Prenatal Visualization of Cebocephaly with a Prominent Nose in a Second-trimester Fetus with Alobar Holoprosencephaly and Trisomy 13

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A 39-year-old, gravida 7, para 3, woman was referred to the hospital at 18 weeks' gestation because of advanced maternal age. Initial two-dimensional (2D) ultrasound revealed alobar holoprosencephaly (Figure 1), congenital diaphragmatic hernia, and endocardial cushion defect. Level II 2D ultrasound showed a prominent nose, a large common nasal cavity, absence of nasal septum, and micrognathia (Figure 2). The nasal length measured 18 mm, and the external nasal diameter measured 25 mm. Three-dimensional (3D) ultrasound (Voluson 730D; Medison, Seoul, Korea) demonstrated hypotelorism, a single nostril, and a prominent nasal bridge (Figure 3). The diagnosis of cebocephaly was established. Genetic amniocentesis revealed a karyotype of 47,XY, +13. Quantitative fluorescent polymerase chain reaction using polymorphic small tandem repeat markers specific for chromosome 13 showed that the aneuploidy arose from nondisjunction in maternal meiosis II. The parents opted to terminate the pregnancy. The findings at autopsy were consistent with the prenatal diagnosis (Figures 4 and 5).

We have presented the prenatal visualization of a prominent nose and a large common nasal cavity associated with trisomy 13 and cebocephaly. Prenatal sonographic diagnosis of nasal malformations has been well described [1–9]. It is suggested that fetal nose is a target in the prenatal sonographic screening for malformations in the early mid-trimester [9]. Smallness of the nose and absence of nasal bone at 11–14 weeks of gestation are common findings of fetuses with trisomy 21 [10]. A prominent or broad nasal bridge and a broad nasal root are likely to be associated with an abnormal karyotype or multiple congenital anomalies. For example, Baller-Gerold syndrome and Seckel syndrome are associated with a prominent nasal bridge; Ehlers-Danlos syndrome, fragile X syndrome, Freeman-Sheldon syndrome, and fetal aminopterin, hydantoin, trimethadione and valproate effects are associated with a broad nasal bridge; and frontonasal dysplasia, generalized gangliosidosis syndrome and trisomy 8 syndrome are associated with a broad nasal root [8].

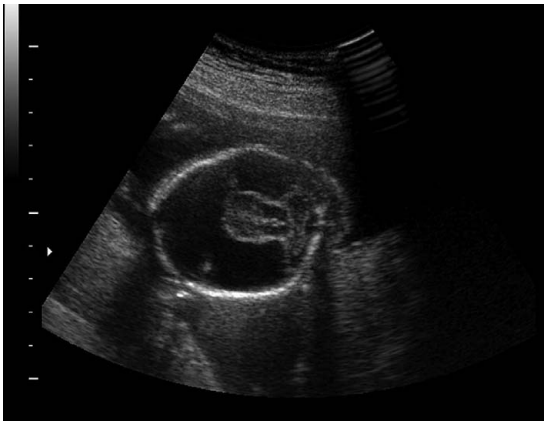

Figure 1. Two-dimensional ultrasound of the fetal head at 18 weeks' gestation shows alobar holoprosencephaly with fused thalami and a single ventricle.

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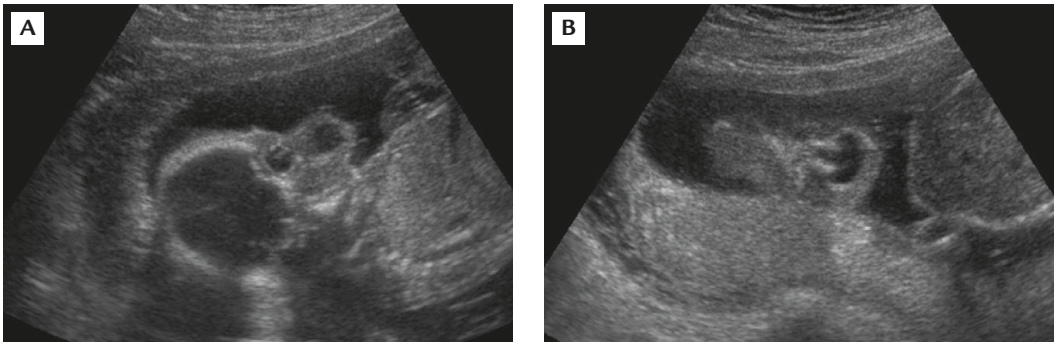

Figure 2. Two-dimensional ultrasound of (A) coronal section and (B) sagittal section of the fetal face reveals a prominent nose, a large common nasal cavity, absence of nasal septum, and micrognathia.

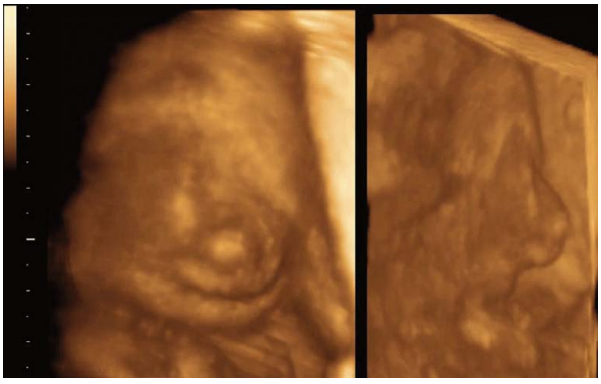

Figure 3. The anterior (left) and lateral (right) three-dimensional ultrasound surface-rendering views of the fetal face.

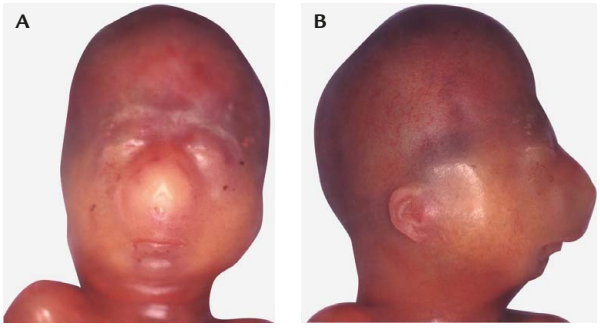

Figure 4. The fetus at birth.

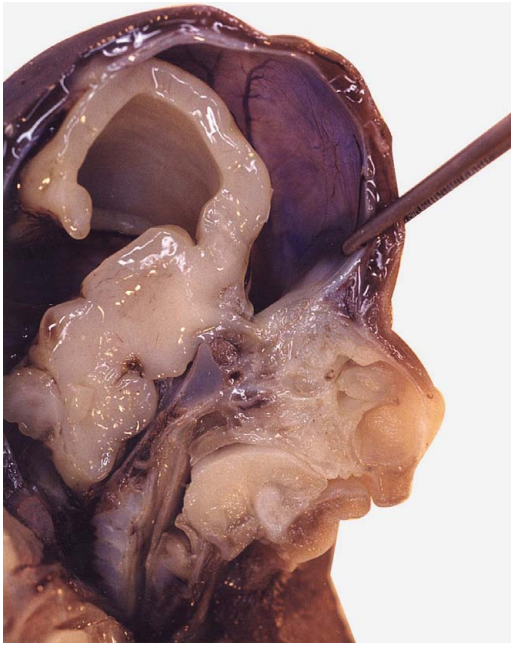

Figure 5. Postnatal autopsy findings of alobar holoprosencephaly, a prominent nose, and a large common nasal cavity without nasal septum.

Holoprosencephaly is characterized by congenital malformations of the forebrain and mid-face and is associated with various dysmorphisms ranging from severe alobar holoprosencephaly with cyclopia, ethmocephaly, cebocephaly or premaxillary agenesis, to microforms with microcephaly, corpus callosum agenesis/dysgenesis, mental retardation, ocular hypotelorism only, or a single maxillary central incisor. Chromosomal aberrations, mendelian mutations, and teratogens are well-known causes of holoprosencephaly. Cytogenetic abnormalities have been reported in half of the infants born with holoprosencephaly, with trisomy 13 being the most common. Other chromosomal abnormalities include trisomy 18, triploidy, del(2p), dup(3p), del(7q), del(13q), del(18p), and del(21q) [11]. Chen et al [12] previously described the dysmorphism of cebocephaly and a prominent nose in a fetus with *de novo* isochromosome 13q. This report further illustrated the 2D and 3D prenatal imaging findings of a prominent nose and a large common nasal cavity associated with trisomy 13 and cebocephaly. Such features may be included as part of the characteristic sonographic findings of fetuses with trisomy 13 in at-risk pregnancies.

References

1. Turner GM, Twining P. The facial profile in the diagnosis of fetal abnormalities. *Clin Radiol* 1993;47:389–95.

2. Pretorius DH, Nelson TR. Fetal face visualization using three-dimensional ultrasonography. *J Ultrasound Med* 1995;14: 349–56.
3. Devonald KJ, Ellwood DA, Griffiths KA, et al. Volume imaging: three-dimensional appreciation of the fetal head and face. *J Ultrasound Med* 1995;14:919–25.
4. Lee A, Deutinger J, Bernaschek G. Three-dimensional ultrasound: abnormalities of the fetal face in surface and volume rendering mode. *Br J Obstet Gynaecol* 1995;102:302–6.
5. Merz E, Weber G, Bahlmann F, Miric-Tesanic D. Application of transvaginal and abdominal three-dimensional ultrasound for the detection or exclusion of malformations of the fetal face. *Ultrasound Obstet Gynecol* 1997;9:237–43.
6. Goldstein I, Tamir A, Itskovitz-Eldor J, Zimmer EZ. Growth of the fetal nose width and nostril distance in normal pregnancies. *Ultrasound Obstet Gynecol* 1997;9:35–8.
7. Hull AD, Pretorius DH. Fetal face: what we can see using two-dimensional and three-dimensional ultrasound imaging. *Semin Roentgenol* 1998;33:369–74.
8. Ben-Ami M, Weiner E, Perlitz Y, Shalev E. Ultrasound evaluation of the width of the fetal nose. *Prenat Diagn* 1998;18: 1010–3.
9. Bronshtein M, Blumenfeld I, Zimmer EZ, Ben-Ami M, Blumenfeld Z. Prenatal sonographic diagnosis of nasal malformations. *Prenat Diagn* 1998;18:447–54.
10. Cicero S, Curcio P, Papageorghiou A, Sonek J, Nicolaides K. Absence of nasal bone in fetuses with trisomy 21 at 11–14 weeks of gestation: an observational study. *Lancet* 2001; 358:1665–7.
11. Chen CP, Devriendt K, Lee CC, Chen WL, Wang W, Wang TY. Prenatal diagnosis of partial trisomy 3p(3p23 → pter) and monosomy 7q(7q36 → qter) in a fetus with microcephaly, alobar holoprosencephaly and cyclopia. *Prenat Diagn* 1999; 19:986–9.
12. Chen CP, Chern SR, Lee CC, Chen LF, Chuang CY, Chen MH. Prenatal diagnosis of *de novo* isochromosome 13q associated with microcephaly, alobar holoprosencephaly and cebocephaly in a fetus. *Prenat Diagn* 1998;18:393–8.