CASE REPORT

Unilateral proximal focal femoral deficiency, fibular aplasia, tibial campomelia and oligosyndactyly in an Egyptian child – Probable FFU syndrome

Rabah M. Shawky a,*, Heba Salah Abd Elkhalek a, Shaimaa Gad a, Shaimaa Abdelsattar Mohammad b

a Pediatric Department, Genetics Unit, Ain Shams University, Egypt
b Radio Diagnosis Department, Ain Shams University, Egypt

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Abstract We report a fifteen month old Egyptian male child, the third in order of birth of healthy non consanguineous parents, who has normal mentality, normal upper limbs and left lower limb. The right lower limb has short femur, and tibia with anterior bowing, and an overlying skin dimple. The right foot has also oligosyndactyly (three toes), and the foot is in vulgus position. There is limited abduction at the hip joint, full flexion and extension at the knee, limited dorsiflexion and plan tar flexion at the ankle joint. The X-ray of the lower limb and pelvis shows proximal focal femoral deficiency, absent right fibula with shortening of the right tibia and anterior bowing of its distal third. The acetabulum is shallow. He has a family history of congenital cyanotic heart disease. Our patient represents most probably the first case of femur fibula ulna syndrome (FFU) in Egypt with unilateral right leg affection. We suggest that the condition in our patient may be due to a rare autosomal dominant mutation with possible gonadal mosaicism and with variable expression in the family, as limb anomaly in one child and cyanotic congenital heart disease in another child.

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1. Introduction

Fibular hemimelia is a congenital deficiency or absence of the fibula, and it is one of the rare congenital malformations. However it is the most frequent reduction malformation of long bones [1].

Fibular hemimelia ranges from mild hypoplasia to aplasia and may be unilateral (common) or bilateral (rare). The ipsilateral tibia may be hypoplastic, bowed or normal. Three types of fibular hemimelia have been recognized. Type I includes...
cases with unilateral or partial absence of the fibula with mild or no bowing of tibia (10% of cases). The leg may or may not be shortened. Type II includes cases with unilateral absence of the fibula, anterior bowing of the tibia with skin dimpling, and foot deformity with absent rays and marked shortening of the leg (35% of cases). Type III has unilateral or bilateral absence of the fibula, with same leg and foot deformities and multiple skeletal defects (55% of cases) [2].

Fibular hemimelia can be frequently associated with other skeletal anomalies including proximal focal femoral deficiency (PFFD) which is the most common (20% of patients) [3], as well as peromelia, dislocation of the head of the radius, and absent tarsal bones [4]. Other associated anomalies include, cardiac, thrombocytopenia, absent radius (TAR) syndrome, thoracoabdominal schisis, spina bifida and renal anomalies [5].

Fibular hemimelia is due to interference with limb bud development at about the 5th or 7th week of intrauterine life. The fibular field of the limb bud controls the development of the proximal femur which explains the frequent association of femoral abnormalities. Other associated abnormalities of the knee, leg, ankle and foot are also related to the fibular field of the lower limb bud [6].

Fibular hemimelia is usually sporadic, although a familial incidence (autosomal recessive) has been reported in a small percentage of cases [7].

We report for the first time an Egyptian child with a rare unilateral lower limb reduction defect after taking consent of the parents.

2. Case report

Our patient is an Egyptian male child, fifteen months old, the third in order of birth of healthy non consanguineous parents. The mother’s age is 28, and the father’s age is 38 years old. The patient presented to the Genetics Clinic complaining of right lower limb shortening and deficient toes in the right foot detected at birth. Pregnancy and delivery were uneventful. There is no history of hypertension or diabetes in the mother. However she received progesterone from the 1st trimester for 5 months because of vaginal bleeding. There is a family history of cyanotic congenital heart disease in a previous female sib who died at the ICU before surgical operation at the age of one month. Also there is a family history of cyanotic congenital heart disease in a paternal female cousin who died at the age of ten years shortly after the 2nd stage repair operation. There is also a family history of mental retardation and motor disability in a maternal male cousin and no family history of limb anomalies (Fig. 1).

On examination the skull circumference is 47 cm (at 50th centile), length is 79 cm (at 50th centile), and weight is 11 kg (at 50th centile). The mental and physical developments are normal. The eyes show bilateral medial epicanthic folds with no other dysmorphic facial features. The upper limbs and left lower limb are completely normal. The right lower limb has short femur, and tibia with anterior bowing, and an overlying skin dimple. The right foot has oligosyndactyly (3 toes only), with complete syndactyly between the 2nd and 3rd toes which are short (brachydactyly). The foot is in a vulgus position. There is limited abduction at the hip joint, full flexion and extension at the knee, limited dorsiflexion and plantar flexion at the ankle joint. The nails are normal (Figs. 2 and 3).

Cardiac, abdominal, neurological and external genitalia examinations as well as mentality are completely normal.

The X-ray of the lower limbs and pelvis shows under trabeculation of the femur and tibia. The right femur is short and its ossific center is small compared to the left, its long axis is oval in shape and longitudinally oriented (rather than

![Figure 1](image1.png) Family pedigree, A: Patients with congenital cyanotic heart disease. B: A cousin has mental retardation and motor disability.

![Figure 2](image2.png) There is marked discrepancy between the two lower limbs, the right lower limb has short thigh, leg and skin dimple.

![Figure 3](image3.png) The right foot has 3 toes with syndactyly between the 2nd, and 3rd toes, with normal nails.
horizontal) (proximal focal femoral deficiency). The right fibula is absent with shortening of the right tibia and anterior bowing of its distal third (type II). The acetabulum is shallow (Fig. 4). The foot shows only 3 metatarsal bones with 3 toes only (the 4th and 5th toes are absent). The 2nd toe contains only 2 phalanges with absent middle phalanx. Absent calcaneus is detected as its ossific center is not seen, cuboid and cuneiform lateral bones are also absent (Fig. 5).

ECHO cardiography, pelviabdominal ultrasonography, and karyotype are normal.

3. Discussion

We report a male child born to non consanguineous Egyptian parents, with congenital lower limb deficiency. This deficiency consists of shortness of right leg, anterior bowing at the distal third of the tibia, with associated overlying soft tissue dimpling, together with oligosyndactyly (3 toes) of the right foot. Both upper limbs and left leg are completely normal. The infant has neither dysmorphic facial features nor other associated anomalies. There is a family history of congenital cyanotic heart disease in a sib and a cousin. Radiographic examination revealed complete absence of right fibula (fibular aplasia, FA type II), anterior bowing and shortness of right tibia (tibial camptomelia, TC), and absence of lateral rays of the foot (3 toes only – oligosyndactyly) with absence of calcaneous, cuboid, and cuneiform lateral bones. There is also dysplastic proximal femur and acetabulum (proximal focal femoral deficiency (class A) [8]. No other abnormalities were detected on skeletal survey. There is also no family history of limb anomalies. To our knowledge this is the first report in Egypt.

Changes reported in the leg of our patient are typical of those described as Fibular Aplasia, Tibial Campomelia, and Oligodactyly (FATCO) syndrome described previously by Hecht, and Scott, as well as others [9–13].

Our patient has in addition short thigh due to proximal focal femoral deficiency (PFFD) which was not reported in any patient with FATCO syndrome where the femur is...
completely normal. In our patient the heart is not affected, however there is a family history (sib and cousin) with congenital cyanotic heart disease. In the 2 cases reported by Hecht and Scott [8], the girl is typical of FATCO syndrome while her half brother has tetrameric transverse defect and a cyanotic congenital heart.

The findings in our patient are similar to the antenatal sonographic findings reported in a fetus with normal karyotype [14]. This patient has PFFD in addition to the absence of the ipsilateral fibula, an anterior bowed tibia, absence of two toes, a normal contralateral leg and normal upper limbs.

Proximal focal femoral deficiency (PFFD), which is present in our patient, is a rare developmental disorder of the proximal femur that results in failure of formation or differentiation of the proximal femur and associated acetabulum. Its association with fibular a/hypoplasia is reported in approximately 50% of cases [15]. Also it has been reported in a variety of syndromes including Fuhrman syndrome. This syndrome is characterized by fibular a/hypoplasia in addition to a/hypoplasia of the femur, oligosyndactyly, aplasia or hypoplasia of the ulna plus dysplastic nails. This syndrome can be excluded in our patient by the presence of bowing of the femur, hypoplasia of the pelvis, congenital dislocation of the hip, postaxial polydactyly, dysplastic nails and other anomalies not present in our patient. Also in Fuhrman syndrome the tibia is normal in length, and slender [16].

Other syndromes having both PFFD and fibular a/hypoplasia include the femur–fibula–ulna (FFU) syndrome or complex. FFU syndrome is a non-lethal syndrome. Its original description includes absence of the proximal part of the femur, absence of the fibula and malformation of the ulnar side of the upper limb, with normal axial skeleton, internal organs and intellectual function [17,18]. Later cases of bilateral femur and fibula defects with normal arms were included in the same category [19]. In a study of 491 cases with FFU syndrome by Lenz [18], FFU patients were divided into 4 groups. Group I includes patients with one limb affected in nearly half the patients (44.4%). Group II includes patients with two limbs affected (33.6%). Group III includes patients with tree limbs affected (11.2%). Group IV includes patients with four limbs affected. Generally boys are affected twice as often as girls and upper limbs are affected more than the lower limbs, with the right side and males more preferentially affected [18]. An important characteristic is that the limb defects are asymmetrical. The precise diagnosis of FFU complex is particularly difficult because cases which belong to this complex can differ widely from one another [17,20]. It is also characterized by highly variable combination of congenital anomalies of the femur, fibula and/or ulna which can appear along with finger/toe anomalies at the ulnar/fibular side. It is usually not associated with internal malformations. However of the 493 cases with fibular hemimelia, only 0.8% was associated with non skeletal malformations, including two patients with neural tube defects, one patient with cardiac anomaly and one patient with renal anomaly [21]. Ergin et al. [22] reported a case of PFFD and fibular a/hypoplasia associated with urogenital anomalies (left descended testis and hypospadias). Also Sarma [23] reported a patient with agenesis of the fibula and meningocele. An extensive study of nearly 500 FFU cases supported the hypothesis that even if only one arm or leg is affected the case may still be classified as FFU complex [24].

Our patient most probably belongs to FFU syndrome with affection of the right lower limb (group I) with normal ulna. The etiology remains unknown. Neither iatrogenic agent, radiation or drug exposure nor infectious disease can be incriminated [25]. However Kumar and Krishnamurthy [26] reported a rare association of congenital absence of femur and fibular hemimelia with maternal hyperpyrexia.

The inheritance of this syndrome seems uncertain so far. Most cases are sporadic and familial recurrence is quite unusual and extremely rare. However familial cases were described by some investigators [18,27–30]. Also no transmission from a parent to a child has been observed. The rate of consanguinity is not increased among the parents, and there has been no maternal or paternal age effect.

In our patient the parents are non consanguineous although consanguinity rate is high in Egypt [31]. Also there is a family history of cyanotic congenital heart (in a sib and a cousin). So we suggest that the condition in our patient may be due to a rare autosomal dominant mutation with possible gonadal mosaicism and with variable expression in the family. It manifests its effect as limb reduction defect in some family members and cyanotic heart in other family members. Also some authors support early somatic mutation as a cause of FFU syndrome [24].

To conclude: we report the first case of FFU in Egypt with unilateral right leg affection with a family history of cyanotic congenital heart. Our case may allow understanding the mode of inheritance of this syndrome.

Conflict of interest

The authors declare no conflict of interests.

References


