

Three-dimensional prenatal diagnosis of frontonasal malformation and unilateral cleft lip/palate

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ABSTRACT

Frontonasal malformation includes a spectrum of anomalies involving the eyes, nose, lips, forehead and brain. We present a case in which a fetal labial cleft was initially identified using traditional two-dimensional sonography. Three-dimensional sonography with multiplanar reconstruction and surface-rendering were essential to establish the diagnosis of frontonasal malformation with severe nasal hypoplasia and unilateral complete cleft lip/palate.

INTRODUCTION

Frontonasal malformation is a term for an etiologically and pathogenically heterogeneous spectrum of midfacial anomalies that involve the eyes, nose, forehead and occasionally the brain¹. The common features are high grade orbital hypertelorism and abnormal nose (bifid, hypoplastic or cleft) that is sometimes associated with cleft lip. In severe cases, an anterior basal encephalocele may also be present. These midfacial defects can also include an abnormal frontal hairline, sometimes forming a widow's peak^{1–3}.

While the prenatal sonographic detection of cleft lip and palate is well established, the antenatal diagnosis of major frontonasal anomalies has rarely been made. We present a case of frontonasal malformation with hypertelorism, nasal hypoplasia and labial cleft, correctly identified antenatally using three-dimensional (3D) sonography. Although the presence of major nasolabial clefting was initially observed with traditional two-dimensional sonography, the precise diagnosis of frontonasal malformation with the severe nasal hypoplasia and unilateral complete cleft lip was made definitively using 3D scanning with multiplanar reconstruction and surface rendering.

CASE REPORT

The patient was a 37-year-old woman, gravida 1, para 0, who had conceived by *in-vitro* fertilization that was complicated

by ovarian hyperstimulation early in her pregnancy requiring bedrest. At 16 weeks of gestation, she had an abnormal serum triple screen with an elevated maternal serum alpha-fetoprotein (2.03 multiples of the median) and a positive screen for Down syndrome at a risk of 1/257.

At that time, two-dimensional ultrasound examination (Voluson, Medison America Inc., Cypress, CA, USA) showed

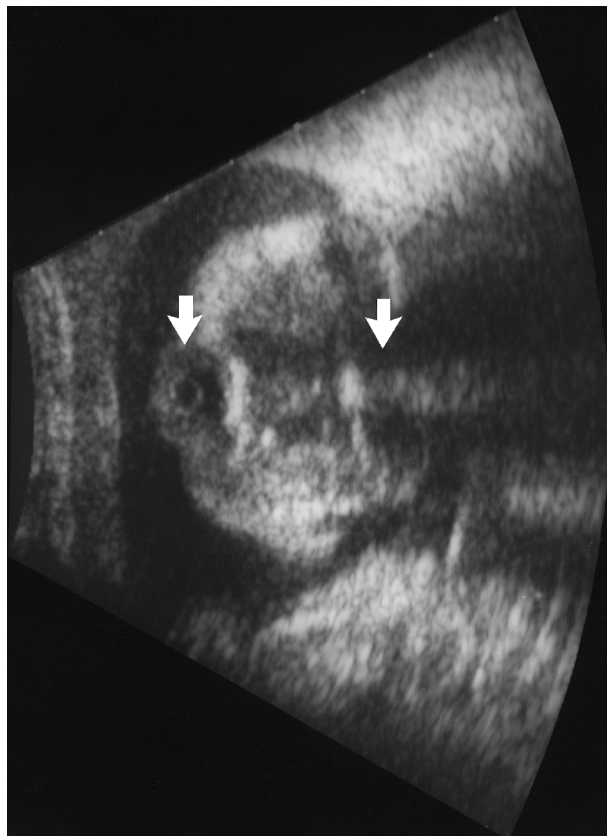


Figure 1 Coronal image of the fetal face at 19.5 weeks of gestation showing asymmetric orbital hypertelorism. (Arrows indicate orbits.)

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Figure 2 Sagittal image of the head at 19.5 weeks of gestation demonstrating flattening of the nose and forward displacement of the frontal bones.



Figure 3 Axial image of the head at 19.5 weeks of gestation at the level of the orbits demonstrating protrusion of the brain (arrows).

a right unilateral complete cleft lip/palate and unilateral choroid plexus cysts. An amniocentesis revealed a normal karyotype (46,XX). The patient returned for follow-up sonography at 19.5 weeks of gestation, when the more severe extent of the frontonasal malformation was discovered. There was obvious asymmetrical orbital hypertelorism (Figure 1), a right unilateral complete cleft lip and palate (Figure 2), as well as forward displacement of the frontal

bones with herniation of a portion of the frontal lobes (Figure 3). A 3D sonographic study (Voluson) demonstrated the exact extent of the protrusion of the frontal lobes and bones, associated with orbital hypertelorism and asymmetrical broad nose (Figure 4). Although this appearance was similar to a frontal encephalocele, there was no anterior cranial defect, and the findings were ascribed to a frontonasal abnormality or cranium bifidum occultum. Because of the sonographic

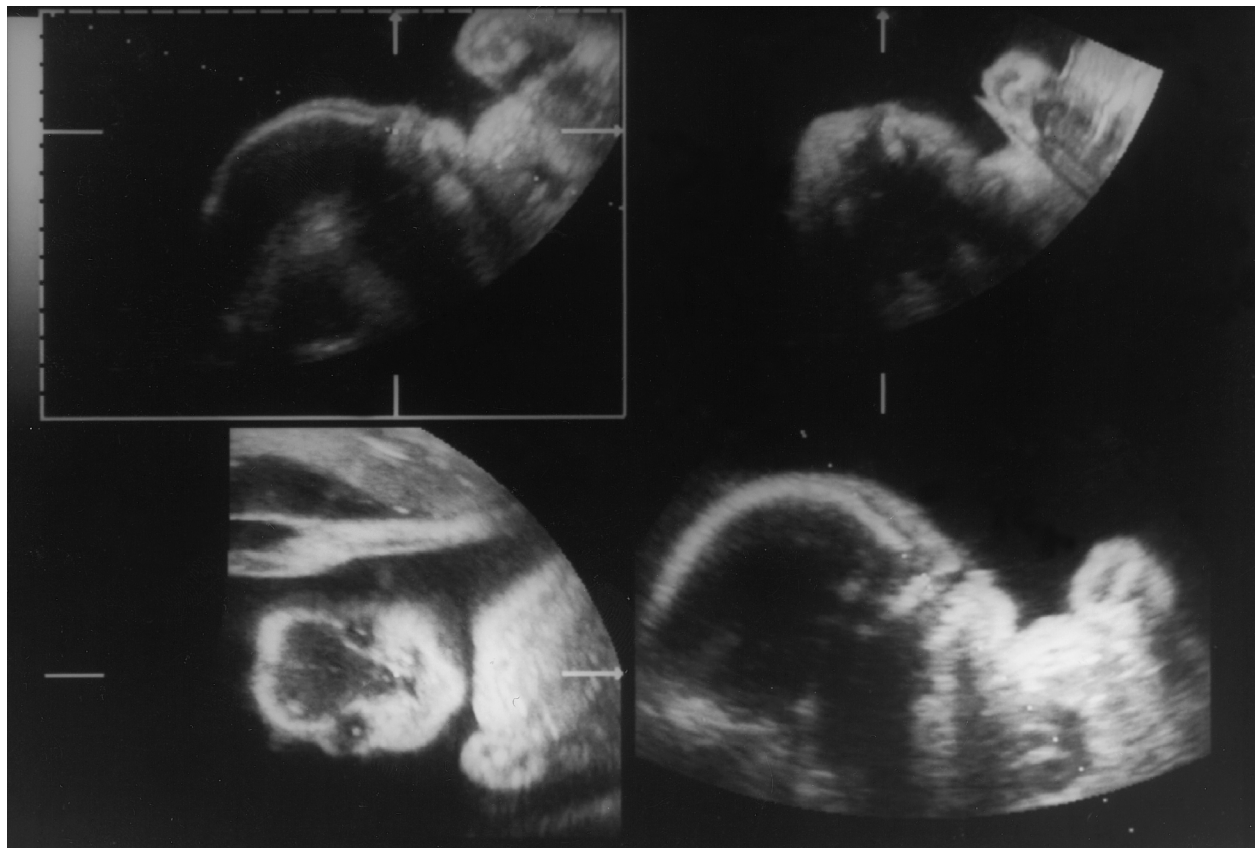


Figure 4 Three-dimensional acquisition and orthogonal planes at 19.5 weeks of gestation confirming protrusion of a portion of the frontal lobes of the brain and forward position of the frontal bones.

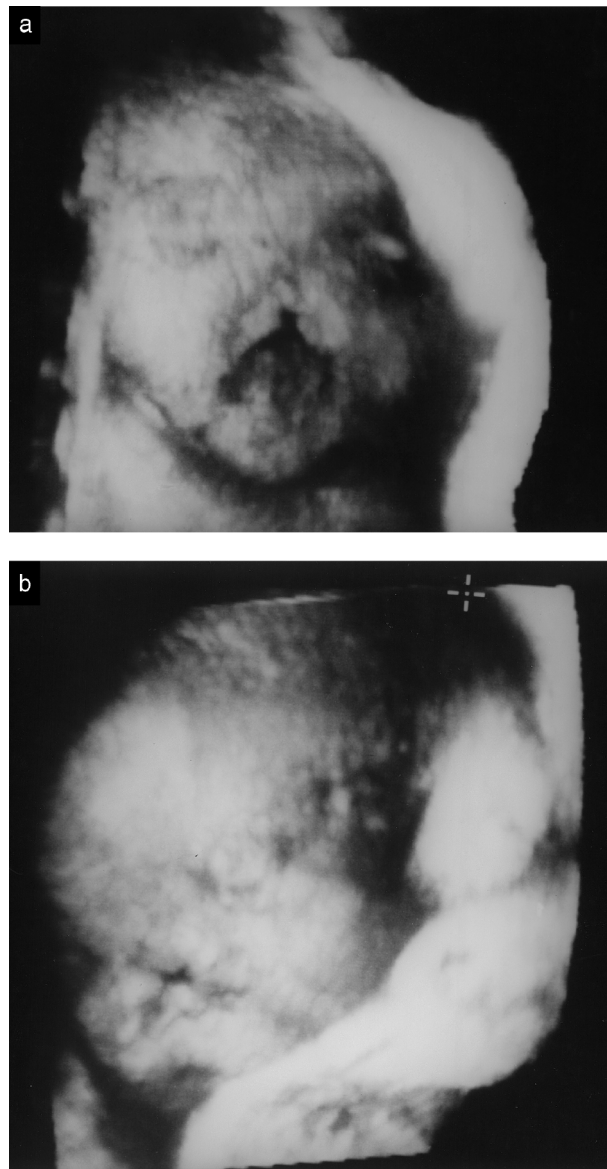


Figure 5 Three-dimensional surface reconstruction at 29 weeks of gestation demonstrating hypertelorism and right labial cleft (a) and hypertelorism, unilateral cleft and broad flattened nose (b).

findings, the patient was referred to a pediatric plastic surgical specialist for counseling.

The patient returned at 29 weeks of gestation, manifesting moderate polyhydramnios and preterm labor. She was treated with terbutaline for tocolysis and bedrest was recommended. Sonography with 3D surface reconstructed images was performed to aid in discussion for postnatal care (Figure 5). The patient returned for one more ultrasound evaluation at 33.5 weeks of gestation when abnormally increased fetal activity was noted.

Labor was induced at 39 weeks of gestation, and the patient delivered a female infant weighing 2.8 kg, with Apgar scores of 7, 8 and 8, at 1, 5, and 10 min, respectively. The postnatal assessment of the infant confirmed the prenatal findings of a frontonasal malformation (Figure 6), and imaging studies were performed to evaluate the possibility of

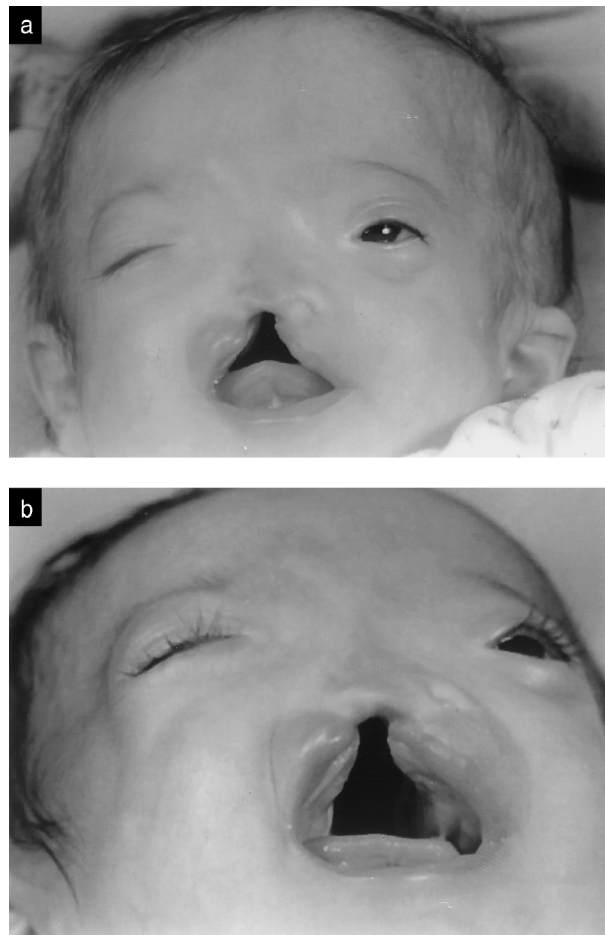


Figure 6 Postnatal photographs confirming the prenatal findings of frontonasal malformation with unilateral labial cleft, nasal hypoplasia and contralateral choanal atresia.

an anterior encephalocele. This was excluded; the pseudo-nasal mass seen by magnetic resonance imaging was identified as a mucus-filled sac that was a blind-ended nasal cavity caused by left-sided choanal atresia.

The infant underwent several craniofacial procedures; the first was 360° orbital osteotomies and medial translocation to correct the hypertelorism. She was fitted with a molding helmet that was adjusted daily for several months to further narrow the interorbital distance. The atretic left choana was opened endoscopically and stented and she had staged repair of the complete cleft lip and palate.

Developmentally, she showed some delay in motor skills and had sensorineural loss of hearing, although she had normal cognitive function at 1 year of age. The final postnatal diagnosis was asymmetrical frontonasal malformation with Grade 3 hypertelorism, nasal hypoplasia and right unilateral complete cleft lip/palate.

DISCUSSION

DeMyer⁴ was the first to describe 'median cleft face syndrome'. Sedano *et al.*⁵ recognized that this condition does not fulfil the definition of a syndrome, and renamed the disorder

'frontonasal dysplasia'. Later, Sedano and Gorlin⁶ proposed the term 'frontonasal malformation' for this non-specific developmental field defect that includes orbital hypertelorism, cranium bifidum occultum (which represents a deficit in the midline frontal bone and widow's peak hairline), as well as a broad nasal root, a broad flattened nasal tip or nasal clefting, and rarely cleft lip and palate^{1,2,6,7}. Occasional abnormalities include microphthalmia, agenesis of the corpus callosum, and lipoma of the corpus callosum, basal anterior encephalocele and tetralogy of Fallot^{1,2,6-10}. In a study of 21 patients with frontonasal malformation, there was a 2 : 1 male : female sex ratio. These 21 patients had a high incidence of agenesis of the corpus callosum (12 of 21 cases) encephalocele (10 of 21 cases), and lipoma of the corpus callosum (4 of 21 cases)¹⁰. The prognosis depends on the presence and severity of associated anomalies. Intelligence is normal in most; however, moderate to severe developmental delays complicate up to 20% of cases. Conductive deafness and optic abnormalities are occasionally seen².

The development of these frontonasal anomalies can be understood at a gross level as an embryological field defect. The face initially develops early, with the formation of bilateral nasal placodes into nasal tubes, until the embryo reaches a crown-rump length of 17 mm. The internasal groove is present between the nasal tubes, and, at this stage of development, the normal embryo has a flat nose and hypertelorism. Later in development, the nasal septum grows and the distance between the eyes decreases. If the nasal capsule fails to develop normally, the primitive brain fills the space which is normally occupied by the nasal capsule, producing an anterior cranium bifidum occultum¹¹. This results in a morphological arrest of the upper facial development at that stage, with the eyes and nostrils maintaining their fetal positions, thus resulting in hypertelorism and nasolabial clefting¹¹. The etiology of frontonasal malformations is unknown. It is considered to be a sporadic anomaly, although there are rare reports of familial recurrence¹².

There are many different forms of frontonasal malformation with hypertelorism, which may or may not be related in their etiology. Orbital hypertelorism can be graded as first, second or third degree based on standard deviations from the normal mean, age, and size-matched control values¹³. In severe cases, the nasal root is broad and the tip is bifid. There is also a rare form of frontonasal malformation called rugose nasal deformity in which the overlying skin has a corrugated appearance¹³. Less frequently, there can be symmetrical or asymmetrical clefting of the nose or notching (coloboma) of the alae nasi. The associated labial clefts are in the usual paramedian position, and are the result of a failure of fusion between the nasomedial process and the maxillary portion of the first pharyngeal arch.

In our case, the 3D evaluation of the abnormalities was particularly useful, as it enabled us to navigate through the three orthogonal planes to establish standard views of the face rather than being limited by difficult fetal positions. The surface rendering made it easier to view the fetal appearance and enabled the plastic surgeon and the parents to discuss the proposed surgical procedures.

The correct diagnosis of a frontonasal anomaly with labial clefting was suspected with standard two-dimensional sonography at 19 weeks of gestation. However, it had not been made correctly at 16 weeks of gestation, when only a cleft lip/palate was detected. The final diagnosis of frontonasal malformation with hypertelorism was entertained in the differential diagnosis at 19.5 weeks of gestation due to the sonographic findings of major nasal and frontal abnormalities. However, 3D surface rendering at that time exposed the full extent of the frontonasal malformation, based on the sonographic appearance of the fetal face and forehead.

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