Slovenian Medical Journal

FATCO syndrome (fibular aplasia, tibial campomelia, and oligosyndactyly) in newborn in Serbia – A case report

Sindrom FATCO (fibularna aplazija, tibialna kampomelija in oligosindaktilija) pri novorojenčku v Srbiji – prikaz primera

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Abstract

FATCO syndrome (Fibular aplasia, tibial campomelia, and oligosyndactyly) is a very rare malformation of an unknown genetic basis. It more commonly occurs in male children, and the lower extremities are more frequently affected. This is a case of a male newborn with the rare FATCO syndrome. It is the first child of healthy, unrelated parents. The pregnancy, being the first, was regular, monitored, and concluded with a cesarean section at 39 weekswithout any complications. The 33-year-old mother denies taking medication during pregnancy but reports having had COVID-19 in the fourth month of pregnancy. The newborn has normal upper extremities and the left lower extremity. The right lower extremity exhibits a shorter, curved lower leg with reduced circumference. A dimple is observed on the skin on the anterior side of the shin. There is a missing fifth toe on the right foot. Treatment involves a multidisciplinary approach and orthopedic-surgical corrections after birth to avoid varying degrees of disability.

Izvleček

Sindrom FATCO (fibularna aplazija, tibialna kampomelija in oligosindaktilija) je zelo redka razvojna nepravilnost, katere genetsko ozadje je neznano. Pogosteje se pojavlja pri otrocih moškega spola in pogosteje so prizadete spodnje okončine. Prikazan je primer novorojenčka moškega spola z redkim sindromom FATCO. Gre za prvega otroka zdravih nesorodnih staršev. Ta prva nosečnost je bila normalna, nadzorovana in se je končala s carskim rezom v 39. tednu brez kakršnih koli zapletov. Triintridesetletna mati zanika jemanje zdravil med nosečnostjo, navaja pa, da je v četrtem mesecu nosečnosti prebolela COVID-19. Novorojenček ima normalne zgornje okončine in levo spodnjo okončino. Desna spodnja okončina ima krajši, ukrivljen podkolenski del z zmanjšanim obsegom. Na koži na sprednji strani goleni je opazna vdolbina. Na desni nogi manjka peti prst. Multidisciplinarno zdravljenje vključuje ortopedsko-kirurško korekcijo po rojstvu, da se preprečijo različne stopnje invalidnosti.

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Key words: FATCO sy; fibular aplasia; oligosyndactyly; tibial campomelia

Ključne besede: FATCO sindrom; fibularna aplazija; oligosindaktilija; kampomelija golenice

Received / Prispelo: 25. 3. 2024 | **Accepted / Sprejeto:** 15. 10. 2024

Cite as / Citirajte kot: Kajevic A, Plojovic H, Detanac DS, Malicevic S, Kajevic A, Detanac AD, et al. FATCO syndrome (fibular aplasia, tibial campomelia, and oligosyndactyly) in newborn in Serbia – A case report. Zdrav Vestn. 2024;93(11–12):410–14. **DOI:** https://doi.org/10.6016/ZdravVestn.3531

1 Introduction

Congenital anomalies of the lower extremities fall into a group of rare and diverse inborn disorders. Limb deficiency can be defined as hypoplasia/absence of fingers, long bones, or a combination of both, and it is more commonly observed in the upper extremities (1). The overall prevalence of all types of limb deficiency is approximately 1 per 1000 live births (1). The incidence of fibular hemimelia, with or without associated anatomical abnormalities in the lower extremity, is very low, up to 20/million births (2,3). The condition is of unclear etiology, and can occur independently, most often as unilateral or as part of certain malformation syndromes.

According to Achterman and Kalamachi et al., fibular hemimelia can be present as minimal fibular hypoplasia (Type I) and absence of the fibula (Type II) (4). It can manifest as a part of various malformation syndromes, with FATCO syndrome being one of them (4).

Unilateral or bilateral fibular aplasia, tibial campomelia, and oligosyndactyly of the lower extremities constitute a rare syndrome, describing this condition observed in newborns, identified as FATCO syndrome (3,5).

Herein, we present a male newborn with malformations characteristic of FATCO syndrome.

2 Case presentation

We present a male newborn on the 1st day of life with the rare FATCO syndrome, born as the first child of healthy unrelated parents via cesarean section at 38 weeks of pregnancy, which transpired without complications. The 33-year-old mother denies taking medications and narcotics during pregnancy. This was her first pregnancy, and she was regularly monitored. There is no family history of diseases. The mother (previously unvaccinated) contracted COVID-19 infection in the 4th month of pregnancy (with mild clinical presentation), and there were no other obvious teratogenic exposures.

At birth, the infant weighed 3170 g, measured 56 cm in length, had a head circumference of 36 cm, and an APGAR score of 9 at 1st minute. On the first examination after birth, the newborn exhibited normal upper extremities and the left lower extremity, with a shorter right lower extremity (Figure 1). Absence of the fifth toe on the right foot, shortening, and reduced circumference of the right shin with a discrete skin dimple on the anterior side was noted. The right extremity was 2 cm shorter than the left one. Hypertelorism was also present (partially familial, observed in the mother as well) (Figure 2). Other findings were unremarkable.

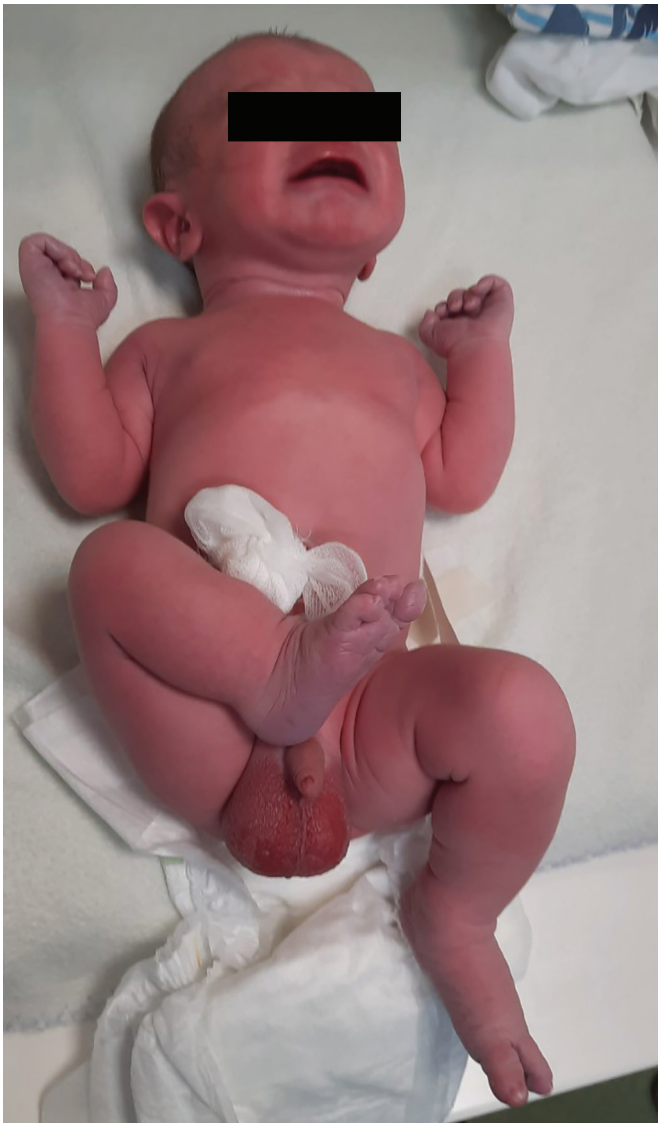

Figure 1: Male newborn at the first examination after birth. Source: Image is from the 1st author dr Almir Kajevic's archive.

Radiography of the right lower extremity revealed the absence of the right fibula with shortening of the right tibia and the absence of bones in the right foot (calcaneus, tarsal bones (all 5), fifth metatarsal bone, and corresponding phalanges of the fifth toe) (Figure 3). An echocardiographic examination detected a fissured defect with minimal left-to-right shunting in the central part of the interatrial septum (IAS). Upon a follow-up examination on the 7th day of life, closure of the defect was observed. Cranial and abdominal ultrasound showed normal findings. Laboratory test results were within normal ranges.

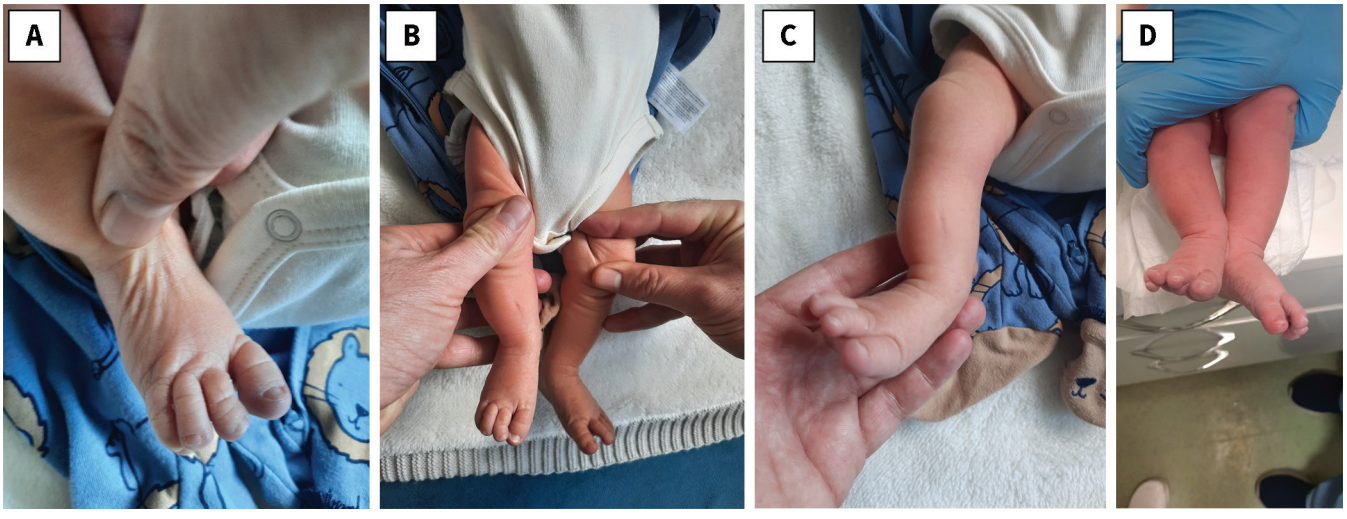

Figure 2: Finding at the first examination at birth (A,B,C,D).
Source: Image is from the 1st author dr Almir Kajevic's archive.

As part of the genetic investigation, clinical exome sequencing (CES) and whole exome sequencing (WES) with mitochondrial genome sequencing turned out negative. The parents were advised on the possibilities of orthopaedic treatment with further supervision by a paediatric orthopedist.

After discharge, further monitoring and treatment of the patient continued in a tertiary institution, on an outpatient basis, by a paediatric orthopedist. Treatment with physical exercises and orthopedic aids was started. An operation to lengthen the Achilles tendon and later,, tibia lengthening in an older child is planned.

The newborn was followed on an outpatient basis for 6 months in our hospital, after which the parents ceased bringing the child for follow-up examinations.

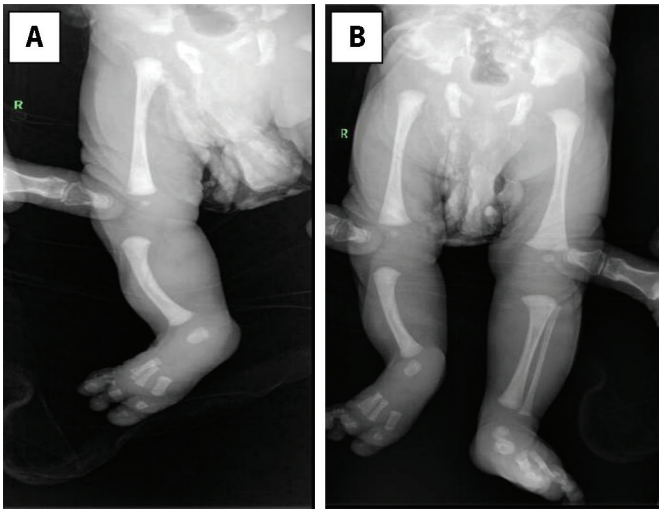

Figure 3: Radiography of the lower extremities (A and B).
Source: Image is from the 1st author dr Almir Kajevic's archive.

3 Discussion

FATCO syndrome in newborns is a very rare congenital disease of unknown aetiology, with an estimated prevalence of less than 1 per million births. Hecht and Scott first described this syndrome in 1981, but the name FATCO was proposed by Courtens et al. in 2005, describing the syndrome with fibular aplasia, tibial campomelia, and oligosyndactyly (6,7). According to the literature available to us, 43 cases of FATCO syndrome have been reported worldwide so far, and no consistent genetic cause has been identified (8). As far as we know, this is the first case published in Serbia.

Sifre-Ruiz et al. state that among the published cases so far, about two-thirds of patients with FATCO syndrome were male. Considering the malformations characteristic of FATCO, changes more commonly affect only the lower extremities, often occurring unilaterally, slightly more on the right side. As for the upper limbs, only the hands were affected in 39.5%, and bilateral involvement of both extremities was reported in ten cases (8). The cause of FATCO syndrome is still unknown (3-6,8). The genetic basis of this disease remains unclear. Due to similarities with some other syndromes (Furhmann syndrome and Al-Awadi syndrome), genetic testing was performed in some patients with FATCO syndrome for possible gene mutations, including WNT7a, TP63, and WNT10B. However, no mutations were found (4-9). Due to male predominance, some authors

have suggested that FATCO syndrome is X-linked. Further tests are needed to shed light on the genetic background of this pathology in the future (5-10).

Our case report involves a male newborn from a regular pregnancy with a multifactorially induced musculoskeletal anomaly of the right shin and foot. Genetic testing yielded negative results.

Children with FATCO syndrome usually have normal mental development, mainly with no facial dysmorphism or other anomalies. In some previously published cases, other associated anomalies were described, such as micrognathia, tracheo-esophageal fistulae and esophageal atresia (9), cleft lip (5), spina bifida occulta (8), brachycephaly (1), Klinefelter syndrome (11). In our patient, hypertelorism is present (also observed in the mother), and in the central part of the interatrial septum (IAS), a fissured defect with minimal left-to-right shunting was detected, which spontaneously closed by the seventh day of life. Other findings were unremarkable.

The diagnosis of FATCO syndrome is usually made at birth, but prenatal diagnosis is possible, as confirmed by Izadi M et al. in the first prenatally diagnosed FATCO syndrome (4).

Any infection during pregnancy carries the risk of complications. Congenital viral infections can cause death, multisystem organ damage, sepsis, and permanent disability in newborns. Data from the literature show that newborns whose mothers tested positive for COVID-19 during pregnancy can have these problems (12). It is also stated that neonates of mothers with positive COVID-19 had a comparable risk of malformations compared to those of mothers without COVID-19 (12). Molnarova et al. indicate in their study the possibility of the influence of COVID-19 infection during pregnancy on the formation of non-syndromic orofacial clefts (13). There are also studies such as Popescu DE et al., which found no correlations between COVID-19 infections during pregnancy and neonatal heart, brain, and kidney damage, as well as auditory or visual function (14). Hernández-Díaz et al. stated in their study that there is no evidence of a major teratogenic effect associated with maternal SARS-CoV-2 infection during the first months of pregnancy, but also stated that larger studies are needed to confirm the conclusions (15).

Because there are discrepancies in published studies regarding the impact of COVID-19 infection during pregnancy on fetal damage, all of this points to the complex nature of the viral impact on the health of newborns as well as the importance of other factors.

Given that in our case report, the mother had COVID-19 during pregnancy, with a mild clinical picture, this infection cannot be linked with certainty to malformation in the child.

The therapeutic approach to these patients should be individualized and customized to each specific patient. The main principle is the preservation and elongation of shorter limbs for their equalization, which can be achieved through surgical correction or by means of prosthetics. Surgical amputation with early prosthetic use should be considered in cases with a non-functional foot and a high degree of shortening at birth compared to the expected length (16-18).

4 Conclusion

FATCO syndrome is a rare disorder and poses challenges for both parents and the child. Treatment involves a multidisciplinary approach and surgical corrections after birth to prevent various degrees of disability. Therefore, adequate prenatal diagnostics, parental counselling, and preparation for what awaits them upon the child's birth are integral components of the treatment.

Conflict of Interest

None declared.

Funding

No.

Author contribution

All authors have contributed equally.

Inform consent of the parent

The parent of a case patient signed the informed consent form for the publication.

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