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Letter to the Editor

No Involvement of Distal Lower Limbs in The First Report of Iranian Patient with Acromesomelic Dysplasia, Maroteaux Type: A Case Study

Running Title: A Variant of AMDM

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Dear Editor,

Acromesomelic dysplasia, Maroteaux type (AMDM), is an autosomal recessive form of acromesomelic dysplasia which is characterized by disproportionately short stature, shortening of the middle and distal segments of the limbs as well as vertebral involvement. AMDM is the result of a mutation in the natriuretic peptide receptor 2 (NPR2) genes which impairs the skeletal growth (1-3).

A 2-year-old boy, the 2nd pregnancy of non-consanguineous parents, was referred to the endocrine and metabolic referral center of Nemazee Hospital in the southwestern Iran for evaluation of short stature. He was born at 38 weeks of gestation with good Apgar score by cesarean section. At birth, he had a weight of 3100 g, a length of 45cm and a head circumference of 35 cm; he had no other dysmorphic features of general physical examination. There was no satisfactory length gain after birth, as noticed by his parents. At the referral time (2 years old), the case had a weight of 8200g (-4SD), a length of 71cm (-4SD), with a head circumference of 48 cm (0.3 SD). Fingers of the hand were extremely short and broad with small nails; there was no redundant skin on the fingers (Figure 1). His foot was normal without brachydactyly. Frontal bossing, low set ears and wrist joint hyperflexibility were prominent. All developmental milestones were within normal limits. His older sibling was of normal stature. His mother's height was 156cm (-1.6 SD) and the father was 163cm (-1.9 SD) tall. His older sibling was of normal stature. None of the other family members were affected.

Radiographic findings showed curved radius, relative short ulna, and broad metacarpals with wide phalanx. The vertebrae were of normal size and without beaking. Iliac wings and metatarsal bones were normal in radiography (Figure 1). DNA was extracted from the peripheral blood by standard technique and microsatellite analyses were performed. Whole exome sequencing test of the patient was followed by mutation confirmation by direct Sanger screening for comparing it to the normal reference sequence, AMDM maps to 9p13.3. Furthermore, parents and the other older sibling could not do cytogenetic study. Informed consent was obtained from his parents for this report. The mutation of the case was displayed in NPR2 with cytogenetic location of 9p13.3. This mutation overlaps with two diseases: firstly, autosomal dominant epiphyseal chondrodysplasia, miura type (ECDM) which is characterized by tall stature, long hands and feet with arachnodactyly, and secondly, short-rib thoracic dysplasia 5 with or without polydactyly (4,5). Both diseases have completely different clinical patterns and radiographic manifestations from AMDM.

Considering the skeletal changes, radiological findings and sequence analysis of mutation, we firstly presented AMDM from Iran; the presented case with severe short stature had no obvious abnormality in the distal segment of his lower limb. It is suggested to be a new variant form of AMDM in cases with severe short stature; however, the distal segment of the lower limbs might be pronounced throughout childhood.

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Figure 1. Clinical characteristics and radiographic features of the case. Frontal bossing, low set ears and wrist joint hyperflexibility as well as short and broad fingers of the hand with small nails. Radiographic findings showed radial bowing with posterior dislocation, short lower end of the ulna than the radius, and broad metacarpals with wide phalanx

