Clinodactyly – A Clinical Clue to Diagnose a Hereditary Periodic Paralysis

To the Editor,

A 26-year-old male had recurrent episodes of proximal weakness affecting lower limbs more than upper limbs for the last 10 years, which were predominantly related to physical activity and heavy meals. The weakness was severe enough to restrict the patient to the bed. During the episode, he had 3/5 power in proximal lower limb muscles and absent deep tendon reflexes with a normal neurological examination in between the episodes. General physical examination (GPE) revealed bilateral fifth digit clinodactyly, which was also present in his asymptomatic mother [Figures 1 a and b]. The thyroid profile, creatinine kinase, and potassium levels were normal both during and in between the episodes. Holter monitoring showed ventricular premature contractions (VPCs). The prolonged exercise test showed a 38% decline in compound muscle action potential (CMAP) amplitude at 40 minutes. Genetic testing of the patient and his mother revealed heterozygous pathogenic (chr17:68171425G>A c.245G>A p.Arg82Gln) variant in exon 2 of the KCNJ2 gene consistent with the diagnosis of Andersen–Tawil syndrome (ATS). He was treated with acetazolamide (1000 mg/day). On follow up, the patient has decreased frequency (from once in 2-3 months to once in 6-9 months) and severity of episodes such that now he could walk with support during the episodes. This case shows the importance of GPE and identification of clinodactyly as a clinical clue to diagnosing a hereditary periodic paralysis.

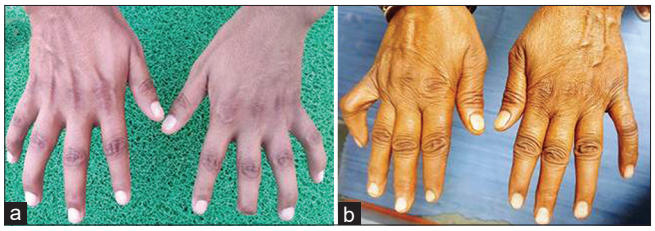

Figure 1: Bilateral fifth digit clinodactyly in the patient (a) and his mother (b)

Discussion

ATS is an autosomal dominant disorder characterized by a triad of periodic paralysis, cardiac abnormalities, and skeletal dysmorphism. ATS is classified as Type 1 (due to mutation in the KCNJ2 gene on 17q - 60% of cases) and Type 2 (for which the cause is not known). KCNJ2 gene encodes for inwardly rectifying K channel (kir 2.1) in skeletal muscles and cardiac muscles. In total, 58% of KCNJ2 patients have a complete triad of cardinal features; 81% have 2/3 cardinal features.[1] Careful physical examination is the key to early diagnosis. Fifth digit clinodactyly in the patient and mother was the major diagnostic clue for ATS in our case. Other skeletal manifestations include short stature, low set ears, ocular hypertelorism, broad nasal root, small mandible, 2nd-3rd toe syndactyly, and scoliosis

Episodic weakness, usually the first presenting symptom, occurs between 4 and 18 years.[2] Skeletal weakness sparing bulbar and respiratory musculature, lasting for hours to days, can occur spontaneously or by triggers like prolonged rest or rest following exertion, emotional stress and high carbohydrate diet.[2,3] Attack frequency, duration, and severity usually vary.[4] Permanent proximal weakness can develop later in the course.[1,3]

The most common cardiac symptom is palpitation.[2] The patient may be asymptomatic or develop syncope, cardiac arrest, or sudden death.[1] Electrocardiogram (ECG) can show prolonged QTc or QUc, enlarged U-waves, VPCs, ventricular bigeminy, polymorphic VT or bidirectional ventricular tachycardia.[1] Serum potassium concentration during episodes of weakness may be elevated, normal, or, most commonly, reduced (<3.5 mmol/U), which requires supplementation.[1] Routine nerve conduction electrophysiology is normal between episodes; the long exercise protocol may reveal an immediate post-exercise increment followed by an abnormal decrement in the CMAP amplitude (>40%) or area (>50%) 20–40 minutes postexercise. In a study of 11 individuals with ATS, 82% met long-exercise amplitude decrement criteria for abnormal testing, 100% had an abnormal area decrement of >40% from baseline suggesting area decrements from baseline may be a more sensitive parameter in ATS.[5] Our patient had a 38% decrement in amplitude from baseline after prolonged exercise.

Carbonic anhydrase inhibitors (acetazolamide 250–500 mg/day or dichlorphenamide 50–100 mg/day) have been reported to prevent episodic weakness.[1,2,4]

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.

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Conflicts of interest

There are no conflicts of interest.

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