Pediatric patients with KCNJ2 mutations: wide clinical spectrum in a special disorder

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Introduction Andersen–Tawil syndrome (ATS) is a rare disorder characterized by periodic paralysis, cardiac arrhythmias and dimorphic features. ATS has been associated with mutations in the KCNJ2 with autosomal dominant inheritance pattern.The aim of the study is to analyze the electrocardiographic pattern of these patients.

Methods: Retrospective review of patients with KCNJ2 mutations in our unit. Clinical features, treatment, procedures, EKG measurements, stress test, 24h-Holter and follow up are described. QT and QU intervals were measured in lead V2 with Bazzet formula, and electrocardiographic criteria for ATS.
Results: Family history, clinical features, genetics and treatment are shown in table 1.

Patient	Age (y)	Family History	Dimorphic features	Arrhythmia	Mutation	Treatment
1	8	Mother KCNJ2 asymptomatic	Yes	PVC and PMVT	KCNJ2 p.189 R>I	Flecainide Beta-Blocker
2	6	Mother KCNJ2 + ICD	Yes	No	KCNJ2 p.144G>A	No
3	11	Mother KCNJ2 + asymptomatic	No	No	KCNJ2 p.82R>Q	No
4	15	Mother KCNJ2 + asymptomatic	No	PVC - couplet	KCNJ2 p.82R>Q	Beta-blocker
5	5	No	Yes	PVC, PMVT, TV bidirectional	KCNJ2 p.218 R>W	Flecainide Beta-blocker

All patients were females, mean age at diagnosis of 7.6 y (IQR 7; SD5.1). Four were index cases. Prominent U-waves in leads V2-V5 and in the inferior leads were detected in all patients. “U on P” sign was observed during tachycardia in all cases. Patients 1, 4 and 5 had the “tee on pee” sign and prolongation of the QT interval after premature ventricular contractions (PVC). Mean QT interval was 433ms (IQR60, SD4), mean QU interval was 591ms (IQR32.5, SD106). Two patients required sympathectomy due to refractory polymorphic ventricular tachycardia; the others are asymptomatic or well controlled with pharmacological therapies.The mean follow up time was 4 years, there were no malignant events and none need ICD.

Conclusions Patients with KCNJ2 mutation have wide clinical and electrocardiographic manifestation, since asymptomatic until refractory PMVT. EKG features constantly seen were “U on P” during tachycardia, “tee on pee” sign and QT interval prolongation after PVC. Oral flecainide and beta-blocker therapy seems to be effective, but in patients with refractory PMVT we may need other therapies and sympathectomy to prevent malignant events.