CASE REPORT

Andersen-Tawil Syndrome – Periodic Paralysis with Dysmorphism

MAHESH KAMATE AND VIVEK CHETAL

From Department of Pediatrics, KLE University's J N Medical College, Belgaum, Karnataka, India.

Correspondence to:
Dr M. Kamate,
Asstt. Prof. (Pediatrics),
KLE University's J N Medical College, Belgaum 590 010, Karnataka, India.
drmaheshkamate@gmail.com
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Andersen-Tawil syndrome is a rare type of channelopathy characterized by the presence of periodic paralysis, cardiac arrhythmia (prolonged QT interval or ventricular arrhythmia) and distinct dysmorphic abnormalities. It is a type of potassium channelopathy that occurs sporadically or by autosomal dominant inheritance. We report a 14 year old boy with Andersen-Tawil syndrome.

Key words: Andersen-Tawil syndrome, Channelopathy, Periodic paralysis, QT interval.

Andersen-Tawil Syndrome (ATS) is a heterogeneous autosomal dominant or sporadic disorder characterized by the clinical triad of periodic paralysis, dysmorphic features, and ventricular arrhythmias [1,2]. The presence of developmental abnormalities which result in dysmorphic features is the most striking difference from other forms of periodic paralysis [3]. The presence of dysmorphic features in this patient with periodic paralysis led us to the diagnosis of ATS. To the best of our knowledge, this is the first report of ATS in Indian children.

CASE REPORT

A 14-year-old boy born to non-consanguineously married couple presented with episodic weakness since ten years of age, with normal muscle strength between attacks. The episodes of weakness had variable duration (from hours to few days) and started during rest after playing or carrying heavy weights. Leg muscles were mostly affected but later, arms were also involved. The attacks were usually more frequent during cold weather. The frequency of attacks varied according to intensity and duration of physical exercise. Initially the attacks occurred once to twice in a month but had increased to once to twice a week 3 months prior to presentation. Other provocative factors, such as fasting or carbohydrate intake, were not reported. The patient did not complain of muscle pain or cramps. His father has similar complaints and an elder brother of 18 years age had one such episode 3 years back. His prenatal, natal and postnatal history was unremarkable, and his school performance was good.

Physical examination revealed micrognathia, retrognathia, clinodactyly of fifth fingers, hypertelorism, high arched palate and short stature. There was no clinical evidence of thyrotoxicosis. Examination of the nervous system revealed an intact sensorium and cranial nerves. There was weakness of proximal limb muscles (MRC grade 3) in both upper and lower limbs with areflexia. Potassium levels were normal and serum CPK was mildly raised (454 IU/L). His thyroid, renal and liver function tests were within normal limits. QTc interval was mildly prolonged (0.45 seconds). There was no evidence of any arrhythmias or ectopic beats. Trans-thoracic echocardiography confirmed a structurally and functionally normal heart. Nerve conduction studies and electromyography were normal with no evidence of myotonia. His weakness improved gradually in 36 hours. Based on the clinical and laboratory abnormalities he was diagnosed with Andersen-Tawil syndrome. Due to

lack of availability of genetic studies in our country and positivity rate of 65% for genetic studies in ATS(1), mutational studies were not done. Paralysis was treated with carbonic anhydrase inhibitors (acetazolamide at 20 mg/kg/day in 3 divided doses). The child was advised close monitoring for occurrence of urinary lithiasis and to avoid QTc prolonging medications.

DISCUSSION

Andersen-Tawil syndrome is caused by a dysfunction of the inward-recitifying potassium channel Kir 2.1, and several mutations have already been identified in the gene coding for this channel, KCNJ2(4). While mutations in KCNJ2 account for the majority of ATS cases, 35% of patients with the ATS phenotype are KCNJ2 mutation-negative [1].

Diagnosis of ATS is not straight forward due to the great variability in clinical presentation. Moreover the full syndrome is not always present [5]. The diagnosis of ATS is made in the presence of two of the following three features: (*a*) periodic paralysis; (*b*) KCNJ2 mutation with electrocardiographic abnormalities (enlarged U-waves, ventricular ectopy, nonsustained ventricular tachycardia or a prolonged QTc interval); and (*c*) characteristic physical features (at least two). A patient with only one of the features above can be diagnosed with ATS when there is one family member with an established diagnosis [8]. The case presented had periodic paralysis, prolonged QTc interval and dysmorphism.

Periodic paralysis, which begins in the first two decades and may be associated with hypokalemia, hyperkalemia or normokalemia but it is usually of the hypokalemic type [5]. Dysmorphic features seen in ATS include facial and skeletal abnormalities like low-set ears, ocular hypertelorism, small mandible, palatal defects, single palmar crease, slight bilateral ptosis, short stature, fifth digit clinodactyly and syndactyly. The most common feature seen is clinodactyly [5]. These provide a diagnostic clue but may be difficult to identify and should thus be methodically sought. Clinical expression is variable, even within the same family [6,8].

Due to the genotypic and phenotypic heterogeneity in disease, along with erratic and paradoxical worsening of symptoms with therapy, no therapeutic standards exist to date. Ventricular arrhythmias post the most immediate risk [7]. The cardiac arrhythmias are well controlled when the plasma potassium levels is in the high normal range (4.2-4.5 meq/L). Tocainide and flecainide have been tried with variable efficacy and implantation of pacemaker/defibrillator devices is sometimes required. Acetazolamide and dichloro-phenamide may be useful to control attacks of paralysis. Some patients need potassium sparing diuretics and potassium supplements. Prognosis depends mainly on the management of cardiac arrhythmia. Though muscle weakness is disabling, patients usually remain ambulatory throughout adult life [5].

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