CASE REPORT

Leri-Weill dyschondrosteosis: An under-recognised cause of short stature

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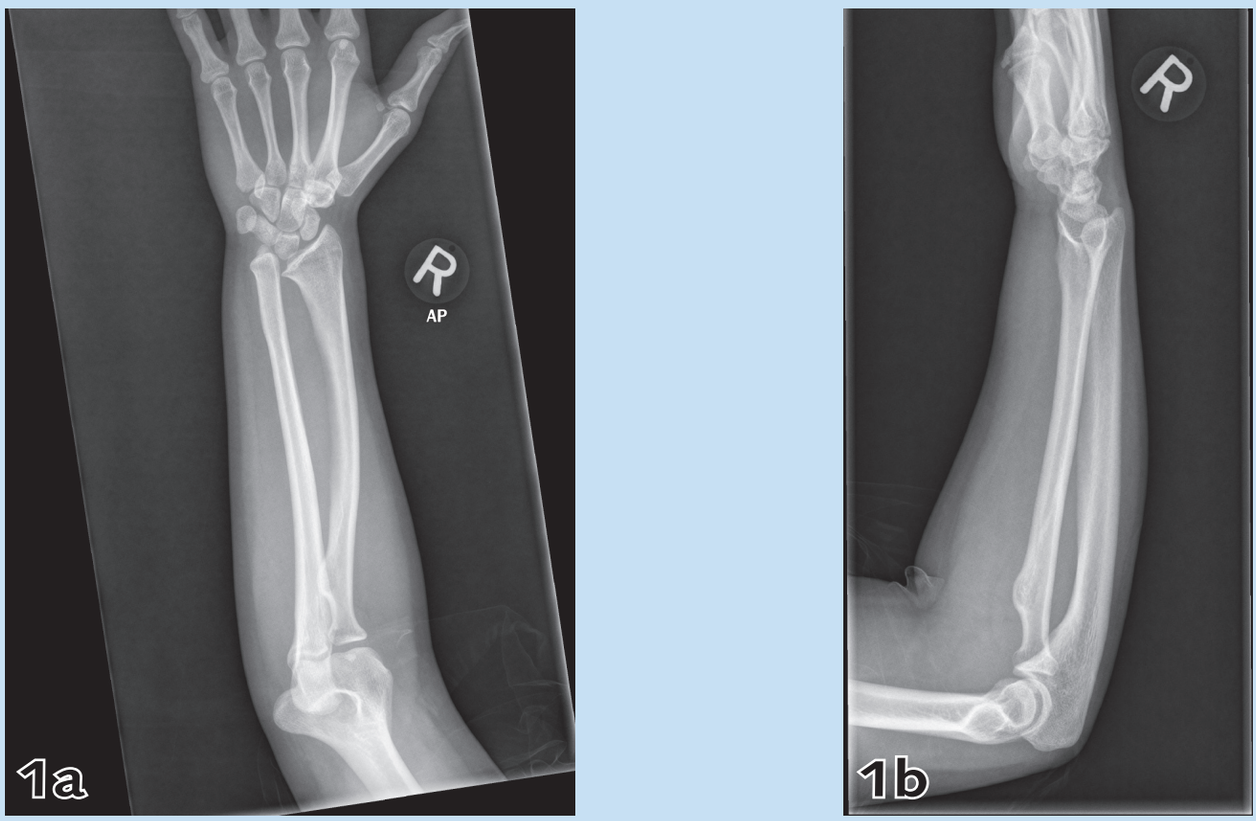
Introduction

Short stature is a frequent presenting problem in the paediatric population. Various causes including endocrinopathies, skeletal dysplasias, dysmorphic syndromes and malabsorption have been implicated. In girls with short stature, Turner syndrome is frequently considered in the differential diagnosis and can easily be ruled out with chromosome analysis. However, it is not uncommon for a child to have no identifiable cause of their short stature.

Advances in the field of genetics have estimated that about 2% of idiopathic short stature is related to haplo-insufficiency of the short stature homeobox (SHOX) gene, which is found on the short arm of the X and Y chromosomes in the pseudo-autosomal region. Heterozygous carriers of SHOX mutations may be minimally affected or may present with disproportionately short stature, Madelung deformity and other radiographic findings, as in Leri-Weill dyschondrosteosis (LWD). In this report, we discuss a 14-year-old girl with mesomelic short stature and bilateral Madelung deformities caused by LWD and describe the radiographic findings.

Case report

The subject was born at term following an unremarkable pregnancy. Birth parameters were: length 54 cm (90th centile), weight 3 985 g (80th centile) and head circumference 36.5 cm (70th centile). The newborn period was unremarkable and the patient was discharged on day 2. Developmental milestones were met appropriately. She was an above-average student at school.



Figs. 1a and 1b. Antero-posterior and lateral radiographs of the right forearm demonstrating the typical features of Madelung deformity: bowing and shortening of the distal radius, widening of the distal radial-ulnar joint, and triangulation of the distal radial epiphysis, producing an ulnar slant to the articular surface.

She had always been one of the shortest students in her class. Menarche occurred at age 10 years, preceded by a growth spurt when, for a brief period, she reportedly was of average height among her peers until they also entered puberty. Her sister, three years her junior, is now taller than her.

Past medical history was remarkable for surgical excision of a congenital cholesteatoma and insertion of transtympanic tubes to correct a conductive hearing loss. The family history was unremarkable, and her parents were both approximately 170 cm tall. A number of investigations were performed: she was found to have an advanced bone age on X-ray; somatomedin C and TSH levels were normal; and chromosome studies revealed a normal female karyotype – 46XX. She was referred to the Medical Genetics Division for further assessment.

On physical examination at age 14 years and 7 months, the patient presented with disproportionately short stature and relative macrocephaly. Clinically, she appeared to have mesomelic limb shortening with bilateral Madelung deformities, which was confirmed by measurements. Her growth parameters were as follows: height 151 cm (5th centile), weight 54 kg (60th centile) and head circumference 56.25 cm (90th centile). Other measurements included a reduced arm span (148 cm) to height ratio (normal >1.0 and <1.05 for age) and an increased upper segment (83 cm) to lower segment (68 cm) ratio of 1.22 (normal ~1.0 for age).[1] A diagnosis of LWD was advanced clinically, and additional X-rays were requested to confirm the diagnosis radiographically.

Radiographs supported the clinical diagnosis (Fig. 1). The prominent Madelung deformity (shortening and bowing of the radii and triangulation of the distal radial epiphysis producing an ulnar slant to the articular surface) of the distal radius and ulna is a well-described feature of dyschondrosteosis (Leri-Weill disease). The lunate carpal bone wedges between the deformed distal radial ulnar joint are slightly subluxed.[2]

The patient and her family declined genetic testing.

Discussion

SHOX-related haplo-insufficiency disorders are estimated to have a prevalence of 1/4 000 and are known to account for a not insignificant proportion of cases of idiopathic short stature.[3] The SHOX gene is located on the pseudo-autosomal regions of the short arms of the X and Y chromosomes. Consequently, transmission appears to be autosomal dominant because recombination occurs, but it is more correctly termed pseudo-autosomal dominant.

The majority of SHOX gene mutations are deletions, but point mutations are also known to occur. Most affected individuals have inherited the mutation from one of their parents, but rarely it can be caused by a *de novo* mutation. Penetrance is known to be incomplete, meaning that some carriers of a SHOX mutation may appear to be normal or minimally affected. Homozygosity or compound heterozygosity for SHOX mutations leads to a more severe skeletal dysplasia – Langer mesomelic dysplasia.

The clinical spectrum of SHOX mutation carriers is quite variable, ranging from normal to the mesomelic short stature of LWD. Mesomelia leads to a reduction in the arm span and an increase in the upper-to-lower segment ratio. Disproportionately short stature was observed in our patient, which led us to suspect LWD. The radiographic finding of the Madelung deformity supported the clinical diagnosis.

The differential diagnosis includes Turner syndrome, growth hormone deficiency and idiopathic short stature. The diagnosis of Turner syndrome was excluded in our patient by karyotype analysis. Interestingly, the short stature seen in Turner syndrome is in part related to SHOX haplo-insufficiency caused by the missing X chromosome. Madelung deformity is also an occasional feature of Turner syndrome but is not commonly associated with isolated growth hormone deficiency or idiopathic short stature.

1. Hall JG, Allanson JE, Gripp KW, Slavotinek AM. *Handbook of Physical Measurements*. 2nd ed. New York: Oxford University Press, 2007: 196, 243-244.
2. Taybi H, Lachman RS. *Radiology of Syndromes, Metabolic Disorders, and Skeletal Dysplasias*. 4th ed. St Louis, USA: Mosby, 1996.
3. Munns C, Glass I. SHOX-Related Haploinsufficiency Disorders (updated 1 February 2008). *GeneReviews* at GeneTests: Medical Genetics Information Resource, University of Washington. http://www.genetests.org (accessed 2 February 2009).