary arrhythmias [17-19].

The cardiovascular part of the re-evaluation of a diagnosis of presumed epilepsy basically follows the initial evaluation of syncope in general: a careful history, a physical examination including orthostatic blood pressure measurement, and an ECG [20].

Then echocardiography and exercise testing should be part of the initial evaluation to identify or exclude the presence of heart disease. Vasovagl syncope - or neuromediated reflex syncope – is one of the most common causes of convulsive syncope, and when history alone does not allow for a diagnosis, the head-up tilt test is preferred diagnostic tool. The diagnostic yield of the invasive electrophysiological evaluation is, however, limited in the absence of ECG abnormalities or evidence of structural heart disease, although pharmacological provocation might improve the yield [3].

Documentation on the usefulness of the implantable loop recorder in patients with “presumed epilepsy” is limited [18,19] while data on its value in the evaluation of “unexplained syncope” (negative tilt and electrophysiological testing without pharmacological provocation) is starting to come forth [20].

Our case is an example of misdiagnosis of epilepsy and inappropriate treatment of the underlying heart condition with a significant risk of mortality. CPVT is a rare arrhythmogenic disorder characterized by the presence of polymorphic VT and bidirectional VT caused by physical or emotional stress [21]. Mutations in the Ryanodine Receptor-2 gene (RyR2) are implicated in approximately half of cases and pathologic arrhythmias arise from inappropriate handling of calcium release in the cardiomyocyte [22].

These arrhythmias predispose affected individuals to syncope, seizure, cardiac arrest and SCD. Exercise stress test is pathognomonic and demonstrates increasing ventricular ectopy with progressive adrenergic drive, often culminating in bidirectional or polymorphic VT. In cases associated with a seizure-like presentation, physicians may misinterpret the symptoms to vasovagal or neurological causes or may fail to associate the syncope and arrhythmia with physical and emotional stress triggers [21].

Anamnestic history, as well as the onset of polymorphic VT induced by adrenergic stimulation, or the absence of structural heart disease and ECG abnormalities are essential criteria to identify CPVT. There are 2 diagnostic tests that are useful: (1) Holter monitoring for up to 48 hours; and/or (2) an exercise stress test [21,23].

As the majority of CPVT cases are familial, genetic testing for CPVT-related mutations may be fundamental for early diagnosis. Therefore, the screening of asymptomatic family members is crucial and can be accomplished through the use of exercise tests (or isoproterenol infusion) and genetic evaluation [21].

CPVT can be successfully managed if diagnosed early. Lifestyle changes, such as limiting competitive sports and strenuous exercise, can decrease the risk for arrhythmogenesis in CPVT patients [24].

Life-long administration of β-blockers is currently the firstline therapeutic option for CPVT patients; they should receive the highest tolerable β-blockers dose and should be re-evaluated consistently to increase the dosage accordingly as the child grows [21,24-26].

The most commonly used β-blocker is nadolol, which is long-acting (half-life 20–24 hours) and effective in treating symptoms, and as a prophylactic agent. In addition, due to the significant prophylactic effect of nadolol, genetically-positive but asymptomatic family members of CPVT patients should also be prescribed β-blockers [21,24-27].

The case report we have reported might suggest to clinicians to consider convulsive syncope and a diagnostic re-evaluation when EEG is not diagnostic or treatment with AEDs is not effective. This would lead to timely identification of high-risk cardiac diseases, such as CPVT, that need prompt management to avoid significant cardiac events [28,29].

Conclusion

Syncope accompanied by involuntary movements is very frequent and should be differentiated from epileptic seizures.

A detailed history, careful physical examination, routine laboratory tests and electrocardiogram must be conducted in every child with syncope for correct management and accurate risk stratification.

Further laboratory and instrumental investigations should be performed in selected patients. It could be lifesaving to identify the underlying cause of syncope and to apply the right treatment.

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