A case of catecholaminergic polymorphic ventricular tachycardia masquerading as an intractable seizure

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ABSTRACT

A 5-year-old boy with the history of intractable seizure for the past 2 years was transferred to the emergency room for cardiopulmonary resuscitation because of the prolonged seizure and profound cyanosis. He was intubated and resuscitated by cardioversion for a bizarre shape ventricular tachycardia (VT). After noxious stimulation, he showed multiple polymorphic ventricular premature beats that were followed by a bidirectional VT in favor of catecholaminergic polymorphic VT. The genetic assessment was positive for CASQ2 mutation. In the follow–up, the arrhythmia was controlled by nadolol, however with a prominent neurological sequela.

Keywords: Arrhythmia, catecholaminergic polymorphic ventricular tachycardia, channelopathy, intractable seizure

INTRODUCTION

Myoclonic jerk and occasionally tonic movements that occur due to the brain anoxia following the syncope make it difficult to distinguish from epilepsy. It has been reported that up to one-third of the epileptic patients, particularly those treated with multiple anti-epileptic drugs were misdiagnosed. Here, we present a child with drug-resistant epilepsy that finally was diagnosed with a case of catecholaminergic polymorphic ventricular tachycardia (CPVT). Occasionally, the CPVT clinical presentation might be vague and misleading.

CASE REPORT

A 5-year-old boy with the history of refractory seizure in the past 2 years was visited by our neurologist while having an episode of tonic-clonic seizure. He was resuscitated according to the guideline of advanced pediatric life support. The initial electrocardiogram showed a bizarre shape ventricular tachycardia (VT) [Figure 1] that was successfully aborted to the sinus rhythm after the second attempt of defibrillation at 2J/kg. The corrected QT interval was 430ms, and there was no evidence of short PR interval or delta wave either. Moreover, shortly after the resuscitation, he had an episode of supraventricular tachycardia with a rate of 210bpm that was aborted spontaneously [Figure 2]. The patient was transferred to the cardiac intensive care unit (CICU) for invasive monitoring and arrhythmia management. In CICU, he had multiple polymorphic ventricular premature beats [Video 1] after nasogastric tube insertion and tracheal tube suctioning. The serum

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DOI: 10.4103/apc.APC_73_19

How to cite this article: Shabanian R, Ahani M, Zandiyeh S, Nikdoost A, Dadkhah M, Asbagh PA, *et al.* A case of catecholaminergic polymorphic ventricular tachycardia masquerading as an intractable seizure. Ann Pediatr Card 2020;13:141-3.

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Submitted: 17-May-2019 **Revised:** 24-Oct-2019 **Accepted:** 19-Feb-2020 **Published:** 02-Apr-2020

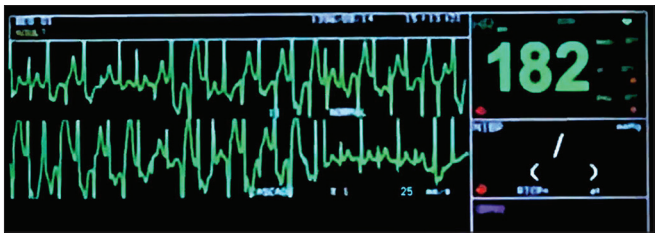

Figure 1: An episode of catecholaminergic polymorphic ventricular tachycardia

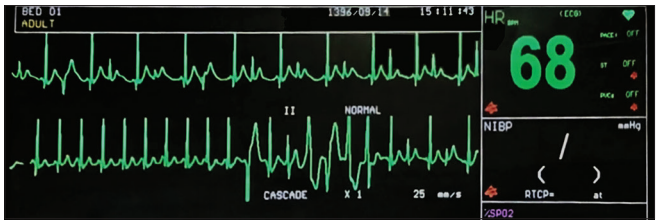

Figure 2: The electrocardiographic monitor (25mm/s) shows the alternate polymorphic premature ventricular contractions with an episode of atrial tachycardia followed by the polymorphic ventricular tachycardia; heart rate of 68bpm on cardiac monitoring corresponds to the low amplitude premature ventricular contractions that are not counted as heartbeats by the monitor

magnesium, calcium, and potassium levels were all within the normal limits. Echocardiography revealed mild systolic dysfunction without any structural abnormalities. The diagnosis of CPVT was suspected, and because of the stable hemodynamic, we decided to control the arrhythmia by combination therapy of esmolol infusion (100μg/kg bolus followed by 25–50μg/kg/min) and flecainide (2mg/kg/day divided into two doses). Reviewing the child's medical history revealed that his seizure was usually provoked by physical activity or noxious stimulation. His parents claimed that the seizures were often aborted by carotid sinus massage. The brain computed tomography scan did not have any abnormal findings and the electroencephalogram testing revealed no evidence of epilepsy. Parents did not have a consanguineous marriage, and the family history of stress-induced syncope and juvenile sudden death was negative either. The next day the combination therapy was replaced by nadolol 2mg/kg/day once daily that was tapered to 1mg/kg/day because of the profound bradycardia. Direct DNA sequencing was performed for all exons of RYR2, CASQ2, TRDN, and CALM1 genes. There was a homozygote pathogenic variant in exon3 of the CASQ2 gene defined as c.406G>T (E136*) in favor of CPVT type 2. Genetic analysis for his 6-month-old brother showed a heterozygote mutation in this region. Six months follow-up was negative for arrhythmia recurrences while the patient receiving nadolol. Unfortunately, he suffered from a prominent neurological sequela of the hypoxic brain damage.

DISCUSSION

CPVT is a rare and dangerous kind of polymorphic VT encountered in childhood with clinical manifestation of palpitation, syncope, or sudden cardiac death.[1] It may also present with convulsive syncope masquerading seizure disorders that are usually refractory to antiepileptic therapy.[2] A prevalence of about 1 in 10,000 has been reported in some centers. Hayashi *et al.* reported seizure as the initial presentation in 15% of the patients later diagnosed as CPVT, with about half of them suffering from drug-resistant epilepsy.[3] The genetic mutation in CPVT as a calcium channelopathy may occur in RyR2, CASQ2, TRDN, CALM1, KCNJ2, and ANK2, with the first two as the most prevalent and familiar mutations.[4] The mutated proteins will cause calcium overload as a substrate for delayed after depolarization and subsequent arrhythmia. Changes in the autonomic tone and the reentry mechanism have also been suggested as the underlying cause of this arrhythmia. Runs of atrial tachycardia have been frequently reported in these patients.[5] Conspicuously, like cardiac myocytes, ion channels play an important role in the creation of excitation in neuronal cells. Hence, a mutation in voltage-gated channels will lead to hyper-or hypoexcitability of the affected tissue that may present as either arrhythmia or seizure in the heart or central nervous system, respectively.[6]

It is prudent to diagnose the convulsive syncope from epilepsy to provide the proper management and preventing the risk of unexpected sudden death. This may need antiarrhythmic medication and implantable cardioverter defibrillator implantation instead of antiepileptic drugs. Moreover, unnecessary prescription of the antiepileptic drugs will add the hazard of cardiotoxic side effects. Although it has been shown that antiepileptic drugs (e.g., phenytoin, carbamazepine, and sodium valproate) could have an antiarrhythmic effect,[7] there are multiple reports of their proarrhythmic complications in the literature. Therefore, their administration without having established the appropriate diagnosis might be hazardous to the patient. Since we were not aware that our patient is a case of CPVT, his arrhythmia was aborted by cardioversion. However, it is important to know that direct current shocks are associated with pain and stress resulting in catecholamine release which can be proarrhythmic and provoke a VT storm in patients with CPVT. Therefore, any run of VT should not be directly cardioverted, especially when the hemodynamic is stable, and the background of CPVT is suspected.[8]

It is noteworthy to remind that there are reports of cases with both arrhythmia and seizure that either the arrhythmia or seizure precedes the other. Hence, some patients may need to be treated with both antiepileptic drugs and antiarrhythmic medication or devices. It is postulated that in these cases, channelopathy might affect both the heart and brain causing the patients

vulnerable to cardiac dysrhythmia and epilepsy at the same time. Central apnea is also a potential mechanism that contributes to the sudden unexpected death in epilepsy.[9] Recently, a human leaky RyR2 mutation R176Q has been found in autopsies of cardiorespiratory collapse that lower the threshold for spreading depolarization in the dorsal medulla.[10] These data point to the neuronal intracellular calcium hemostasis as a previously unrecognized contributing mechanism to sudden death in patients with CPVT.

Consequently, regarding our patient's ominous fate, it is reasonable to consider the channelopathies in the differential diagnosis of patients presenting with drug-resistant epilepsy or patients having an unusual manifestation of seizure after exercise or emotional stresses. The interaction of epileptic discharges, dysrhythmia, and central apnea in the pathogenesis of the channelopathies is the key point for the therapeutic management of mysterious cases.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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