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SCIENTIFIC LETTER

Pathological Fracture in Autosomal Recessive Cutis Laxa Type 2B

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To the Editor: Cutis laxa is also known as elastolysis. It includes a wide spectrum of rare genetic disorders characterized by loose, redundant and wrinkled skin [1]. We present a rare case of pathological fracture in a case of autosomal recessive cutis laxa type 2B (MIM#612940) due to novel homozygous missense variation (Proline for leucine at codon 66) in exon 3 of the *PYCR1* gene transcript (ENST00000329875) (chr17:79893334;A>G), which is a likely pathogenic variant (c.197T>C) detected by Sanger sequencing.

A term male infant with birth weight of 1.95 kg was born of consanguineous marriage to a primigravida mother. The antenatal scans were suggestive of intrauterine growth restriction. The infant was noted to have microcephaly, progeroid facial appearance, cutis laxa, hypermobile joints, wide open anterior fontanelle and congenital vertical talus. Screening echocardiogram and MRI were normal. The infant was discharged on day 10 of life and was asymptomatic until discharge. At 3 wk of age, the infant was noted to have a tender swelling on the right thigh region. Skiagram showed fracture of the right femur bone with osteopenic changes. The infant had normal serum calcium, low phosphorous (1.5 mg/dl), elevated alkaline phosphatase (1150 IU/L) and low serum vitamin D levels (17.5 ng/ml). The fracture was treated with immobilization and supportive care. The neonate was treated with vitamin D (800 IU/d), calcium (150 mg/kg/d) and phosphorous (90 mg/kg/d) supplementation. At three months of age the infant had normal phosphorous and vitamin D levels with decline in alkaline phosphatase levels (750 IU/L).

The common differential diagnosis of hypermobile joints with cutis laxa includes deBarsy syndrome, autosomal recessive cutis laxa type 2A and 2B, wrinkly skin syndrome and Geroderma osteodysplastica [2]. The infant presented in the above clinical case had novel homozygous mutation in *PYCR1* gene which is likely pathogenic variant of autosomal recessive cutis laxa type 2B/3B [3]. *PYCR1* gene helps in synthesis of proline from glutamate. Hence defective proline synthesis results in fragile bones and pathological fractures. These neonates require calcium, phosphorous, vitamin D supplementation and routine follow-up for bone mineral density apart from long term neurodevelopmental outcome [3].

Compliance with Ethical Standards

Conflict of Interest None.

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