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Case Report / Olgu Sunumu

Prenatal diagnosis of Apert syndrome: a case report

Apert Sendromunun prenatal tanısı: olgu sunumu

Kubra Boynukalin[1,1], Cem Baykal[2], Oguzhan Dolar[3], Nahit Ozcan[4]

[1]Anatolia Women's Health and Infertility Clinic, Ankara; [2]Department of Obstetrics and Gynecology, Florence Nightingale Hospital, Istanbul; [3]Department of Pediatrics, Camlıca Erdem Hospital, Istanbul; [4]Sonomed Radiologic Imaging Center, Istanbul

Abstract

Apert syndrome is characterized by craniosynostosis, midfacial hypoplasia and symmetric cutaneous and bony syndactily of the limbs. We report a rare case of Apert syndrome with cloverleaf skull deformity, prenatally diagnosed at 20 weeks' gestation in which the ultrasonographic features of a characteristic trilobed skull shape, abnormal biparietal diameter and head circumference, as well as malformations of the all extremities confirmed the diagnosis. Our case demonstrates the possibility of prenatal diagnosis of Apert syndrome with cloverleaf skull using ultrasound.

Keywords: Craniosynostosis, Apert syndrome, syndactily, prenatal diagnosis

Özet

Apert sendromu, kraniosinositoz,midfasial hipoplazi ve ekstremitelerde simetrik kutenöz ve kemik sindaktili ile karakterizedir. Bu makalede nadir görülen bir sendrom olan Apert Sendromunun 20. haftada yapıln detaylı ultrasonografik değerlendirmede saptanan trilobule kafa şekli, anormal biparietal çap ve kafa çevresi e aynı zamanda belirlenen ekstremite malformasyonları ile konulan tanısından bahsedilmektedir.

Anahtar sözcükler: Kraniosinostozis, Apert sendromu, sindaktili, prenatal tanı

Introduction

Apert syndrome is characterized by the triad of coronal craniosynostosis, midfacial hypoplasia, and bony syndactily of the hands and feet. The prevalence of Apert syndrome at birth is estimated to be 1 in 160,000 to 1 in 164,500 [1]. It has an autosomal dominant

[1] Corresponding author:
Dr. Kubra Boynukalin, Anatolia Women's Health and Infertility Clinic, Ankara.
Email: drkubraboynukalin@yahoo.com.tr

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mode of inheritance but most of the cases are sporadic, as a result of a de novo mutation [2]. Advanced paternal age can be a risk factor [3]. Although it is difficult to visualize, the affected fetus can be detected by ultrasound in the second trimester. Various nonspecific ultrasonographic findings have been reported in the literature, many of which lead to a more detailed examination that detects the specific triad of features. Apert syndrome can be associated with a variety of visceral malformations. Cardiovascular and genitourinary anomalies are found most commonly [4]. Molecular tests that evaluate 2 recurrent missense mutations of the fibroblast growth factor receptor 2 gene (FGFR2) involving 2 adjacent amino acids (S252W and P253R) are used to confirm the diagnosis [5, 6]. We report a case of prenatally diagnosed craniosynostosis.

Case

A 27 year old, gravida 1 woman was referred to our clinic for first trimester screening for Down syndrome (nuchal translucency (NT) combined with maternal biochemistry including PAPP-A, and hCG). Ultrasound at 12 weeks of gestation revealed vanishing twin. There was a fetus with a crown rump length (CRL) measured as 8 weeks and 4 days but no fetal heart beat in the first gestational sac and in the second sac there was a fetus with a crown rump length (CRL) measured as 12 weeks fetal heart beat was positive. Combined test was not performed because the presence of a vanishing twin may lead to errors in risk estimation. Down syndrome screening was restricted to NT and found as 2 mm.

At 20 weeks of gestation routine second trimester ultrasound for possible detection of fetal anomalies was performed. Examination of the fetal cranium revealed ventriculomegaly (Figure 1a). The skull showed the trilobed shape of a cloverleaf deformity, hypertelorism, depressed nasal bridge, frontal bossing (Figure 1b) and a fairly wide metopic suture caused by synostosis of coronal sutures was present on lateral view of the face. There was hyperecogenic fetal cardiac focus but structural cardiac deformity was not detected. Fetal stomach was viewed smaller than as usual. Bilateral hydronephrosis was also detected. There seemed to be syndactily of the digits of both the hands and feet on the examination of the extremities. (Figure 2) And also clenched hands were present. Trisomy 18 was highly suspected. Amniocentesis was performed at 20 weeks of gestation. Cytogenetic analysis revealed a 46, XY karyotype. The parents were informed that the findings were suggestive of Apert syndrome and counseled about the option of termination. But they did not accept this option.

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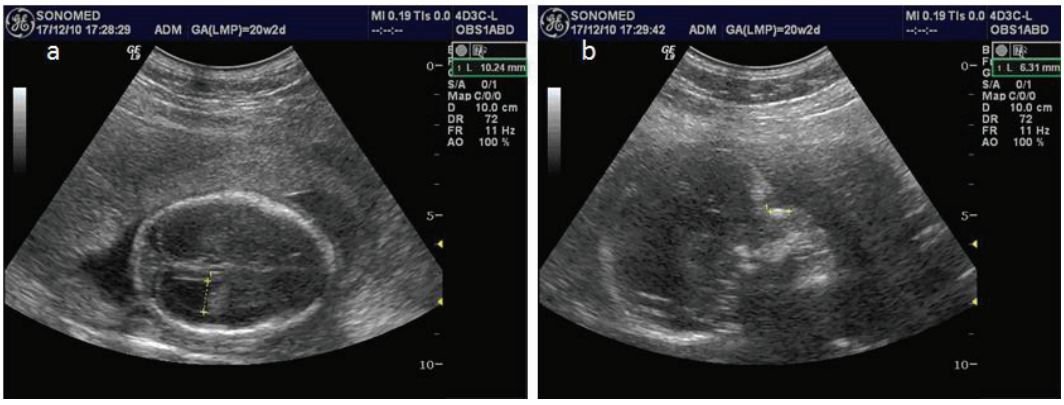

Figure 1. a. A representative picture of bilateral ventriculomegaly. b. Frontal bossing detected by ultrasonography.

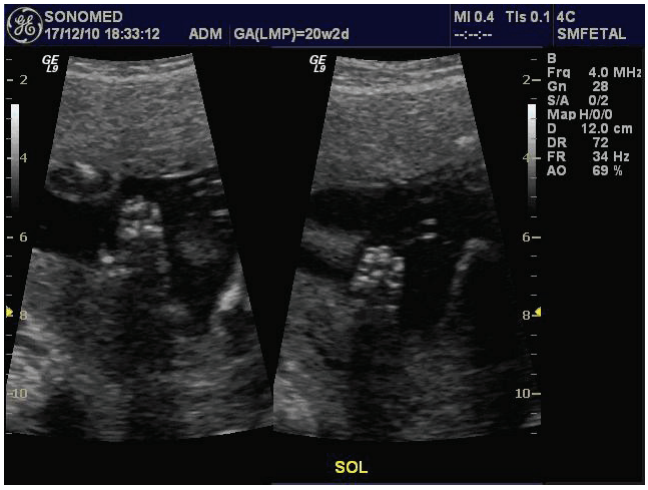

Figure 2. Ultrasonographic image representing syndactily.

Fetus was delivered by elective cesarean section at term in the 39th gestational week. Postpartum, the first evaluation of the newborn (3280 g) revealed that bilateral choanal atresia was present. The classic signs of Apert syndrome, including malformations of the skull and extremities, were obvious after birth (Figure 3). Male baby was evaluated by neonatologists and neurosurgeons and an immediate surgery was planned for choanal atresia. Baby was followed up in neonatal intensive care unit for 4 weeks with a gastrostomy tube placed for nutrition and successfully operated for choanal atresia thenafter. The patient will return at 2 months of age for cranioplasty and possible ventriculoperitoneal shunting. Hand reconstruction will begin at 6 months of age. Molecular analysis of missense mutations of the fibroblast growth factor receptor 2 gene (FGFR2) was confirmed the diagnosis.

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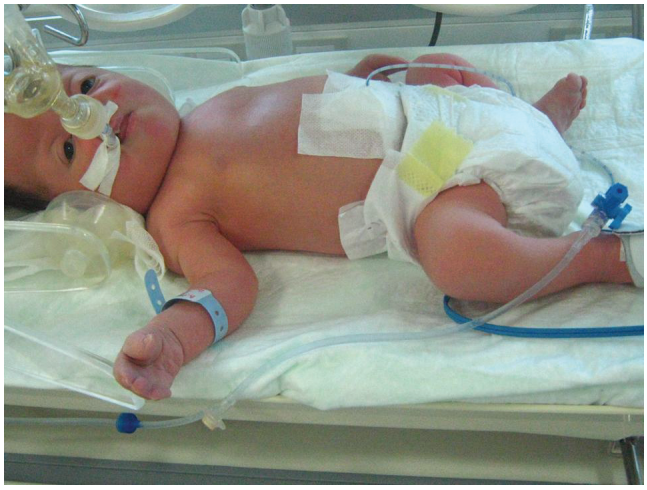

Figure 3. Picture of the baby after delivery.

Discussion

Prenatal ultrasonographic detection of craniosynostosis is usually straightforward in late gestation because craniofacial deformities become more evident and also differential diagnosis of the craniosynostosis syndromes may be very difficult, due to overlapping morphologic features. Syndromes involving craniosynostosis may be associated with abnormalities of the digits. Crouzon syndrome is associated with normal hands and feet. Jackson-Weiss syndrome is associated with normal hands, medially deviated broad great toes and cutaneous syndactily of the second and the third toes. Apert syndrome is associated with symmetric syndactily of the hands and feet. Pfeiffer syndrome is associated with broad abducted thumbs, broad great toes, and brachymesophalangy and partial syndactily of the hands and feet [7]. Differential diagnosis of the craniosynostosis syndromes can be done by using two- and three- dimensional ultrasound in the second trimester. The confirmation of the diagnosis is by amplification of the FGFR gene in fetal DNA samples.

In the present case, prenatal ultrasonographic diagnosis of Apert syndrome was based upon detection of the characteristic triad of symmetrical syndactily in the hands, midfacial hypoplasia and abnormal cranial shape. Visseral abnormalities such as ventriculomegaly were detrimental for the differential diagnosis of the craniosynostosis syndromes. Chromosomal analysis was performed antenatally, genetic analyses was performed postnatally. Though the karyotype of patients with Apert syndrome is usually normal, rare cases with chromosomal anomalies have been reported and thus, prenatal chromosomal analysis is necessary [8].

Perinatalogy specialists should inform parents that there is increased risk of mental retardation and multiple postnatal operations might be needed, due to cranial and limb malformations. Termination of the pregnancy can be an option for these fetuses.

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Conflict of Interest

The authors declare that there is no conflict of interest.

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