TWO FEMALE SIBLINGS FROM TURKEY WITH LANGER MESOMELIC DYSPLASIA (HOMOZYGOUS LERI-WEILL DYSCHONDROSTEOSIS SYNDROME)*

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SUMMARY: Balcı S, Zafer Y, Ünsal M. (Department of Pediatrics, Hacettepe University Faculty of Medicine, Ankara, Turkey). Two female siblings from Turkey with Langer mesomelic dysplasia (homozygous Leri-Weill dyschondrosteosis syndrome). Turk J Pediatr 1999; 41: 531-539.

Leri-Weill dyschondrosteosis is an autosomal dominant syndrome of which the characteristic features are mild-to-moderate shortness of stature and Madelung deformity of the wrist. The homozygous state of the gene for Leri-Weill syndrome causes Langer mesomelic dysplasia which is characterized mainly by shortening of the long tubular bones, more markedly in the middle than in the proximal and distal segment of the extremities. In this paper, we present two sisters with Langer mesomelic dysplasia (12 years and 6 months of age, respectively), from consanguineous parents. The mother of our cases had Madelung deformity. Father, mother and grandmother also had a slight deformity of both forearms. Unfortunately, despite the well documented case of the older sister with Langer mesomelic type dysplasia, the first and second trimester ultrasonographies of the younger sister were performed by inexperienced staff of a local urban hospital and the prenatal diagnosis of this case was not made. In this paper, we also discuss the prenatal diagnosis of Langer type mesomelic dysplasia. *Key words: Langer mesomelic dysplasia, homozygous Leri-Weill dyschondrosteosis syndrome, hypoplastic ulna-fibula, hypoplastic mandible, prenatal diagnosis.*

Leri-Weill dyschondrosteosis is an autosomal dominant syndrome of which the characteristic features are mild-to-moderate shortness of stature and Madelung deformity of the wrist. The homozygous state of the gene for Leri-Weill syndrome causes Langer mesomelic dysplasia[1]. The first Turkish case of Langer type mesomelic dysplasia was reported from Germany in 1980[2] and the second by Diren et al.[3] 1985. This report from Turkey is the third such report of Langer type mesomelic dysplasia, documented in this case in two siblings.

Case Reports

Case 1

The 12-year-old female patient was the first child born to consanguineous parents who were cousins. She was first seen at 21 months of age with chief complaints

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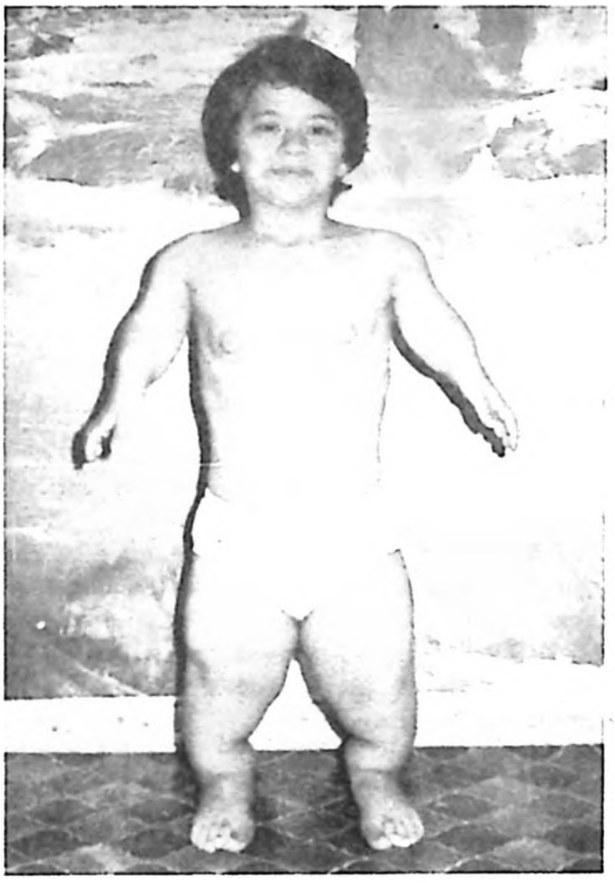

Fig. 1: The first case at the age of 12 years. Note the striking shortness of the middle segments of the extremities, ulnar deviation at the wrists, and normal appearance of hands and feet.

of short stature mainly due to short extremities. Her length was 67 cm (<3rd percentile), weight 12 kg (50th percentile), and head circumference 48 cm (75th percentile). She was seen again at 12 years of age (Fig. 1). Her psychomotor development was normal. Physical examination revealed marked bilateral shortening of the proximal and middle segments of upper and lower limbs. Her height was 106 cm (<3rd percentile) and weight 30 kg (<3rd percentile). She had hypertelorism, pectus excavatum and lumbar lordosis.

Radiological examination: Skull X-ray showed basilary impression and mildly hypoplastic mandible (Fig. 2). Symmetrical shortening of the radius and ulna was associated with bowing of the radius. Humerus was also short and thickened. Caput humeri showed varus deformity and the distal epicondyle was broad. Tuberositas deltoidea humeri was prominent. Proximal portion of the radius and distal portion of the ulna were hypoplastic (Fig. 3).

Spina bifida occulta malformation at 5th lumbar vertebra was observed. The femur and the tibia had a broad shaft and were shortened. Diaphysis of the femur was also short and trochanter major, trochanter minor and condyles were broad (Fig. 4).

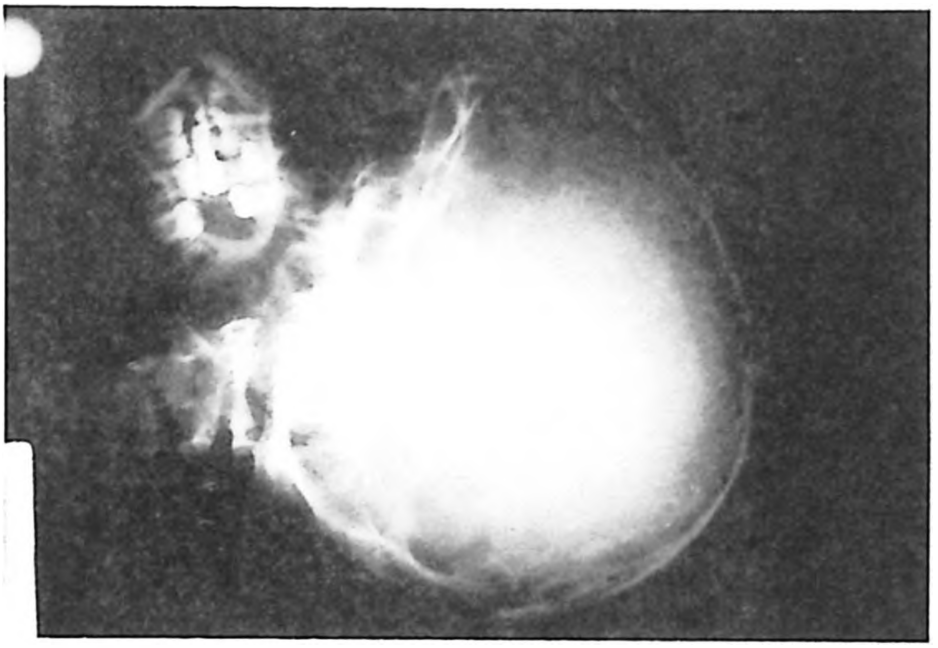

Fig. 2: Skull X-ray: basilary impression and mildly hypoplastic mandible.

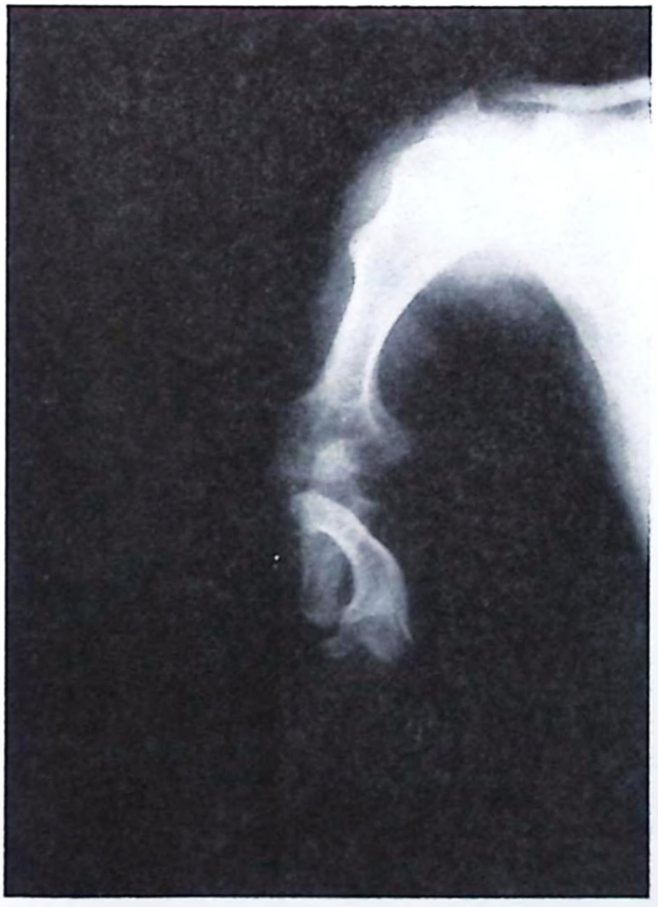

Fig. 3: Forearm, anteroposterior radiograph: shortening of he radius and the ulna and associated bowing of the radius. Proximal portion of the radius and distal portion of the ulna are hypoplastic. Slight broadening of the humenus.

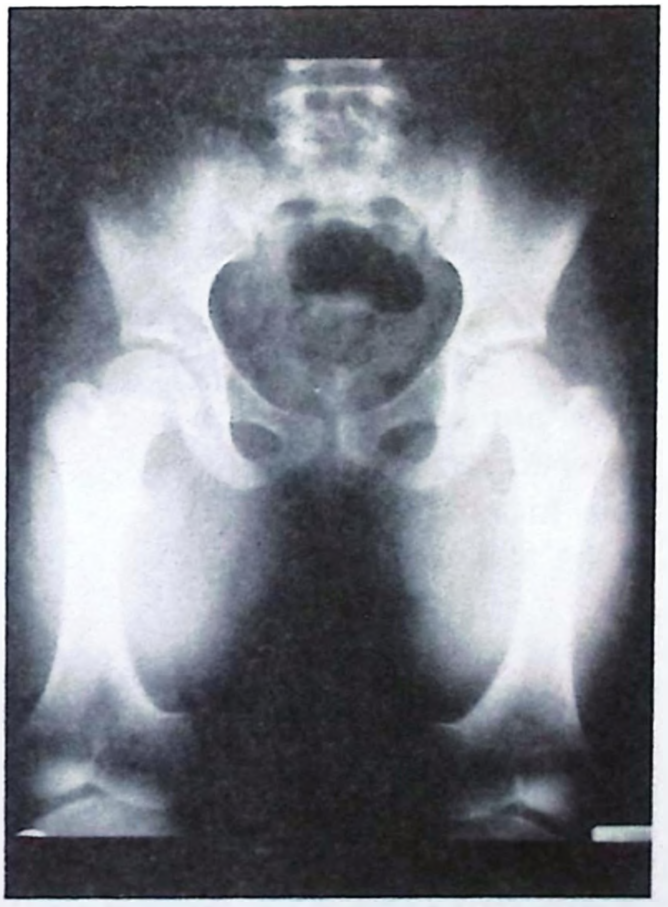

Fig. 4: Hip and thigh, anteroposterior radiograph: the femur is broad and short. Spina bifida malformation at 5th lumbar vertebra.

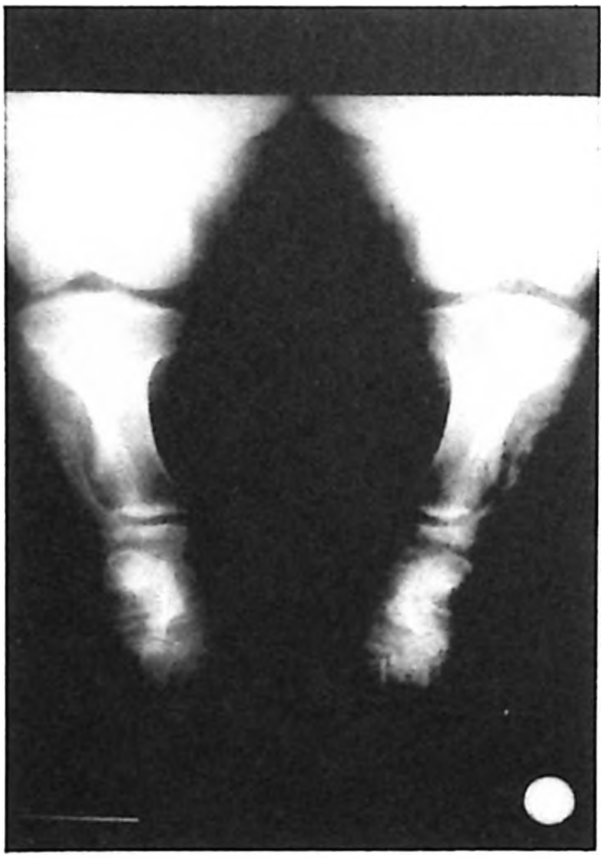

Fig. 5: Shank, anteroposterior radiograph: the tibia is broad and short. Early fusion in tibial proximal epiphyseal ossification center is observed. Proximal segment of the fibula is hypoplastic.

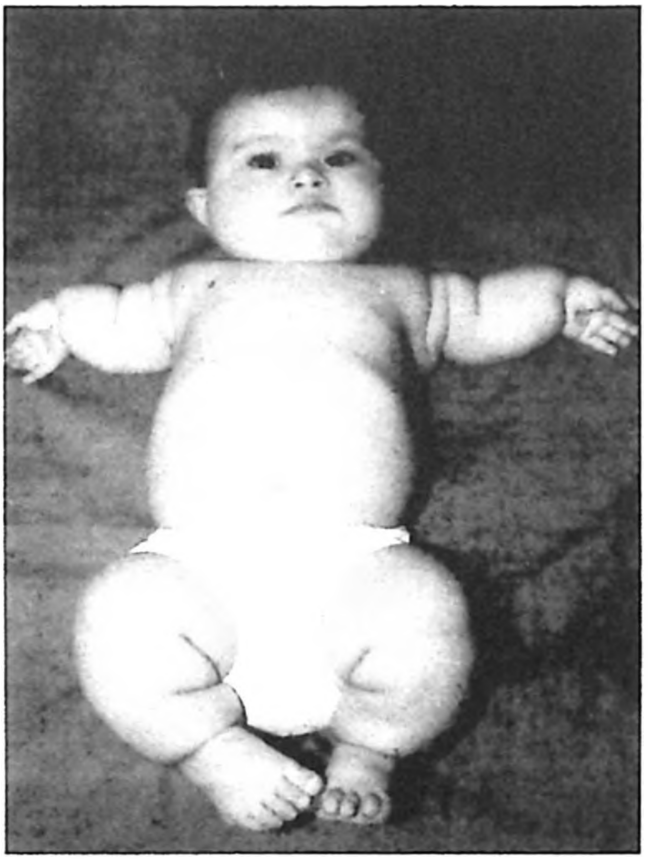

Fig. 6: The second case at six months. Limb shortening is most obvious in the forearms and shanks.

Hand and foot roentgenograms showed no abnormalities. Tibial plates were flattened, and eminentia intercondylaris was not clearly seen. Early fusion in tibial proximal epiphyseal ossification center was observed. Proximal segment of the fibula was hypoplastic (Fig. 5).

Case 2

When the first affected daughter was 14 years old, the mother became pregnant again. She was 37 years old and the father was 33 years old. Although the parents were invited to the hospital many times, financial problems prevented their coming. The family did not apply to our center for prenatal ultrasonography of this third pregnancy. Routine prenatal ultrasonography was performed by inexperienced staff. Unfortunately, the third child was born with similar findings. Birth weight was 3,700 g and length was 49 cm. After six months, her weight was 9 kg (90-97th percentile) and her length was 61.5 cm (3rd-10th percentile) (Fig. 6). On physical examination, bowing and shortness of upper and lower

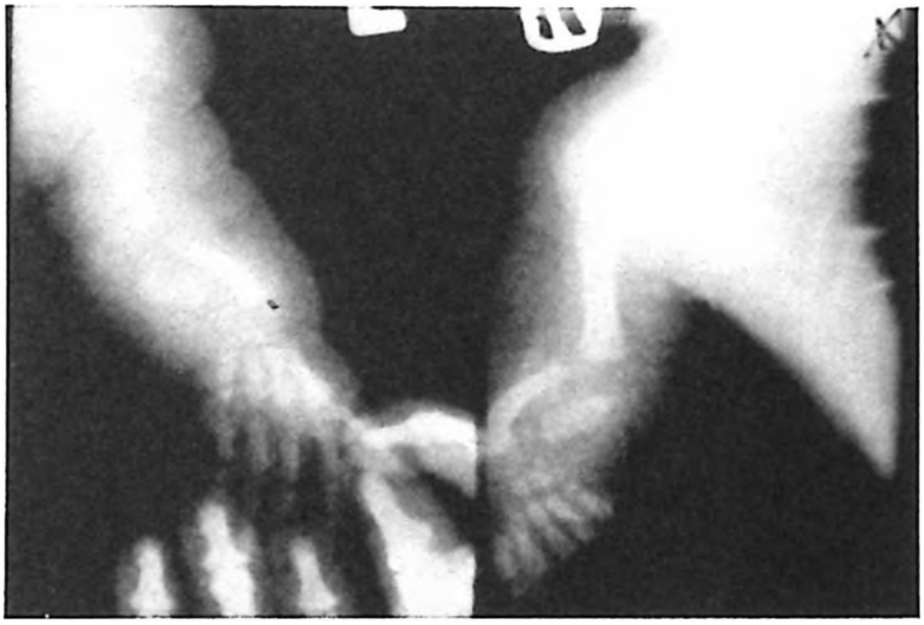

Fig. 7a

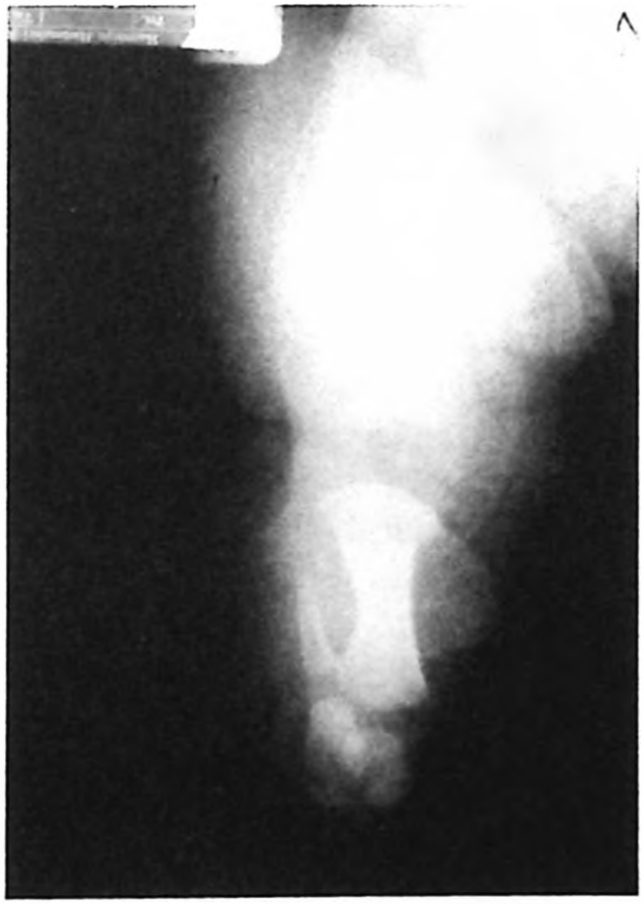

Fig. 7b

Fig. 7a-b: a: Right arm, anteroposterior radiograph: broadening of the humerus. Radial bowing of the radius and absence of the ulna including the epiphysis. b: Right leg, anteroposterior radiograph: shortened tibia with broad shaft, rudimentary fibula. Absent upper portion including the ossification center of the fibular head.

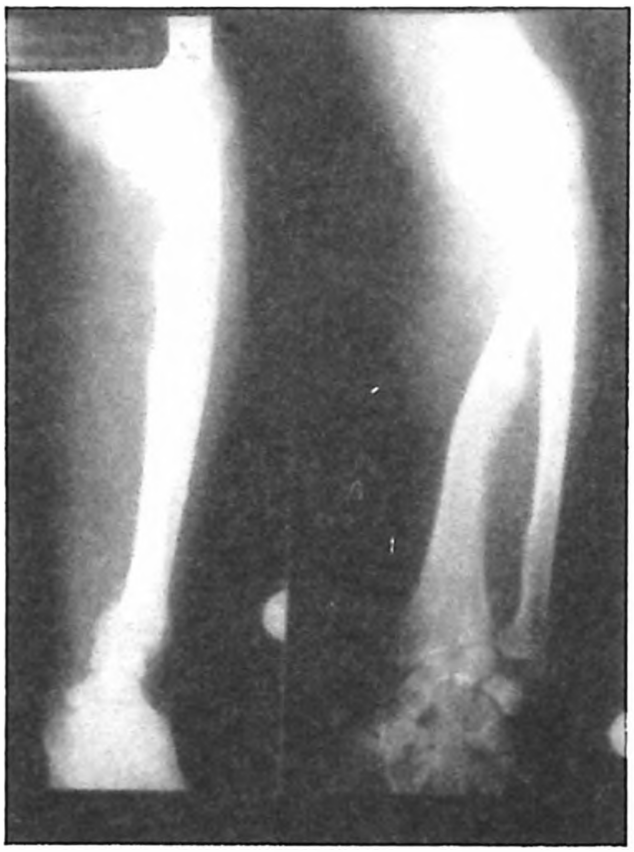

Fig. 8a

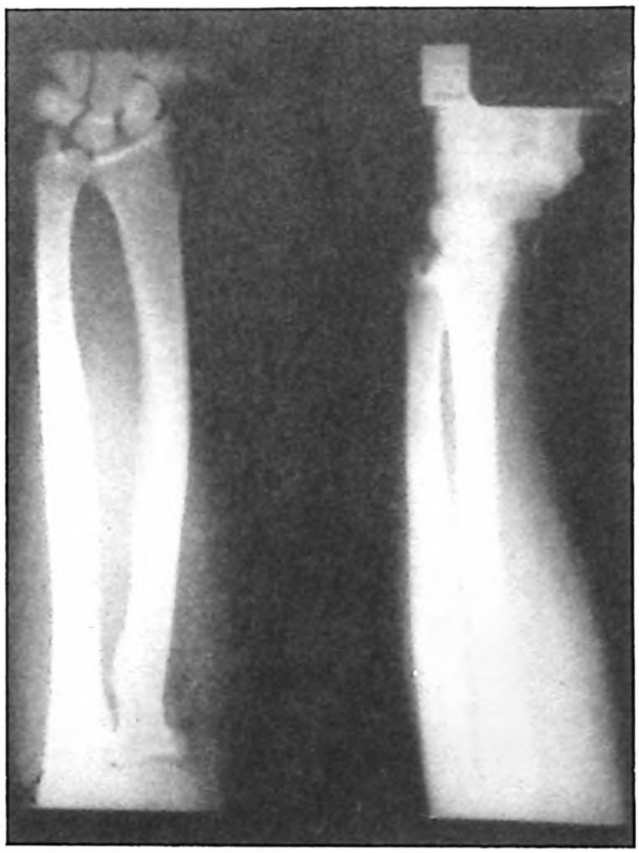

Fig. 8b

Fig. 8a and b: Right forearms of the parents with typical changes caused by Madelung deformity.

extremities were detected. Radiological examination: Roentgenograms obtained at six months showed symmetrical shortening of the radius and ulna with bowing of the radius. The humerus was short and thickened. The ulna was hypoplastic and the distal portion including the epiphysis absent. The middle segments of the lower extremities were considerably shortened. The tibia had a broad shaft and was shortened. The fibula was rudimentary: the upper portion, including the ossification centers of the tibia, was small and moderately deformed. The radiological findings of the second affected female patient are shown in Fig. 7a, 7b. The mother measured 141 cm and demonstrated typical Madelung deformity (Fig. 8a). The father measured 171 cm and had a slight deformity of both forearms (Fig. 8b). The maternal grandmother was 59 years old, and roentgenograms of her upper extremities showed slight bowing of the radius (Fig. 9). Figure 10 summarizes this current pedigree of kinship.

Discussion

Langer[1] described three families and referred to the entity as 'mesomelic dwarfism of the hypoplastic ulna, tibia, mandible'. Langer mesomelic dysplasia is characterized mainly by shortening of the long tubular bones, more markedly

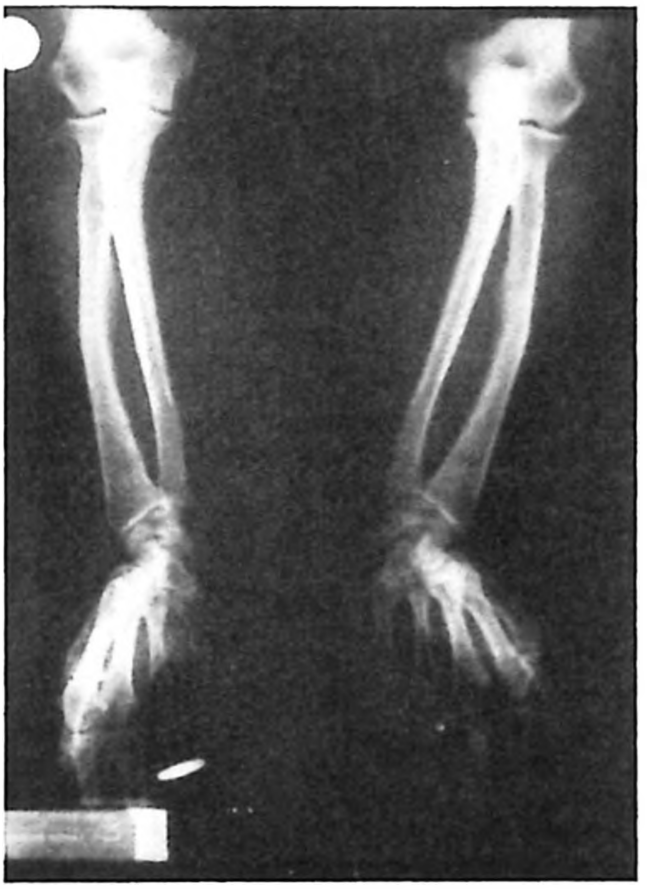

Fig. 9: Right forearms of the maternal grandmother showing slight bowing of the radius.

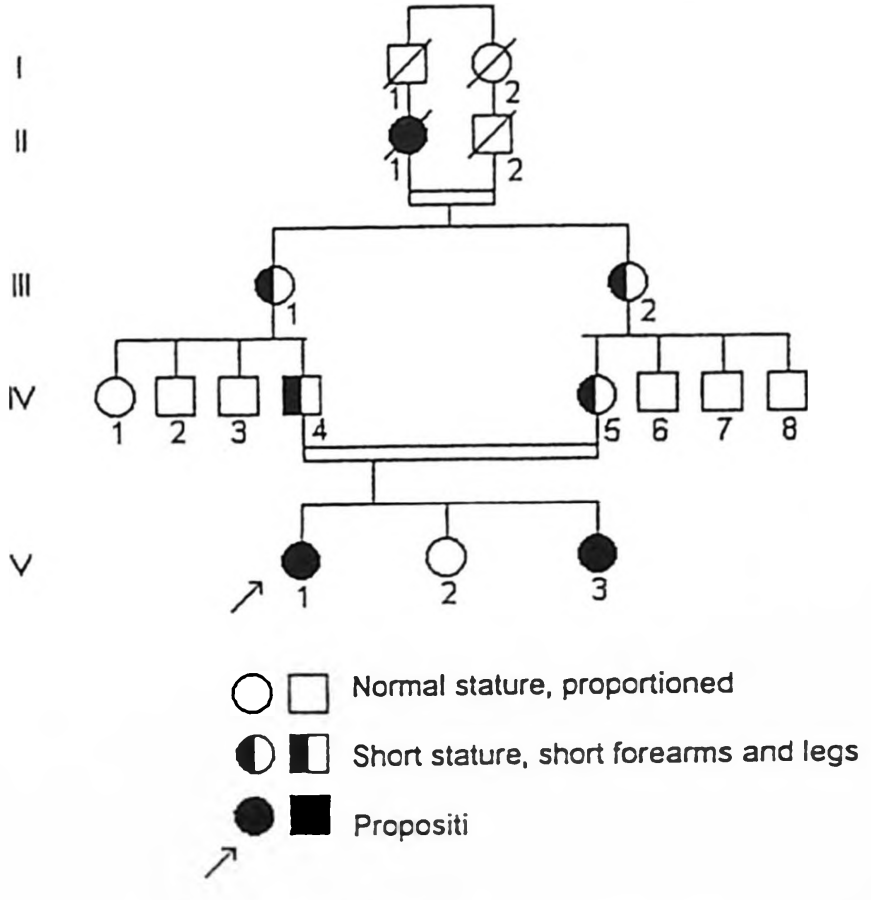

Fig. 10: Pedigree of kinship. Members IV-5, V-1 and V-3 have classical dyschondrosteosis.

in the middle than in the proximal and distal segments of the extremities. The second most common finding is radial bowing of the radius with additional radial and volar curvature, hypoplasia of the distal part of the ulna and absence of an ossified distal ulnar epiphysis, such as was seen in our case[3,4]. The third common finding is marked shortening of the tibia with lately developed, moderately deformed and prematurely fused epiphyseal ossification centers[3].

Mesomelic is a nonspecific term representing shortening, most apparent in the forearm and lower leg, and referred to as 'dyschondrosteosis'. In addition to these findings, a hypoplastic mandible and normal skull are the other characteristic features. There are no extraskeletal abnormalities and intelligence is normal[3].

The mesomelic dysplasias are a heterogeneous group of disorders characterized by shortness predominantly in the radioulnar and tibiofibular segments. Five have been delineated: Nievergelt, Langer, Robinow, Rheinhardt-Pfeiffer, and Werner[3].

Included in the differential diagnosis of mesomelic dysplasia is also Ellis-van Creveld syndrome. This syndrome can be differentiated from Langer mesomelic dysplasia by the presence of cardiac malformations, oligodontia with conical teeth, polydactly and nail dysplasia. The mode of inheritance of this syndrome is autosomal recessive. Heterozygote individuals show mild-to-moderate shortness of stature and relatively short forearms with Madelung deformity. The homozygous state is associated with a much more severe shortness of stature.

Book[6] described the first kindred with Langer type mesomelic dwarfism from northern Sweden in 1950. Heterozygotes in this family were short (the father was 160 cm and the mother 150 cm) and had relatively short fingers, and broad hands. Motor and mental development were normal. The adult height was approximately 130 cm. In our cases there was first-degree consanguinity between the parents, and there was a history of the maternal great grandmother being of short stature. Heterozygotes in the family were also short (the mother was 141 cm tall and the great grandmother was even shorter, with relatively short fingers and hands). The first Turkish case of Langer type mesomelic dwarfism was reported by Kunze and Klemm[2] in 1980. They reported two female cases of separate unrelated Turkish families. Both parents of affected females had signs of dyschondrosteosis, including Madelung deformity. The first three cases with Langer mesomelic dysplasia from separate unrelated families from Turkey were reported in 1985 by Diren[3] et al.

Goldblatt et al.[7] described a case of Langer type mesomelic dysplasia with a mild deformity of the forearms similar to but different from Madelung's deformity of the forearms.

Evans et al.[8] described the first prenatally diagnosed (2nd trimester) case of Langer type mesomelic dwarfism by sonography, and reported the pathologic findings in this case. The mother of this fetus also had Madelung deformity. Madelung deformity or mild deformity of the forearm may be an important sign for mesomelic dysplasias.

In this report two sisters from consenguineous parents with Langer type mesomelic dysplasia are presented. There is no report of this dysplasia occurring in a related family in the literature. This observation suggests that this dysplasia may be due to an autosomal recessive gene. In our cases despite the older sister's illness being well documented, prenatal diagnosis of the younger sister was not made, probably due to misinterpretation of the first and second trimester sonographics by inexperienced staff at a local urban hospital. This highlights the importance of early prenatal recognition of this rare dysplasia. We believe increased reporting of such cases will prompt early diagnosis.

Acknowledgements

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