Prenatal diagnosis of frontonasal dysplasia with anterior encephalocele

Anterior ensefaloselin eşlik ettiği frontonazal displazinin prenatal tanısı

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Abstract

Frontonasal dysplasia is a rare congenital anomaly affecting the eyes, nose and forehead, and occurs sporadically in most of the cases. A 24-year-old woman was referred to our unit at 27 weeks gestation due to the preliminary diagnosis of encephalocele. The sagittal and axial sonography of the fetal face depicted a midline mass measuring 3.8 x 4.2 cm, projecting anteriorly between the fetal orbits and extending from the the upper aspects of the forehead to the nasal bridge, which was consistent with the frontal (anterior) encephalocele. There were prominent hypertelorism and two facial clefts, and the nostrils were extremely separated. Following genetic counseling, the couple requested termination of pregnancy. Fetal pathologic examination confirmed the diagnosis of frontonasal dysplasia and anterior encephalocele with no additional major malformation. The fetal karyotype was normal and no mutation in the ALX1 gene was found, excluding ALX1-related frontonasal dysplasia in the differential diagnosis. Fetuses with neural tube defect may suffer from associated syndromes and disorders, as with our case. The presence of frontonasal dyplasia should be considered when an anterior encephalocele is detected by ultrasonography. (J Turkish-German Gynecol Assoc 2013; 14: 50-2)

Key words: Frontonasal dysplasia, anterior encephalocele, prenatal diagnosis, ultrasound, congenital anomaly

Received: 30 July, 2012 **Accepted:** 22 August, 2012

Özet

Frontonazal displazi gözleri, burnu ve alnı etkileyen nadir bir konjenital anomalidir ve çoğunlukla sporadik olarak meydana gelir. 24 yaşındaki bir kadın 27. gestasyonel haftada ensefalosel ön tanısıyla kliniğimize refere edildi. Fetal yüzün sagital ve aksiyal ultrason kesitlerinde 3.8 x 4.2 cm büyüklüğünde, fetal orbitaların arasından öne doğru bir çıkıntı oluşturan ve alnın üst kısmından burun köküne kadar uzanan frontal (anterior) ensefalosel ile uyumlu orta hat yerleşimli bir kitle saptandı. Belirgin hipertelorizm ve iki tane fasiyal kleft mevcuttu ve burun delikleri aşırı derecede ayrık duruyordu. Genetik danışmanlık verildikten sonra çift gebeliğin sonlandırılmasını talep etti. Fetusun patolojik değerlendirmesinde frontonazal displazi ve anterior ensefalosel tanısı doğrulandı ve ek bir majör bulgu saptanmadı. Fetal karyotip normaldi ve ALX1 genininde mutasyon olmaması nedeniyle ayırıcı tanıda ALX-1 ile ilişkili frontonazal displazi dışlandı. Nöral tüp defekti olan fetuslarda bizim olgumuzda olduğu gibi eşlik eden sendrom ve hastalıklar görülebilir. Ultrason ile anterior ensefalosel tanısı koyulduğu zaman, frontonazal displazinin de beraberinde bulunma olasılığı akla getirilmelidir. (J Turkish-German Gynecol Assoc 2013; 14: 50-2)

Anahtar kelimeler: Frontonazal displazi, anterior ensefalosel, prenatal tanı, ultrason, konjenital anomali

Geliş Tarihi: 30 Temmuz 2012 **Kabul Tarihi:** 22 Ağustos 2012

Introduction

Frontonasal dysplasia, also known as median cleft syndrome, frontonasal syndrome and frontonasal dysostosis, is a rare congenital anomaly affecting the eyes, nose and forehead (1). A spectrum of abnormalities can be seen, ranging from mild hypertelorism to cleft face malformation (2). Frontonasal dysplasia is defined as the presence of two or more of the following symptoms: 1) true ocular hypertelorism, 2) anterior cranium bifidum occultum (a skin-covered gap in the bones of the forehead), 3) broadening of the nasal root, 4) median facial cleft affecting the nose, upper lip and palate, 5) unilateral or bilateral clefting of alae nasi, 6) lack of formation of nasal tip, 7) a V-shaped or widow's peak frontal hairline (3). Hypertelorism is the main and invariable component (4), and the male:female ratio has been reported to be 2:1 (5). There are several variations of frontonasal dysplasia, such as cranio-frontonasal dyplasia, oculoauriculofrontonasal dysplasia, acrofrontofacionasal dysostosis 1, acrofrontofacionasal dysostosis 2, Teebi type hypertelorism, acromelic frontonasal dysplasia, frontofacionasal dysplasia, cerebrofrontofacial syndrome, Pai syndrome and Shanske syndrome (2).

Only a few prenatally diagnosed cases have been reported in the literature (4, 6, 7). In this paper, we aimed to present a prenatally diagnosed case of frontonasal dyplasia with anterior encephalocele.

Case Report

A 24-year-old woman, gravida 4 para 1, was referred to our unit at 27 weeks gestation due to the prenatal diagnosis of encephalocele. The sagittal and axial sonography of the fetal

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doi:10.5152/jtgga.2013.12

face depicted a midline mass measuring 3.8 x 4.2 cm, projecting anteriorly between the fetal orbits and extending from the the upper aspects of the forehead to the nasal bridge, which was consistent with the frontal (anterior) encephalocele (Figure 1a and 1d). There were two facial clefts and the nostrils were extremely separated (Figure 1b). There was hypertelorism with an external orbital diameter measuring 51 mm and an internal orbital diameter measuring 23 mm (Figure 1c). Aside from the aforementioned malformations, there were no additional fetal abnormalities and the size of fetus was appropriate for gestational age.

Following genetic counseling, the couple requested a termination of pregnancy. A fetal blood sample was obtained via cardiocentesis and feticide was applied in the same session because of advanced gestational age. Termination of pregnancy was induced with intravaginal prostaglandin and a 1250 g male fetus was delivered. The postmortem examination revealed a soft-tissue mass measuring 4.5 x 5 cm and extending from the hairline to the nasal tip with a palpable bone defect (Figure 2a and 2b). The hypertelorism was prominent due to the encephalocele. The eyes were asymmetrical, with the left eye located more superiorly than the right eye, and the palpebral fissures were short. Two clefts were noted. The nasal root was broad and the nostrils were separated by the cleft on the left-hand side (Figure 2c) The distance between the two alae nasis measured 3.1 cm. The frenulum extended to the tip of the tongue, restricting lingual movement. 3D fetal CT depicted the bone defect between the frontal, nasal and etmoidal bones (Figure 2d). The fetal karyotype was normal and sequencing of ALX1 gene revealed no mutation.

Discussion

Embryologically, frontonasal dysplasia is suggested to be a result of the migration arrest of olfactory epithelium into the nasal capsule between the 4th and 6th weeks of embryogenesis (5). The nasal capsule does not form normally, leaving a central defect in which the forebrain area protrudes forming the anterior encephalocele (4). Anterior encephalocele is a rare condition and diagnosed as a soft-tissue mass overlying the lower aspect of the frontal bone (8). Fetuses with neural tube defects may suffer from associated syndromes and disorders, as with our case in which anterior encephalocele was associated with frontonasal dysplasia. The diagnosis of associated anomalies plays an important role in prenatal care, because the risk of neural tube defect in subsequent fetuses and the preventive effect of maternal folic acid intake in these cases may be different from those of nonsyndromic multifactorial neural tube defects (9).

Frontonasal dysplasia can be isolated or associated with other malformations (5). Distal limb abnormalities such as syndactyly, polydactyly, clinodactyly or tibial/fibular hypoplasia are associated sonographic findings in craniofrontal dysplasia, acrocallosal syndrome, acromelic frontonasal dysplasia, acrofrontofacionasal dysostosis 1 and 2, oral-facia-digital syndromes and Greig acrocephalopolysindactyly (4). Also, an association between frontonasal dysplasia and severe anomalies of the calvarium and central nervous system has been described (4). Therefore, a thorough search for cranial and limb malformations is recommended for the differential diagnosis (4). In our

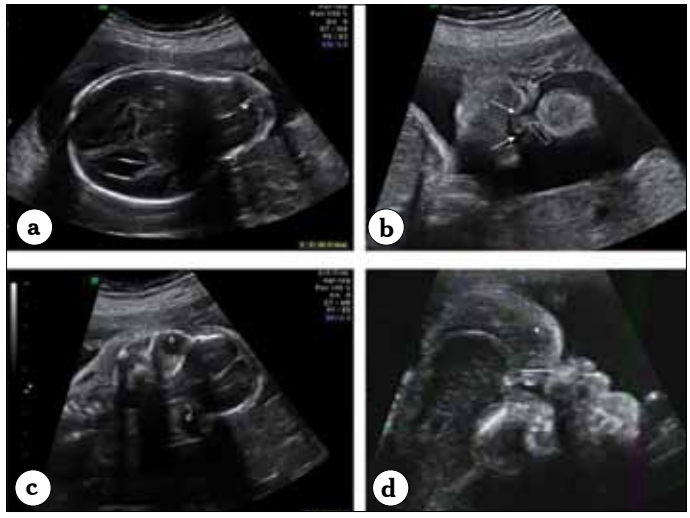

Figure 1. Fetal ultrasonography at 27 weeks gestation. (a) Axial scan of the fetal head showing anterior cephalocele (asterix). (b) Frontal view showing bilateral facial clefts (arrow) and nostrils widely separated (double arrow). (c) Frontal view depicting severe hypertelorism (O, orbits). (d) Sagittal scan showing the abnormal profile and cephalocele (asterix)

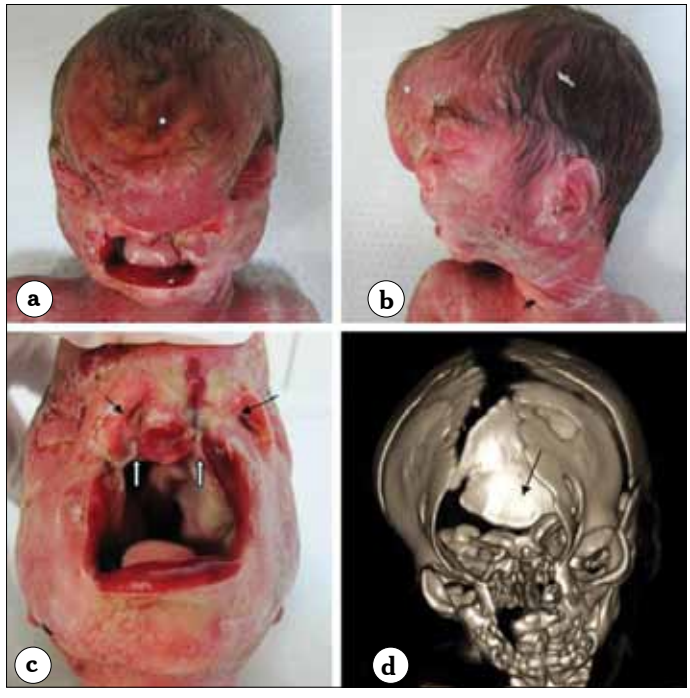

Figure 2. Postnatal appearance of the fetus. (a) Frontal view of the specimen showing anterior cephalocele (asterix). (b) Lateral view of the specimen showing anterior cephalocele (asterix). (c) Frontal view showing two facial clefts (white arrows) and the nostrils extremely separated from each other (black arrows). (d) 3D CT scan showing the cranium bifidum (arrow)

Written informed consent was obtained from the patient for publication of this case report and any accompanying images

case, encephalocele was the only associated finding and there were no extracranial malformations.

Genetic aspects of frontonasal dysplasia are not well-defined. Although frontonasal dysplasia occurs sporadically in most of the cases, autosomal dominant and X-linked patterns, as well as 22q11 microdeletion have been reported in the literature (1,10,11). In general, the possibility of this syndrome occurring in the next sibling is suggested to be 25% (12). Recently, autosomal-recessive mutations in aristaless-like homebox genes ALX1 (13), ALX3 (14) and ALX4 (15) have been described. While ALX3 and 4 predominantly play a role in the formation of the final shape of the nose, ALX1 expression is essential for building oral and nasal cavities as well as proper eye development during early embryogenesis (13). Therefore, ALX1-related frontonasal dysplasia is the most severe form, with a phenotype similar to the fetus in the present report. For this reason, the presence of a mutation in ALX1 gene was investigated but no mutation was found, excluding ALX1-related frontonasal dysplasia in the differential diagnosis.

In this report, we have presented a rare case of prenatally diagnosed frontonasal dyplasia associated with anterior encephalocele. Frontonasal dyplasia should be considered in the differential diagnosis when an anterior encephalocele is detected by ultrasonography.

Conflict of interest

No conflict of interest was declared by the authors.

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