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Case Report

A Fatal Presentation of Catecholaminergic Polymorphic Ventricular Tachycardia in an 18-Month-Old Child: A Case Report

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Abstract

Catecholaminergic polymorphic ventricular tachycardia (CPVT) is a rare inheritable cardiac channelopathy that presents as critical life-threatening ventricular arrhythmias which are catecholamine-mediated. CPVT accounts for a considerable number of sudden cardiac death events in the pediatric population; thus, early diagnosis and appropriate management are crucial. CVPT presents as attacks of syncope or sudden cardiac death, which are predominantly induced by stress, intense emotions, or severe exertion. Patients affected with this condition usually have an anatomically normal heart, which makes it hard to Diagnose early.

With the recent advances in comprehensive genetics testing techniques the etiology of CPVT was found to results from Genetic mutations in either Calmodulin-1 gene (*CALM-1*) or cardiac Calsequestrin 2 gene (*CASQ2*), or Ryanodine receptor gene *RYR2* or Triadin (*TRDN*) gene These mutations affect cardiac calcium channels leading to calcium release from the sarcoplasmic reticulum into the cytoplasm. The increased in intracellular calcium concentration, induce delayed after-depolarizations that produce ventricular arrhythmias.

In spite of the progress done in revealing the genetic etiology, pathophysiology, and clinical presentation of CPVT; the Management of CVPT needs further research. Currently, B blocker constitutes the mainstay of treatment; also, Felcininde has shown to be of benefit. Implantable cardiac devices have been reserved for cases resistant to medical treatment

In this essay, we report a case of an 18-month-old male child who has been diagnosed with CVPT at a young age; also, he has a strong family history of CVPT. Despite receiving B blockers, he presented to the emergency department with sudden cardiac arrest and failed to respond to adequate cardiopulmonary resuscitation.

The aim is to report such rare fatal case and summarize our approach to the diagnosis, and management of CVPT in addition to reviewing the literature.

Keywords: *Sudden Cardiac Death; Ventricular Tachycardia*

Introduction

In Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT), episodic syncope occurs during acute emotion or exercise. The cause of syncope episodes is fast (bidirectional or polymorphic) ventricular tachycardia. Spontaneous recovery may occur, or situation may worsen to ventricular fibrillation, which may lead to death. CPVT is highly fatal; if not treated, almost 30% may experience at least one cardiac arrest and 80% syncopal spells [1].

The affected individual with a structurally normal heart often has normal resting electrocardiography. However, diagnosis can be made by the reproduction of typical ventricular tachycardia during acute adrenergic activation. For adrenergic activation in pediatric group, some propose infusion of catecholamines; however, its sensitivity is not yet precise. The onset of arrhythmia during exercise occurs at a heart rate threshold of 100 - 120 beats per minute. After threshold, heart rate can be further worsened by increasing workload. The other way of establishing the diagnosis is by identification of heterogeneous pathogenic variants of calmodulin-1 (*CALM-1*) or Cardiac ryanodine receptor (*RYR-2*) gene or biallelic pathogenic variants in Triadin (*TRDN*) or Calsequestrin-2 (*CASQ2*) gene.

True prevalence in the population is unknown. Its estimate is 1:10000. The high lethality at a young age and single occurrence of disease in the family are suggestive of a low prevalence of CPVT compared to other arrhythmogenic disorders like Long QT syndrome (1:7000 - 1:5000). Cardiac ryanodine receptor (RYR-2) variants are associated with mild arrhythmogenic right ventricular dysplasia/cardiomyopathy (ARVC) with exercise-induced arrhythmias. Large deletions of *RYR2* are linked with left ventricular non-compaction (LVNC) with or without CPVT. The pathogenic variants of *TRDN* can cause LQTS, atypical CPVT, and borderline prolonged QT interval. *CALM-1* pathogenic variants cause epilepsy, long QT syndrome, neurodevelopmental disorders, and atypical form of CPVT often with QT prolongation. The differential diagnoses are arrhythmogenic right ventricular dysplasia/cardiomyopathy, Long QT syndrome, and Short coupled ventricular tachycardia, and Andersan Tawil syndrome**.** Multiple genetic testing techniques can be utilized to diagnose CPVT. It includes serial single-gene testing, multigene panel testing, and more comprehensive genomic testing such as whole-exome sequencing [2].

Case Study

Background

18-month-old boy, ex-preterm 33 weeks (corrected age 17 months and 1week old), born to first cousins, consanguineous parents. He had average growth and development. Six of his sibling died suddenly in their early childhood (youngest was eight months old, and the eldest was 2 and a half years old). Genetic testing of Mohamed by whole-exome sequencing method revealed homozygous variant detected in *TRDN* gene, which is responsible for CPVT type 5 with or without muscle weakness. His parents are heterozygous.

Past history

The child was delivered at 33rd week of pregnancy via emergency CS (indication: fetal bradycardia) with a Birth weight of 2.080 kg (10th - 50th centile), Length of 32.2 cm (3rd - 10th centile) and Head circumference of 32 cm (90th centile).

He was admitted to the NICU after birth for prematurity and respiratory distress syndrome, where he needed mechanical ventilation for three days. He was discharged after 50 days, with a suspected diagnosis of long QT syndrome because of his positive family history of unexplained deaths beyond the neonatal period in six of his siblings. During NICU stay, electrocardiography and echocardiography were done several times, and all reports were normal. The child had been following up regularly at a pediatric cardiology clinic and pediatric genetic clinic.

Family history

Mohamed is a 13th child born to first cousins, consanguineous parents. Mother is 37 years old, and the father is 38 years old. They have five healthy children age ranging from 6 to 18 years old. Previously, the Mother had four miscarriages. Interestingly Six of his siblings died suddenly in their early childhood (youngest was eight months old, and the eldest was 2 and a half years old) with unknown cause(s). Two of his maternal aunts died in infancy, and one of his paternal aunts died in early childhood with unknown cause(s).

Management

Following discharge from the NICU, the child was initially suspected for suffering from long QT Syndrome, and the parents were explained the list of medication to be avoided. He was scheduled for follow up appointments with pediatric cardiology and pediatric genetics clinics.

At the Pediatric genetics center follow up appointment: The child showed normal development. CBC, renal functions, liver profile, CPK, CK-MB, and other blood tests were normal. Amino acid chromatography: plasma amino acid profile shows a borderline decrease in valine and isoleucine levels. Organic acid screening test: mass spectrometric analysis of organic acids demonstrates an elevated level of oxoglutarate. Amino acid and acylcarnitine profile results were not suggestive of an inborn error of metabolism. Whole-genome sequencing showed homozygous variant c.180G>A (P.Trp60*) was detected in the *TRDN* gene responsible for CPVT type 5 with or without muscle weakness. The Genetic testing results showed that Father was heterozygous; also, the Mother was heterozygous for those genes. The parents were counseled in detail about the condition. The natural history, complications, and prognosis were discussed. The autosomal recessive mode of inheritance was elucidated with a 25% risk of recurrence in the future pregnancies. The availability of pre-implantation genetic diagnosis and different methods of prenatal diagnosis, including chronic villous sampling and amniocentesis with their advantages and risk, were explained. The importance of regular follow up with pediatric cardiology was emphasized. Pediatric cardiology follow-up visits at the age of 9 months and 16 months showed no cardiac symptoms or signs. Repeated ECG and Echo were normal. The child was receiving B blockers with proper compliance. Moreover, He was recommended for Holter monitoring.

Outcome

At the age of 18 months, the child suffered from a sudden attack of cardiac arrest while playing, cardiopulmonary resuscitation started, and the child was transferred to the hospital, where rhythm analysis during CPR showed three attacks of ventricular tachycardia. The child was given synchronized cardioversion 0.5 j/kg. CPR continued for 25 minutes after which the pediatric patient was transported to PICU with permanent brain hypoxic insult. The child died ten days later.

Discussion

As a result of premature delivery was born prematurely, the child was kept in the neonatal intensive care unit (NICU) due to prematurity and respiratory distress syndrome. He received mechanical ventilation for three days in NICU. His heart situation was continuously monitored using echocardiography and echocardiogram inside NICU. Other care protocols were also followed, such as blood pressure monitoring, temperature monitoring, and parenteral nutrition until suckling reflex developed, etc. The patient was discharged on the 50th day from NICU due to his family history of unexplained deaths beyond neonatal age. He was referred for detailed genetic testing.

For detail genetic testing, genetics department tested the pediatric patient for quite a number of diseases using complete blood count, liver function test, renal function test, creatine phosphokinase, and creatine kinase-muscle/brain. He was tested for hemoglobinopathies and metabolic disorders, such as organic acidemia, fatty acid catabolism disorders, and branched-chain amino acids catabolism. All tests were not suggestive of any disease. Moreover, He was tested for rare disorders using Whole Exome Sequencing. There, it was found that the child had a rare genetic mutation; Homozygous variant c.180G>A (P.Trp60*) was detected in the *TRDN* gene. *TRDN* gene was responsible for CPVT type 5 with or without muscle weakness disease. The reports were discussed with parents. They were told about the diagnosis and counseled for management of the disease with possible complications and prognosis. The future possibility of the disease and availability of pre-implantation genetic diagnosis and different methods of prenatal diagnosis, including chronic villous sampling and amniocentesis, with their advantages, and risk were explained to parents. Pediatric cardiology follow-up was recommended for the pediatric patient.

Follow up appointment were scheduled at the age of 9 months and 16 months. He was taking Propranolol with proper compliance. His follow-ups were normal. However, at age 18, he had a sudden cardiac arrest while playing. Cardiopulmonary resuscitation (CPR) was started inside the ambulance while he was being transferred to the hospital. CPR was continued, and rhythm analysis confirmed ventricular tachycardia episodes. Cardioversion was attempted with continuous CPR for 25 minutes, and sinus rhythm was restored. The patient was transferred to PICU with permanent hypoxic brain damage. Unfortunately, he died after ten days due to rare CPVT type 5 with or without muscle weakness. The pediatric patient was also having a unique homozygous variant c.180G>A (P.Trp60*) in *TRDN* genes.

Conclusion

CPVT is a rare critical life-threatening condition which presents in the pediatric population with sudden cardiac death. In this case; a child with previously diagnosed CPVT presents with fatal Ventricular arrhythmias despite receiving B blocker therapy. This case shows the challenges in appropriate diagnosis, prevention, and adequate management of CPVT attacks.

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