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Case Report

FATCO Syndrome with Infant of Diabetic Mother

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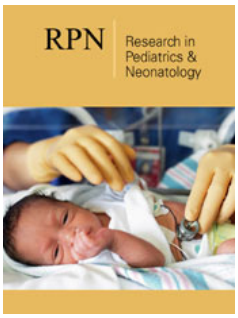

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Abstract

Fibular aplasia, tibial campomelia and oligosyndactyly (FATCO) syndrome (OMIM 246570) is an extremely rare syndrome first described by Hecht and Scott [1]. The etiology of the syndrome is currently unknown. This syndrome is commonly sporadic, but autosomal dominant inheritance has also been proposed. Although fibular aplasia is among the congenital malformations that develop due to diabetes, FATCO syndrome is a separate entity. In addition to the unknown genetic cause of this syndrome, which has typical findings, the mother's pregnancy and diabetes history should also be taken well. Corrective operations, physical therapy and regular development follow-up very important in these patients who do not have mental, cardiac and facial dysmorphism, requires multidisciplinary care.

Keywords: Campomelia; Fibular aplasia; FATCO syndrome; Infant of diabetic mother; Oligosyndactyly

Introduction

Fibular aplasia, tibial campomelia and oligosyndactyly (FATCO) syndrome (OMIM 246570) is an extremely rare syndrome first described by Hecht and Scott [1]. Courtens et al. [2], reported a further case and compare it with earlier four reports of similar conditions [1,3,4]. They proposed the name FATCO as all cases had fibular aplasia, tibial campomelia and oligosyndactyly in common. Individuals with FATCO showed 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. This syndrome is commonly sporadic, but autosomal dominant inheritance has also been proposed [5]. Previous reports have already excluded WNT7A as a potential FATCO candidate gene [6,7]. Mutations in WNT7A cause Fuhrmann syndrome (OMIM 228930) and the Al-Awadi/ Raas-Rothschild syndrome (OMIM 276820), characterized by various degrees of limb aplasia/hypoplasia and joint dysplasia [8]. Conflicting reports have been published concerning inheritance of fibular aplasia with ectrodactyly [9]. We report a 3 years old boy in the FATCO syndrome clinic born to mother with diabetes.

Case

We report a 3 year-old -boy with congenital lower limb deficiency. This deficiency consists of shortness of left leg, anterior bowing at the tibia, with associated overlying soft tissue dimpling, together with oligosyndactyly (4 toes) of the left foot. Both upper limbs and right leg are completely normal. He has neither dysmorphic facial features nor other associated anomalies. The patient was born at full term by elective Cesarean section after an uneventful pregnancy and delivery. He was the third-birth of a mother with diabetes. Birth weight, length, and occipital frontal circumference were 2520g. (<10th percentile), 49cm. (25th-50th percentile), and 35cm. (50th–75th percentile), respectively. Apgar scores were normal. The umbilical cord contained two arteries and a single vein. The first pregnancy of the mother

had been a spontaneous quadruplet pregnancy that had resulted in intrauterine death. A child born after the mother's second pregnancy was a 5-year-old girl in good health [10-17]. The father and mother were 33 and 32 years old, respectively, at the birth. There was no history of consanguinity, although the parents were born in the same small town, which has only about 20000 inhabitants. Family history was unremarkable. The mother had been using insulin for 7 years with the diagnosis of diabetes mellitus and had no history of alcohol, tobacco and exposure to radiation. The pregnant woman who has a follow-up did not have postnatal respiratory distress.

In the newborn physical examination, a difference in length was detected between two legs. Right leg: 18cm (right femur 8cm, right tibia 9cm), left leg: 13cm (left femur 7cm, left tibia 6cm) measured. Left leg was curved and there was a tibial dimple in the 1/3 proximal front side. There were 4 toes on the left foot, and cutaneous syndactyly was present in the second and third toes. Radiographic examination revealed complete absence of left fibula (fibular aplasia, FA type II), anterior bowing and shortness of left tibia (tibial campomelia) and absence of lateral rays of the foot (4 toes only-oligosyndactyly). No other abnormalities were detected on skeletal survey. External genital were normal. He had neither facial dysmorphism nor other associated anomalies. Systemic examination was normal, including fundal examination, auditory evoked potentials, cranial ultrasound examination and abdominal, renal, and cardiac examinations. There were no other associated anomalies. The second hour blood glucose was 46mg/dl. Insulin: 10μIU/mL. c- peptide: 2, 86. Mothers' HbA1c level: 8,33 and BMI was 37.1. Body blood sugar regulation of the patient was achieved with glucose infusion and increased oral intake. All values returned to normal in following controls.

Psychomotor development of the patient was appropriate for his age. He had head control at 2 months, sat up at 6 months, talk at 12 months, and walk at 14 months. The first correction surgery was performed at 21 months of age. The Denver developmental screening test was normal when he was 2 years old. Chromosomal analysis was (46,XY) normal. Other follow-up investigations were all normal, including laboratory examinations, eye fundus, auditory evoked potentials and abdominal renal and cardiac ultrasound examinations. The child is now 3 years, with normal mental development. The second operation was planned at the age of 4 years. The patient still does not have any active health problems other than short legs (Figure 1).

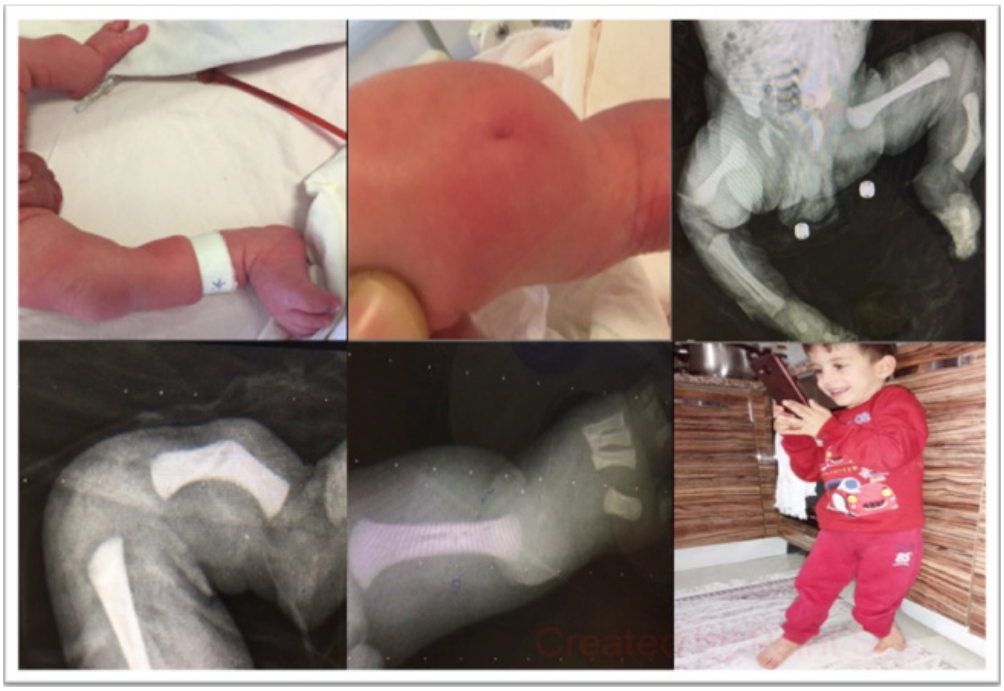

Figure1: Distinct length difference between two legs(A). left tibial dimple(B). X- ray: Congenital total absence of left fibula (C). X ray: Curved left tibia (campomelic) (D). X-ray: Agenesis of finger2 on the left foot (E). The patient still does not have any active health problems other than short legs (F).

Discussion

Congenital limb deficiencies are common birth defects, occurs in 1 in 2000 neonates and characterized by the aplasia or hypoplasia of bones of the limbs [18]. Fibula hemimelia (FH) is a rare congenital anomaly and was described by Gollier in 1698 [2,19]. This term encompasses a spectrum of disease from mild fibular hypoplasia to fibular aplasia. It has been estimated that there are 5.7 to 20 cases per one million births [20]. FH commonly occurs unilaterally, isolated. However it may be a part of a malformation syndrome. These components may include femur and tibia shortening, clubfoot, valgus deformity, flexion contracture, instability of knee and ankle, tarsal coalition with deficiency of lateral rays of the foot. Even though fibular hemimelia is rare among long bone deficiency disorders, it is the most common malformation [19].

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A rare congenital limb malformation syndrome characterized by the left fibular hypoplasia, the right fibular aplasia, tibial campomelia, and lower limb oligosyndactyly involving the lateral rays that was first defined by Hecht and Scott in [1]. Courtens et al. [2] reported on a male infant with oligosyndactyly of the left hand and the right foot, absence of right fibula, and anterior bowing of the ipsilateral tibia with associated overlying soft tissue dimpling and rewieved four other cases [1-4]. All of five cases had same three major findings that fibular agenesis, tibial campomelia and oligo-syndactyly, they proposed to name it Fibular Aplasia-Tibial Campomelia-Olygosyndactytly (FATCO) syndrome [6]. The cases previously reported by various authors had a great deal of phenotypic heterogeneity. We are presenting a phenotypic review of all the previously reported cases to date. A total of 18 cases have been reported to date (Table 1).

Table1: A total of 18 cases have been reported to date.

Reference	Sex	Upper Extremities	Lower Extremities	Others
Hecht and Scott [1]	Female	Oligosyndactyly of the left hand; absence of right hand	Tibial hypoplasia and bowed tibia with overlying skin dimple, absent left fibula 4-ray feet, normal femora and pelvis	Normal development
Capece et al. [3]	Male	Oligosyndactyly of right hand, both ulna-normal	Bowing of left tibia, absent fibula on left side, 4 metacarpals, fifth absent, clubfeet	Fetus at 24 weeks of gestation
Huber et al. [4]	Male	Oligosyndactyly	Tibia hypoplastic and bowed tibia with overlying skin dimple, absent fibula, oligosyndactyly, normal femora and pelvis	Normal development
Huber et al. [4]	Male	Normal	Tibia hypoplastic and bowed tibia with overlying skin dimple unilaterally, absent fibula, oligosyndactyly, normal femora and pelvis	Normal development
Courtens et al. [2]	Male	Oligosyndactyly of left hand, normal right hand, humerii ulnae and radii- Normal	Shortening and anterior bowing of the right lower limb at the distal third of tibia with associated overlying soft tissue dimpling, complete absence of fibula, normal femora	No facial dysmorphism, no other anomalies
Kitaoka et al. [6]	Male	Oligosyndactyly of right hand, both ulnae and humerii- normal	Tibia hypoplastic and bowed with overlying skin dimple, left fibular aplasia, right fibular hypoplasia, bilateral oligosyndactyly	Left cleft lip and palate
Karaman et al. [7]	Male	Normal	Oligosyndactyly of left foot, short angulated left leg associated with overlying skin dimpling, left fibular aplasia, left 3-ray foot	No heart defects, WNT7a mutation absent
Bieganski et al. [5]	Female	Oligosyndactyly of both hand, both ulnae and humerii- normal	Both tibia hypoplastic and bowed with overlying skin dimple, both fibular aplasia, right 3-ray foot, bilateral tarsal coalition, femora,pelvis-normal	İsolated membranous ventricular septal defect. Normal psycomotor development
Bieganski et al. [5]	Male	Bilateral two rays(U-shaped), left hypoplastic nail	Right fibular aplasia, left left fibular hypoplasia, both tibial anterior bowing of the distal one third with overlying skin dimple, bilateral 4-ray feet	Normal development
Bieganski et al. [5]	Male	Normal	Both tibia hypoplastic and bowed with overlying skin dimple,right 2-ray foot, left 3-ray foot.	Normal development
Ekbote et al. [11]	Male	Normal	Shortening of the left leg, with dimpling over the junction of the proximal 2/3 and distal 1/3. Left 3-ray foot. Right leg-normal	no facial dysmorphism or developmental delay
Izadi et al. [12]	Female	Normal	Right fibular aplasia, oligosyndactyly of right foot and mild short tibia	Fetus at 18 6/7 week at gestation
Sezer et al. [13]	Male	Right olygodactyly, left olygosyndactyly.	Bilateral fibular aplasia, tibial campomelia and 4-ray feet	Normal development
Smets et al. [14]	Female	Normal	shortening and anterolateral bowing of the left leg with overlying skin dimpling and oligosyndactyly of both feet.left 3-ray foot, right 4- ray foot.	Normal development
Goyal et al. [15]	Male	Normal	Shortening and anterolateral bowing of the left leg with overlying skin dimpling and oligosyndactyly of right feet	Normal development
Yılmaz et al. [16]	Female	Right hand had 5 fingers with a bigger third finger, left hand had duplication of fourth finger's distal phalanx	Anterolateral bowing of the left leg with overlying skin dimpling, Oligosyndactyly of left feet,	No facial dysmorphisim

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Vyskocil et al. [17]	Male	normal	Tibial campomelia and olygosyndactyly of left foot. Left 4-ray foot, left fibular aplasia	Normal development
Our case	male	normal	shortening and anterolateral bowing of the left leg withoverlying skin dimpling, olygosyndactyly of left foot, left 4-ray foot., left fibular aplasia	Normal development

Upper extremity involvement was present in 50% of patients, and 44% of those affected were unilateral. Skin dimpling and syndactyly in the lower extremity was present in all patients. There was unilateral involvement in the lower extremity at a rate of 55%. Fibular hypoplasia was detected in half of 18 patients. Except for the patient with cleft palate, none of them had facial dysmorphism [6]. The femur, pelvis, ulna, and radius were preserved in all patients. Mental and cardiac effects were not observed in any of the patients. The gene or genes responsible for the FATCO syndrome are not known yet. Most of the cases are sporadic. There was a definitive male predominance (14/18). There was no evidence of consanguinity in any of cases. Bieganski et al. [5] declined that it may be autosomal dominant and inherited X-linked inheritance because of male preponderance [5].

Single or double-sided fibular bone aplasia with tibial bone anomalies syndromes; Acheiropody, Chondrodysplasiacromelic-Genital anomalies Schinzel phocomelia and FATCO syndrome. Of the major components of FATCO syndrome: oligo syndactyly and tibial campomelia are not seen in Acheiropody and Chondrodysplasia Akromelik-Genital anomalies syndrome. Again, Fuhrmann syndrome and Al-Awadi syndrome are diseases with similar clinical features with two alleles and are differentiated by the involvement of pelvis, femur, radius and ulna, and nail deformities with oligo/polydactyly [21]. Fibula aplasia or hypoplasia is the most common long bone developmental defect seen often isolated. In etiology, non-genetic reasons are in place. These; exposure to radiation during pregnancy, cytotoxic busulfan drug use, retinoic acid use, and maternal diabetes mellitus [19].

Diabetes is an important medical condition affecting pregnancy. Gestational diabetes, which comprises approximately 80% of cases of diabetes in pregnancy [22]. Women with Type-1 diabetes who receive optimum pre-conception and antepartum care through a multidisciplinary antenatal clinic achieve a perinatal mortality rate equivalent to that observed in women who do not have diabetes in pregnancy [23]. In a recent study, an increased HbA1c level above 6.5% causes an increase in the prevalence of congenital anomalies, glycaemia and BMI are the key modifiable risk factors. There was no significant difference between type-1 and type-2 diabetes. In our case the mother had high HbA1c (8.82-8.33) and high BMI [24].

Our case is an infant of Diabetic Mother (IDM) but this is the first study with FATCO syndrome with IDM. Although fibular aplasia is among the congenital malformations that develop due to diabetes, FATCO syndrome is a separate entity. The goal of treatment for FATCO syndrome is to correct the leg length discrepancy and to functionally stabilize knee and ankle joints. Commonly accepted avenues of treatment include the use of an orthoses, epiphysiodesis, limb lengthening, and amputation with prosthesis [25]. In our case, he had first corrective surgery at the age of 21 months and his second operation was planned.

Conclusion

The FATCO syndrome is a rare genetic development limb disorder of the long bones with proposed autosomal dominant inheritance and so far has an unknown molecular basis. Chromosomal analysis should be performed in addition to the other investigations in patients with deformity and dysmorphism in selected cases where specific molecular diagnosis is not possible.

We know that diabetes causes congenital joint deformities, but this syndrome has been reported for the first time. In addition to the unknown genetic cause of this syndrome, which has typical findings, the mother's pregnancy and diabetes history should also be taken well. Corrective operations, physical therapy and regular development follow-up very important in these patients who do not have mental, cardiac and facial dysmorphism, requires multidisciplinary care.

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