Cardiac Channelopathies Masquerading as Seizures

Cardiac channelopathies are a group of inherited arrhythmias caused by mutations in the cardiac ion channels. Long QT syndrome (LQTS), the commonest of these disorders, is estimated to affect 1 in 2000 people [1]. The other disorders include Brugada syndrome (BrS), catecholaminergic polymorphic ventricular tachycardia (CPVT) and the short QT syndrome (SQTS). They share a predilection for malignant ventricular arrhythmias, syncope and sudden death. Seizure is a frequent presentation in these disorders and is attributed to arrhythmia related decrease in cardiac output [2]. It is not uncommon for children with these disorders to be inaccurately diagnosed to have epilepsy. We report four children with cardiac channelopathies referred from neurology in whom appropriate therapy resulted in a significant decrease in paroxysmal 'seizure-like' events.

Case 1: A 5-year-old boy was referred to us with multiple seizures after electrocardiographic (ECG) abnormalities were noted during an extended electroencephalogram recording. A younger sibling had multiple episodes of seizures and died at 1 year. There was a history of sudden unexpected death in the family with one drowning. A standard ECG in the present case showed a prolonged QTc (520 ms). Holter evaluation documented multiple self-terminating episodes of Torsades de Pointes (TdP). A provisional diagnosis of LQTS was made. He was started on beta-blockers. The family were unwilling for family screening as well as genetic testing. On follow-up, 6 months later, there were no further symptoms.

Case 2: A 6-year-old girl, the first child of non-consanguineous parents, had a maternal aunt with epilepsy, high pitched sounds being one of the triggers. The child had been diagnosed prenatally to have complete heart block and a pacemaker had been implanted postnatally. She also had multiple episodes of seizures. Three EEGs were reported to be normal. A review of her neonatal ECG showed one episode of TdP (arrow in **Fig. 1a**). On family screening, the mother's ECG showed a prolonged QTc of 480 ms. Anti-epileptic drugs were discontinued, and she was started on beta blockers. Genetic testing revealed a pathogenic mutation in *KCNH2* gene (c.1882G>A), which causes LQTS type 2. Cascade screening confirmed the mutation in both the mother and maternal aunt, and both were started on beta blockers. At follow up of one year, there were no further seizures in the child.

Case 3: A 17-year-old girl, the first child of third-degree consanguineous parents, had recurrent seizures during exertion. Her ECG was normal. There was bidirectional ventricular ectopy on exercise stress testing (arrow in **Fig. 1b**). A clinical diagnosis of CPVT was made and she was started on beta blockers. Genetic testing revealed a pathogenic heterozygous mutation in the *Ryanodine receptor* gene (RyR) associated with CPVT (c.184 C>T). The family refused cascade screening. No further seizures were reported during a follow up period of 6 months.

Case 4: A 9-year-old girl, the first child of non-consanguineous parents, with two younger siblings who had died suddenly and unexpectedly in infancy and multiple sudden unexpected deaths in the father's family was referred for evaluation. She had been treated for seizures from the age of five. A prolonged video-EEG recording was performed. She had one episode of tonic posturing during the recording with normal EEG and TdP on ECG. Baseline ECG showed sinus rhythm with a normal QTc. A presumptive diagnosis of LQTS was made, she was started on beta blocker and genetic testing was organized. There have been no further episodes of seizures for the last 9 months.

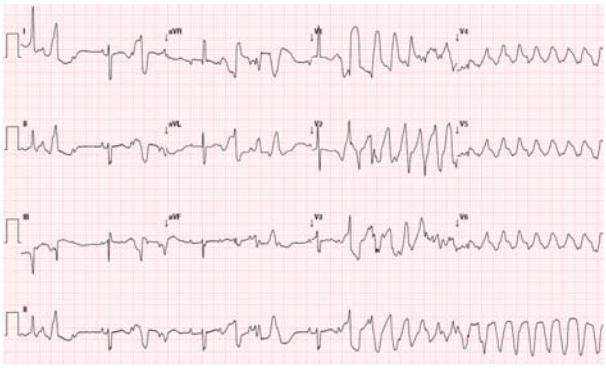

Fig. 1 (*a*) ECG of patient 2 in the newborn period demonstrating polymorphic ventricular ectopy as well as an episode of Torsades de Pointes (TdP).

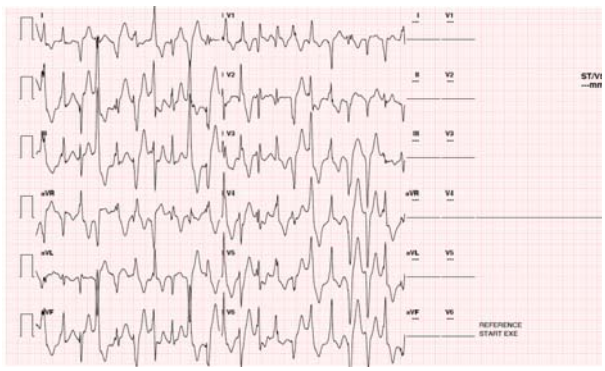

Fig. 1(*b*) ECG tracing from an exercise stress test of patient 3 demonstrating evidence of bidirectional ventricular ectopy.

Cardiac channelopathies are caused by mutations in proteins related to the intra-cellular transport of sodium, potassium and calcium ions. These ion channel abnormalities predispose the patient to episodes of lethal ventricular arrhythmias such as TdP and ventricular tachycardia (VT) or fibrillation (VF). While some may die during such arrhythmias, these lethal arrhythmias can be non-sustained with spontaneous termination. Cardiac output is significantly decreased during these non-sustained episodes and the resultant cerebral hypoperfusion may result in seizures and/or syncope [3]. The term 'torsadogenic seizures' has been used to describe this kind of paroxysmal activity in the past [4]. Misdiagnosis as epilepsy has been shown to be the most important reason for delay in diagnosis and could potentially result in sudden death [5].

A careful history can provide clues to the diagnosis in most patients. A family history of SUD, seizures or syncope in multiple members should raise the suspicion of a cardiac channelopathy [6], as was seen in three of our cases. Recurrent seizures despite appropriate therapy and especially in the absence of pathogenic EEG changes should raise the suspicion of a cardiac channelopathy [6].

Genetic testing by a targeted panel of genes implicated in cardiac channelopathies or an exome wide screening is performed through next generation sequencing. A positive genetic test allows genotype specific therapy [7]. Genetic testing also permits cascade testing in other (even asymptomatic) family members [8] and helps identify individuals at risk and provide appropriate treatment even before clinical manifestations occur. This is especially important in channelopathies as a normal ECG does not rule out the presence of the phenotype. The QTc interval may be normal on a baseline ECG in affected individuals and an exercise stress test or provocative testing with adrenaline may be necessary to identify QTc prolongation. In our series, cascade screening permitted diagnosis in an asymptomatic mother as well as an aunt in whom the symptoms had wrongly been attributed to seizures.

In conclusion, seizures may be the clinical presentation in children with cardiac channelopathy. Red flags such as a family history of sudden death, seizures associated with auditory triggers and recurrent seizures with a normal EEG should raise suspicion and prompt referral to a pediatric cardiologist.The institution of appropriate lifestyle modifications and pharmacological therapy could result in control of symptoms.

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Ivermectin Poisoning – Report of Successful Management

Ivermectin is an endectoparasiticide and is the drug of choice in filariasis, scabies (crusted or if topical treatment has failed), and several other infestations [1]. It has a low rate of adverse reactions with toxicity occurring only with overdosing, resulting in adverse prognosis, as no specific antidotes are available [1,2]. Although rare in children, over 150 cases of serious neurological toxicities have been reported in adults [1]. We report a case of ivermectin toxicity with encephalopathy, shock and aspiration pneumonia in a young child and its successful management.

A 6-year-old previously healthy girl (weighing 20.5 kg) presented with a history of accidental consumption of 60 mL of 1% w/v (600 mg) ivermectin lotion (30 mg/kg). She was undergoing treatment for scabies. After four hours of consumption, she had two episodes of vomiting followed by generalized tonic-clonic movements and loss of consciousness. On arrival, she was unresponsive, with Glasgow Coma Scale (GCS) 6/15, with tachycardia, tachypnea, hypotension and oxygen saturation of 79% at room air. Pupils were equal bilaterally (3 mm) with sluggish reaction. There were no signs of meningeal irritation. There was generalized hypotonia with absent deep tendon reflexes and fundoscopic examination was normal. Excessive salivation and bilateral crepitations were present. The child was admitted to the pediatric intensive care unit. Given the poor GCS and respiratory failure, the child was intubated, ventilated, and started on parenteral antibiotics ceftriaxone and clindamycin, along with supportive measures. In view of continuing seizures, intravenous midazolam and