

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: <http://www.elsevier.com/locate/medici>

Case Report

Bilateral cleft foot: Radiographic and prenatal ultrasound features of two siblings with a review of literature

Mehmet Sedat Durmaz^a, Hakan Demirtaş^{b,*}, Salih Hattapoğlu^c, Taylan Kara^d, Cemil Göya^c, Mehmet Emin Adin^c

^aDepartment of Radiology, Konya Training and Research Hospital, Konya, Turkey

^bDepartment of Radiology, Medicine Faculty, Süleyman Demirel University, Isparta, Turkey

^cDepartment of Radiology, Medicine Faculty, Dicle University, Diyarbakır, Turkey

^dDepartment of Radiology, Medicine Faculty, Mersin University, Mersin, Turkey

ARTICLE INFO

Article history:

Received 26 January 2016

Received in revised form

29 May 2016

Accepted 12 July 2016

Available online 26 July 2016

Keywords:

Cleft foot malformation

Fetal foot

Obstetric ultrasound

Prenatal diagnosis

ABSTRACT

Cleft foot deformity, also known as ectrodactyly, is a rare congenital developmental defect of extremities caused by malformation in continuity of apical ectoderm. The syndrome typically involves malformation or absence of the central rays of the feet and is characterized by deformities like median deep clefts of distal extremities. Routine examination of feet during second-trimester ultrasound (US) may increase the detection rates of foot malformations. Many malformations can be diagnosed with 2-dimensional (2D) US, but 3-dimensional (3D) US also helps better understanding of the foot malformations. In the present study, we report the case of two brothers (a fetus and a 5-year-old) with cleft foot deformity. 2D and 3D second trimester US findings of one case and the foot radiography findings of the other are presented here.

© 2016 The Lithuanian University of Health Sciences. Production and hosting by Elsevier Sp. z o.o. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

1. Introduction

Congenital cleft hand/foot deformity is a rare anomaly with an incidence of 1/90,000 [1–3]. The deformity is usually bilateral.

Cleft foot–hand cases are characterized by congenital deficiency of one or more than one rays including the central ray, sometimes together with metacarpals and metatarsals [4,5]. Various studies suggest that a cleft hand and a cleft foot coexist in about a quarter to a half of the cases [2,5]. The

* Corresponding author at: Department of Radiology, Medicine Faculty, Süleyman Demirel University, East Campus, Çünür 32260, Isparta, Turkey.

E-mail address: demhakan@yahoo.com (H. Demirtaş).

Peer review under the responsibility of the Lithuanian University of Health Sciences.



Production and hosting by Elsevier

<http://dx.doi.org/10.1016/j.medici.2016.07.003>

1010-660X/© 2016 The Lithuanian University of Health Sciences. Production and hosting by Elsevier Sp. z o.o. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

anomaly can appear either as an isolated entity or as part of a genetic or non-genetic syndrome [6]. The most typical one of these syndromes is ectrodactyly, the ectodermal dysplasia of cleft lip/palate (EEC) [7].

The severity of cleft hand-foot deformities varies and in severe cases, the hands and feet have a lobster claw-like appearance [8]. Clinical diversity can occur not only between patients, but between the hands and feet of the same patient. This deformity is accompanied by syndactyly, oligodactyly and rarely polydactyly [6]. The brothers reported in the present study had cleft foot deformities and polydactyly accompanied by these deformities, the findings of the cases were the same. Chromosome analysis of the fetus showed was normal findings, and the parents and parents' family had no history of cleft foot. In the present report, findings of two cases with cleft foot deformity are described and discussed in the light of current literature in English.

2. Case reports

2.1. Case 1

A 26-year-old gravida two para one healthy pregnant woman underwent an US scan for routine screening of fetal anomaly in second-trimester. The obstetric US (Voluson 730 Pro, GE Healthcare, Milwaukee, WI, USA) was performed in B mode

using 2D and 3D transducers. The case was initially evaluated and diagnosed with 2D US. 3D US helped better topographic understanding of the feet deformities. The detailed 2D gray-scale US scan revealed a medial opening in the first two metatarsal bones towards the third metatarsal bone, and a lateral opening in the fourth and fifth metatarsal bones. The first, fourth and fifth toes of the right foot, and the first and fifth toes of the left foot and their phalanges were present. A fusion was observed between the fourth and fifth toes of right foot. No phalanges were observed in the second and third toes of the right foot, and the second, third and fourth toes of the left foot, and a bilateral wide V-shaped cleft was noticed at this level (Fig. 1a and b). Additionally, a little sixth finger attached to the distal portion of right thumb was noted (Fig. 1c).

Findings were confirmed by 3D US. One toe both in the bilateral medial and lateral were present in the foot and a V-shaped deep cleft was observed between them (Fig. 2a-c). The fetal movements including ankle and knee were normal on Four-D US examination. No additional fetal sonographic pathologies were evident at this time. Two weeks later, fetus was lost at 24-week of gestation. Cytogenetic analysis cordocentesis revealed normal karyotype.

2.2. Case 2

It was understood from the patient's history that the patient had a 5-year-old son with bilateral foot anomaly. The 5-year-old



Fig. 1 – Bilaterally split feet in a 22-week fetus. 2D sonograms of the right and left foot show absence of central phalanges, and metatarsal bones show a medial and lateral angulation, V-shaped cleft with syndactyly (a) and (b). A sixth finger (polydactyly) that is adjacent to the thumb of the left hand and fused with the thumb is observed (c).

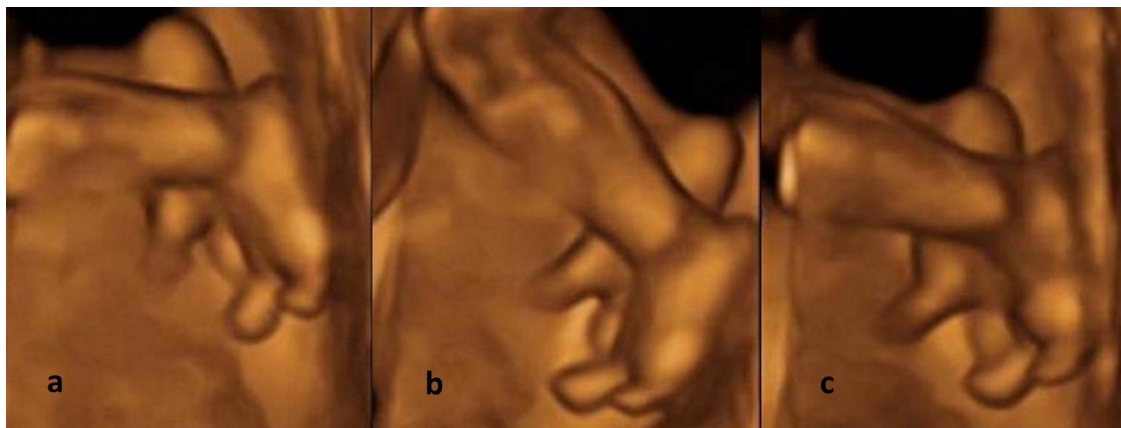


Fig. 2 – 3D sonograms of both feet indicating V-shaped clefts.

boy was invited to the hospital for examination. Direct foot radiography depicted a bilateral deep cleft. The right second and third toes were absent along with their phalanges. The left second, third, and fourth toes and their phalanges were not observed as well. The metatarsal bones were bilaterally present. The metatarsal bones of third, fourth, and fifth toes showed a lateral angulation as opposed to a medial angulation in the second toe. The distal portion of the left third metatarsi was absent. The phalanges of the first, fourth and fifth toes of the right foot, and phalanges of the first and fifth toes of the left foot were present. The fourth and fifth toes of the right foot were observed to be adjacent. Bilateral medial cuneiforms and intermediate cuneiforms were markedly small (Fig. 3a and b). An extra sixth finger attached to the thumb of the right hand was also noted. A surgery history and postoperative appearance due to fused third and fourth fingers of the right hand was evident (Fig. 3c). General and systemic physical examination was normal except for the hand and feet abnormalities. The patient had no other dysmorphic features and his anthropometric measurements were within the normal limits. The patient had not received any medical treatment or intervention for cleft feet. The patient had no walking problems. The ankle and hind foot had normal appearance and movement.

There was no family history of cleft foot or other genetic abnormality in parents and their close families. Chromosome analysis of the fetus showed normal findings, and findings identified in the brother-two cases were literally similar. The family was referred to the Pediatric Department to receive effective genetic counseling for current pregnancy and possible future pregnancies.

3. Discussion

Cleft hand-foot deformity is a rarely seen malformation involving central structures of hands and feet. It can affect a single extremity or distal limbs of all extremities. The deformity is usually bilateral and may be associated with other anomalies. Various studies reported the frequency of this malformation to be between 1/90,000 and 1-9/100,000 [2,3,9]. Historically, these anomalies were named as ectrodactyly or lobster claw-like malformation due to their

appearance in severe cases. The term cleft-hand was also used for partial terminal aplasia. Today, the condition is rather known as split hand-foot [5].

Cleft hand-foot deformity can be observed both as an isolated deformity and as part of a syndrome. More than 50 syndromes associated with this malformation are listed in the London Dysmorphology Database [6,10]. The most common and best known of these syndromes is EEC. The syndrome is characterized by ectrodactyly, ectodermal dysplasia and cleft lip/palate. Apart from these, naso-lacrimal duct obstruction, urogenital abnormalities, conductive hearing loss and mandibulofacial dysostosis can also be seen in EEC. Cleft foot is usually inherited as an autosomal dominant trait, although sporadic cases have been reported [7]. The malformation in two brothers reported here was isolated, with no associated syndromes and pathological findings other than the hand deformity secondary to prior surgery on older brother. Cytogenetic analysis after cordocentesis of the fetus at 22nd week of gestation revealed a normal karyotype. No additional sonographic findings were detected in the fetus except for cleft foot and polydactyly.

Incomplete autosomal dominant inheritance has been described for most of the cases with history of familial inheritance. Moreover, it has been suggested that autosomal dominant inheritances may also be associated with germinal mosaicism [8]. Autosomal recessive and x-linked recessive inheritance is seen mostly in syndromic patients [9]. A great majority of isolated forms and some of syndromic cases are associated with chromosomal fractures in the 7q21 (SHFM 1), Xq26 (SHFM 2), 10q24 (SHFM 3), and 3q27 (SHFM 4) region [6]. DYNC111, 17p13.3, 10q24 and TP63 genes also were found to be associated with this malformation [4]. Deletions of the exons of DYNC111 (3%), 17p13.3 duplications (13%), 10q24 duplications (12%) and TP63 mutations (4%) were detected in 134 unrelated families with cleft hand-foot deformity [4]. Similar malformations in two siblings reported here suggest familial inheritance. However, no detailed genome mapping was done for older brother and his parents. Chromosome analysis performed for the fetus was normal and XY male genotype was detected.

Severity of cleft hand-foot deformities varies. Clinical diversity can occur not only between patients, but between

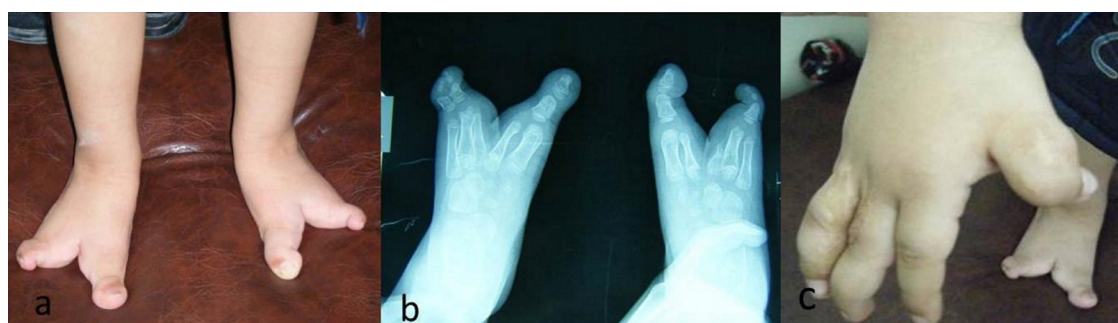


Fig. 3 – A wide, deep cleft in the feet and polydactyly-affected right hand of a 5-year-old patient. The photograph of the feet (a). The foot radiography showing two adjacent toes in the right foot, one toe in the medial of the right foot, and a deep cleft between them and one toe in the medial and lateral of the left foot and a deep cleft between them. Phalanges of the first, fourth and fifth toes of the right foot and only the first and fifth toes of the left foot are present (b). Postoperative appearance of the patient who underwent surgery due to polydactyly in the thumb of the right hand and fusion in the third and fourth fingers of the right hand (c).

hands and feet of the same patient [6]. The fact that deformity is isolated or syndromic does not affect the clinical diversity. This deformity is accompanied by syndactyly, oligodactyly and rarely polydactyly. In our cases, we observed that cleft foot malformation is accompanied by polydactyly in both brothers. We detected polydactyly in the fetus sonographically. We were informed that the five-year old brother had undergone surgery for polydactyly, and we showed postoperative appearances of this 5-year-old patient.

Prenatal diagnosis of cleft hand-foot malformations can be established from the first trimester [11,12]. Various cases reported to be prenatally diagnosed between 12th to 30th week of gestational ages [11,13]. Early diagnosis potentially allows for elective termination, leading to a lower risk of complications, shorter duration of hospitalization, and reduced health care-related costs. Early diagnosis is also important in pregnancies in which the families elect to carry the fetuses to term, allowing delivery planning for associated anomalies that may require special care as well as providing the families with time to be prepared psychologically [13]. In our case, we established the diagnosis when the fetus was 22 weeks when the patient was referred to our radiology department for routine organ scan due to failure by the patient to receive genetic counseling, although the patient had a 5-year-old boy diagnosed previously. However, if the patient had taken an advantage of effective genetic counseling because her first child had split-foot malformation, the diagnosis could have been established earlier in the first trimester. There are studies demonstrating that 3D US is more effective in detecting and showing extremity anomalies in addition to gray-scale [13-15]. We also performed 3D US along with gray-scale scan to better demonstrate the detailed findings.

Rates of pregnancy loss decrease as the pregnancy progresses. Approximately 6% to 8% of pregnancies are lost at 8 to 11 weeks' gestation, whereas stillbirth occurs in 0.3% of pregnancies at 20 to 27 weeks' gestation. Recurrent first trimester losses, fetal malformation and painless rupture of membranes are located in the upper row according to the frequency. Fetal malformation should be considered in second trimester pregnancy loss like our case.

The differential diagnosis of a cleft foot includes brachydactyly, oligodactyly, clinodactyly, hypoplastic middle or distal phalanges, hypoplastic or absent terminal phalanges, symphalangism, and deformed thumbs and big toes [13]. These deformities can be difficult to detect by prenatal US. However, diagnosis and differentiation is easier when 3D US is used together with 2D US. 3D US has enabled to detect fetal foot anomalies more accurately. 3D US provided additional information compared to 2D US. Careful examination over time is required for differentiating foot anomalies, motion seen on real-time imaging may also be helpful [13].

In general terms, surgical treatment for cleft hand-foot aims to provide patients an efficient holding and gripping function and eliminating gait disorders, walking pains and ensuring that patients wear shoes without problem [16]. However, young and adult patients with cleft hand and foot anomalies are usually concerned about appearance rather than function. Therefore, extremities should also be addressed in terms of esthetics and should be improved to the extent possible [5]. No surgery for cleft foot was considered for the

five-year old patient since he did not have any walking problems, but he had a prior surgery for fusion and polydactyly in the third and fourth fingers of the right hand.

4. Concluding remarks

It should be noted that cleft hand-foot deformities have a wide variety of spectrum, and could either be isolated or associated with other syndromes. Diagnosis of cleft hand-foot deformities can be established by prenatal sonographic examination. It should be known that 3D US is effective in prenatal diagnosis of this malformation. Hands and feet should be scanned for this anomaly during routine second-trimester examination. Detailed examination of the fetal feet and hands is an important component of US evaluation of fetuses with congenital anomalies, and of those at risk of chromosomal abnormalities. This routine has been increasingly incorporated into detailed second-trimester US examination of pregnant women who have children with cleft hand-foot deformities. When this anomaly is detected, prenatal counseling should be offered and genetic screening should be performed for all couples for present and possible future pregnancies.

Conflict of interest

The authors declare that they have no conflict of interest.

REFERENCES

- [1] Basel D, Kilpatrick MW, Tsipouras P. The expanding panorama of split hand foot malformation. *Am J Med Genet A* 2006;140:1359-65.
- [2] Barsky AJ. Cleft hand: classification, incidence and treatment. *J Bone Joint Surg* 1964;46:1707-20.
- [3] Blauth W, Borisch NC. Cleft feet. Proposals for a new classification based on roentgenographic morphology. *Clin Orthop* 1990;258:41-8.
- [4] Tayebi N, Jamsheer A, Flöttmann R, Sowinska-Seidler A, Doelken SC, Oehl-Jaschkowitz B, et al. Deletions of exons with regulatory activity at the *DYNC111* locus are associated with split-hand/split-foot malformation: array CGH screening of 134 unrelated families. *Orphanet J Rare Dis* 2014;9(July):108.
- [5] Okur MI, Yıldırım MA, Köse R. Congenital cleft hand and foot: review of the literature and report of two cases. *Firat Med J* 2004;9(1):23-7.
- [6] Duijf PH, van Bokhoven H, Brunner HG. Pathogenesis of split-hand/split-foot malformation. *Hum Mol Genet* 2003; Spec No 1(12):R51-60.
- [7] Sharma D, Kumar C, Bhalerao S, Pandita A, Shastri S, Sharma P. Ectrodactyly, ectodermal dysplasia, cleft lip, and palate (EEC Syndrome) with tetralogy of fallot: a very rare combination. *Front Pediatr* 2015;3(June):51.
- [8] De Smet L, Devriendt K, Fryns JP. Further evidence for germinal mosaicism in cleft hand/cleft foot syndrome. Two affected half sisters and normal father. *Genet Couns* 2001;12:251-4.
- [9] Kalathia MB, Seta AA, Parmar PN. A case of ectrodactyly in a neonate. *J Clin Neonatol* 2013;2(July (3)):151-2.

- [10] Winter RM, Baraitser M. The London dysmorphology database. *J Med Genet* 1987;24:509-10.
- [11] Haratz-Rubinstein N, Yeh MN, Timor-Tritsch IE, Monteagudo A. Prenatal diagnosis of the split hand anomaly: how early is early? *Ultrasound Obstet Gynecol* 1996;8(July (1)):57-61.
- [12] Gonzalez-Ballano I, Savirón-Cornudella R, Alastuey-Aisa M, Garrido-Fernández P, Lerma-Puertas D. Split hand-foot: sonographic detection at 12 weeks. *Ginecol Obstet Mex* 2014;82(July (7)):490-5.
- [13] Lu J1, Vaidya N, Meng H, Dai Q, Romine LE, Jones MC, Pretorius DH. Prenatally diagnosed fetal split-hand/foot malformations often accompany a spectrum of anomalies. *J Ultrasound Med* 2014;33(January (1)):167-76. <http://dx.doi.org/10.7863/ultra.33.1.167>
- [14] Hata T, Aoki S, Akiyama M, Yanagihara T, Miyazaki K. Three-dimensional ultrasonographic assessment of fetal hands and feet. *Ultrasound Obstet Gynecol* 1998;12:235-9.
- [15] Ploeckinger-Ulm B, Ulm MR, Lee A, Kratochwil A, Bernaschek G. Antenatal depiction of fetal digits with three-dimensional ultrasonography. *Am J Obstet Gynecol* 1996;175:571-4.
- [16] Tani Y, Ikuta Y, Ishida O. Surgical treatment of the cleft foot. *Plast Reconstr Surg* 2000;105:1997-2002.