Overlap between Fibular Aplasia, Tibial Campomelia, and Oligosyndactyly and Fuhrmann's Syndromes in an Egyptian Female Infant

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J Pediatr Genet 2017;6:118–121.

Abstract

Keywords

- FATCO
- Fuhrmann's syndrome
- fibular aplasia
- tibial campomelia
- oligosyndactyly

We report a rare congenital limb defect with combined features of both fibular aplasia, tibial campomelia, and oligosyndactyly (FATCO) and Fuhrmann's syndromes. A female newborn infant, born to nonconsanguineous Egyptian parents, presented with isolated abnormalities of the lower limbs comprising bilateral shortening and anterior bowing of the lower limbs at the distal third of the tibia and split foot. Radiographic examination revealed complete absence of both fibulae, anterolateral bowing and shortening of the tibia, bowing of the femora, and absence of several metatarsal and phalangeal bones. The upper limbs were clinically and radiologically normal, and the infant had neither facial dysmorphism nor other associated visceral anomalies. The presented case highlights an extremely rare limb deficiency syndrome, and together with additional case reports, it could be useful to further delineate this condition.

Introduction

Fibular aplasia, tibial campomelia, and oligosyndactyly (FATCO) syndrome (OMIM #246570) is an extremely rare syndrome first described by Hecht and Scott (1981).¹ Individuals with FATCO show shortening and anterior bowing of the lower limb at the distal third of the tibia with overlying soft tissue dimpling, oligodactyly of the foot, and oligosyndactyly of the hand. The etiology of the syndrome is currently unknown. The syndrome is usually sporadic, but autosomal dominant and recessive and X-linked inheritances have been proposed.² The *WNT7A*, *TP63*, and *WNT10B* genes have been investigated in previous cases of FATCO and no mutation was detected.^{2–4}

Fibular aplasia or hypoplasia, femoral bowing, and poly-, syn-, and oligo- dactyly (OMIM #228930), originally known as Fuhrmann's syndrome, is another rare limb malformation disorder.⁵ Fuhrmann's syndrome is mainly characterized by bowing of the femora, aplasia or hypoplasia of the fibulae, and

poly-, oligo-, and syndactyly. Most affected individuals also have a hypoplastic pelvis and hypoplasia of the fingers and fingernails.⁶ The syndrome is caused by homozygous mutations of *WNT7A* gene leading to a partial loss of function.⁷ Thus, it is allelic to Schinzel's phocomelia (or Al-Awadi/Raas-Rothschild syndrome), which results from null mutations in the same gene.⁷

In this report, we document an extremely rare congenital limb deficiency comprising features of both FATCO and Fuhrmann's syndromes.

Case Report

A newborn female child was referred for genetic evaluation because of striking abnormalities of her extremities. She was the first-born baby to a healthy Egyptian couple: mother 25 and father 27 years old. The parents were nonconsanguineous

received

September 19, 2016

accepted after revision

November 30, 2016

published online

January 2, 2017

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DOI <http://dx.doi.org/10.1055/s-0036-1597931>.
ISSN 2146-4596.

and the family history was unremarkable. The patient was born at full term by elective cesarean section and her birth weight was 3 kg. The pregnancy and delivery histories were uneventful, and the mother had no history of chronic illness or use of drugs, alcohol, tobacco, or exposure to radiation during pregnancy.

On clinical examination, the lower limbs showed bilateral shortening and anterior bowing at the distal third of the tibia, associated with soft tissue dimpling over the apex of deformity, and ectrodactyly of both feet (**Fig. 1A, B**). On the right foot there were only two digits: the big toe and another toe with a very wide gap in between (**Fig. 1B**). Four toes in the form of two syndactylous digits were present on the left foot with complete cutaneous syndactyly between digits I–II and IV–V (**Fig. 1B**). The hands and upper limbs were clinically normal. There were no joint contractures. External genitalia were normal. The infant had neither facial dysmorphism nor other external anomalies.

Radiographic examination revealed complete absence of the both fibulae, anterior bowing and shortening of the tibiae and angulated femora bilaterally (**Fig. 1C**). The radiograph of the right foot showed four metatarsal bones, two proximal phalanges, and two distal phalanges, and lacked the three central digits. The left foot also had four metatarsal bones, with the first one duplicated. It also showed four proximal and distal phalanges with the first one duplicated (**Fig. 1D**). There were aplasia of the calcaneus, talus, and cuboid bones. The skeletal survey showed normal humeri, ulnae, radii (**Fig. 2**), and no associated anomalies of the spine, skull, or pelvis.

Other investigations were all normal, including fundus examination, auditory brainstem response (ABR), abdominal ultrasound, and echocardiography. Karyotype analysis revealed normal female karyotype (46,XX).

Discussion

In this report, the described malformations; fibular aplasia, tibial campomelia, and oligosyndactyly, matched with the triad of FATCO syndrome (OMIM #246570). At the same time, the presence of bilateral bowing of the femora overlapped with the phenotype of Fuhrmann's syndrome (OMIM #228930).

In 2005, Courtens et al⁸ proposed the name FATCO to describe the rare syndrome of fibular aplasia, tibial campomelia, and oligosyndactyly first described by Hecht and Scott (1981).¹ This condition shows great variability in expression and its inheritance seems uncertain so far due to lack of information concerning familial transmission. Although almost all reported cases occurred sporadically, autosomal dominant and recessive and X-linked inheritances have been proposed.^{2,8,9} Moreover, there are no consistent associations with environmental exposures. To the best of our knowledge, we are reporting the 15th case of FATCO syndrome and the first from Egypt. The fact that the affected individual is female is also of interest in light of the preponderance of males with this condition (male-to-female ratio = 12:2).^{1–4,8–11}

FATCO shares some characteristics with fibular agenesis with ectrodactyly (OMIM #113310). The two conditions are similar, and it has been argued that FATCO syndrome should be included in the clinical entity of fibular aplasia with ectrodactyly.¹²

Fig. 1 Clinical photographs showing bilateral shortening and anterior bowing of affected lower limbs with overlying dimples (A), and ectrodactyly of both feet (B). Anteroposterior radiographs showing complete absence of the both fibulae, bilateral bowing, and shortening of the tibiae and angulated femora (C). Radiographs of the feet showing missing metatarsal bones and digits (D).

Fig. 2 Anteroposterior radiographs of the upper limbs showing normal features.

Fuhrmann's (fibular aplasia or hypoplasia, femoral bowing, and poly-, syn- and oligodactyly) and Al-Awadi/Raas-Rothschild syndromes (various degrees of limb aplasia/hypoplasia and joint dysplasia; OMIM #276820) are also said to be similar to FATCO syndrome.⁹ The genetic cause of FATCO and fibular agenesis with ectrodactyly is currently unknown and conflicting reports have been published concerning inheritance of these conditions. Although mutations in the *WNT7A* gene have been found to cause Fuhrmann's syndrome, it was excluded as a potential FATCO candidate gene.^{3,4}

The phenotypic data of individuals reported with FATCO show that this syndrome presents considerable clinical variability of limb malformations, which may reflect its underlying genetic heterogeneity. In all described cases, lower limb involvement of variable severity was reported whereas involvement of upper limbs was present in about two-thirds only and was bilateral in one-half.^{1,2,8} In the present case, the upper limbs were clinically and radiologically normal. As far the extraskeletal manifestations, all of the reported cases have shown similar findings, including normal mental development and lack of facial dysmorphism or other anomalies.^{2,3,8–10,13} This information is important in the genetic counseling offered to families.

Interestingly, the presence of femoral bowing in the present case has not been described before. From this perspective, it seems that our patient somewhat resembled Fuhrmann's syndrome. FATCO syndrome differs from Fuhrmann's syndrome in that previously reported cases did not manifest pelvic or femoral abnormalities. A straight femur characterizes FATCO syndrome, whereas skeletal abnormalities in Fuhrmann's syndrome include aplasia/hypoplasia of the ulnae, hypoplasia of the pelvis, aplasia/hypoplasia of the femora, fibulae aplasia, and variable digital abnormalities.¹⁴ However, none of the other manifestations of Fuhrmann's syndrome, such as postaxial polydactyly, hypoplasia of pelvis, congenital dislocation of hips or dysplastic nails, were present in our patient.

The parents were offered a detailed genetic counseling regarding the health consequences of their child's limb deficiency, the proposed modes of inheritance, and our recommendation for the follow-up of next pregnancies. They were then referred to a specialized orthopaedic team to discuss the available surgical therapeutic options and its outcomes.

In conclusion, we report a further case of FATCO syndrome manifesting bowing of the femora, which is considered among the features of Fuhrmann's syndrome and has not been previously reported in FATCO syndrome. The presented case highlights an extremely rare condition, and together with additional case reports, it could be helpful to further delineate this rare limb deficiency syndrome.

Funding

None.

Conflict of Interest

None.

Acknowledgment

The authors are grateful to the patient and her parents for their cooperation.

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