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Otocephaly

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Otocephaly is a rare lethal syndrome of microstomia, aglossia, agnathia, and synotia. This male infant was born to a 19-year-old, gravida 1, para 0, woman who received routine prenatal check-up. Polyhydramnios, low-lying ears, and proboscis were noted by sonography at 29 weeks of gestation. Amniocentesis showed a normal karyotype of 46,XY. Premature rupture of membranes and preterm labor were noted at 32 weeks of gestation. A male infant was delivered preterm and died shortly after birth. The infant showed midline proboscis and absence of mandible. The simple, soft ears were extremely low-set and were near the midline of the neck. Otocephaly is regarded as the most severe form of first arch anomalies. Prenatal diagnosis should be dependent on ultrasound analysis. In the face of polyhydramnios, otocephaly is one of the possible fetal anomalies. [*J Chin Med Assoc* 2007;70(7):298–301]

Key Words: agnathia, fetal anomaly, otocephaly

Introduction

Otocephaly is a rare lethal syndrome of microstomia, aglossia, agnathia, and synotia.[1,2] It is the most severe form of the so-called first-arch anomalies.[3] Arrest in the development of the first branchial arch due to an insult to the neural crest cells was suggested to be the cause of this malformation.[1] It could be caused by gene or chromosomal mutations, or teratogenes.[2,4]

Prenatal diagnosis of otocephaly depends mostly on two-dimensional (2D) and three-dimensional (3D) ultrasound.[5,6] Most cases are diagnosed during the third trimester. Polyhydramnios is frequent in association with otocephaly.[7] Multiple fetal face anomalies, including agnathia, sloped forehead and low set ears, may be seen with ultrasound. Differential diagnoses include Treacher Collins syndrome, Goldenhar syndrome and Mobius syndrome.[7] We describe a case of prenatal detection of otocephaly using ultrasound; the case was diagnosed at 29 weeks of gestation and confirmed at autopsy.

Case Report

This male infant was born to a 19-year-old, gravida 1, para 0, woman. She received prenatal routine check-up at a local clinic. She and her husband were non-consanguineous and healthy. There was neither family history of congenital malformations nor any history of teratogenic medication, recent infection, diabetes mellitus, or hypertension during pregnancy. At 29 weeks of gestation, polyhydramnios was diagnosed. She was then transferred to our hospital for further evaluation where polyhydramnios (AFI: 41 cm), low-lying ears, and proboscis (Figures 1 and 2) were noted on sonography. Fetal biometry was equivalent to the gestational age.

Amniocentesis was performed at 31 weeks of gestation, and the result showed a 46,XY karyotype. Otocephaly was suspected. At 32 weeks of gestation, premature rupture of membranes and preterm labor occurred. A male infant was delivered preterm and died immediately from apnea and bradycardia. The baby was 43 cm in length, 1,450 g in weight, with multiple

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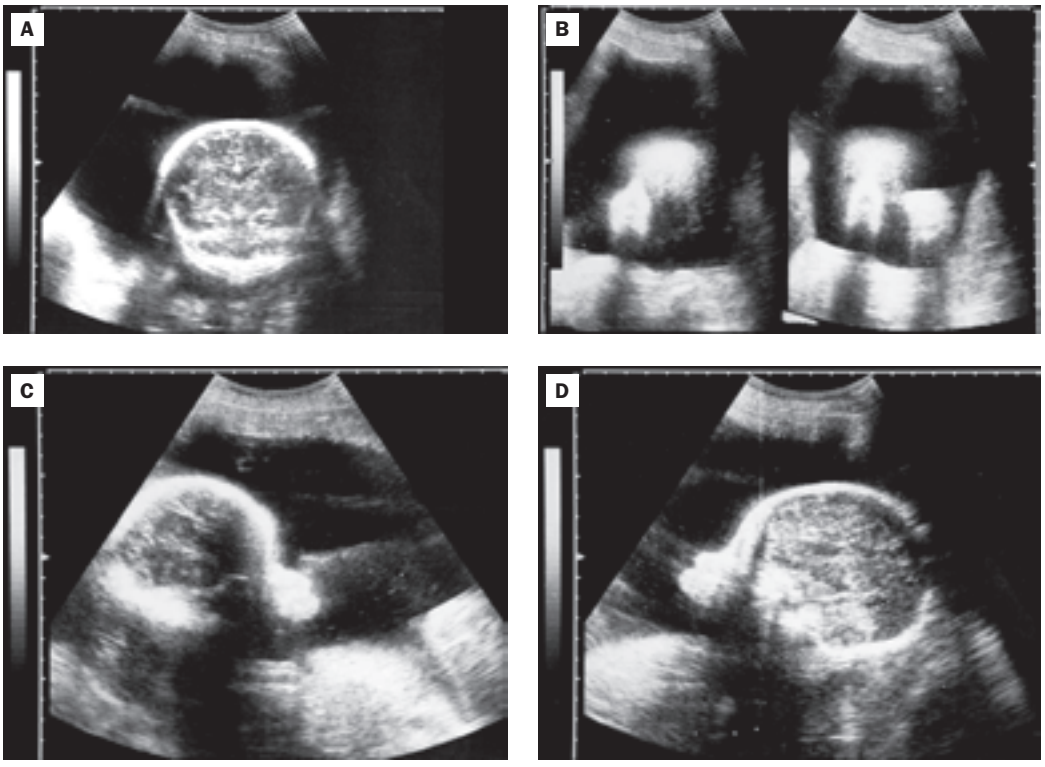

Figure 1. Ultrasound findings of proboscis-like mass and the absence of the mandible: (A) coronal view of brain; (B) frontal view of face; (C, D) different aspects of semi-sagittal view of face.

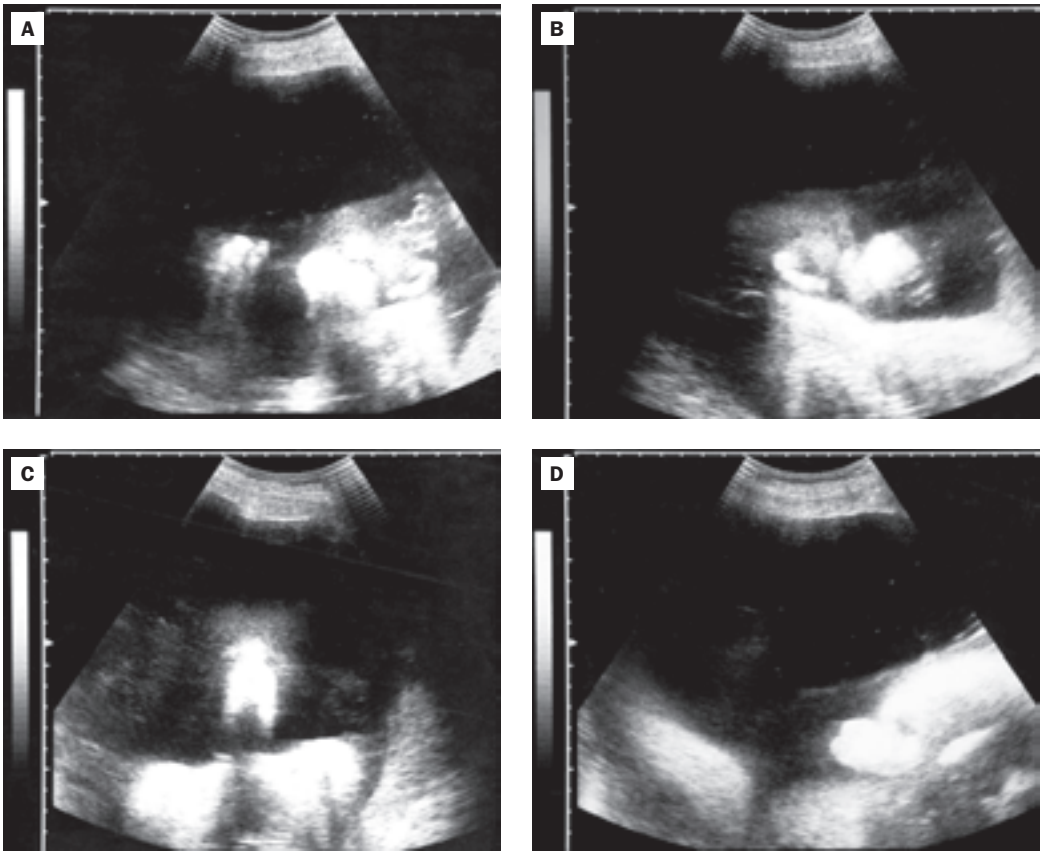

Figure 2. Ultrasound findings of proboscis-like mass and low-set ears: (A, B) bilateral low-set ears; (C, D) proboscis-like mass.

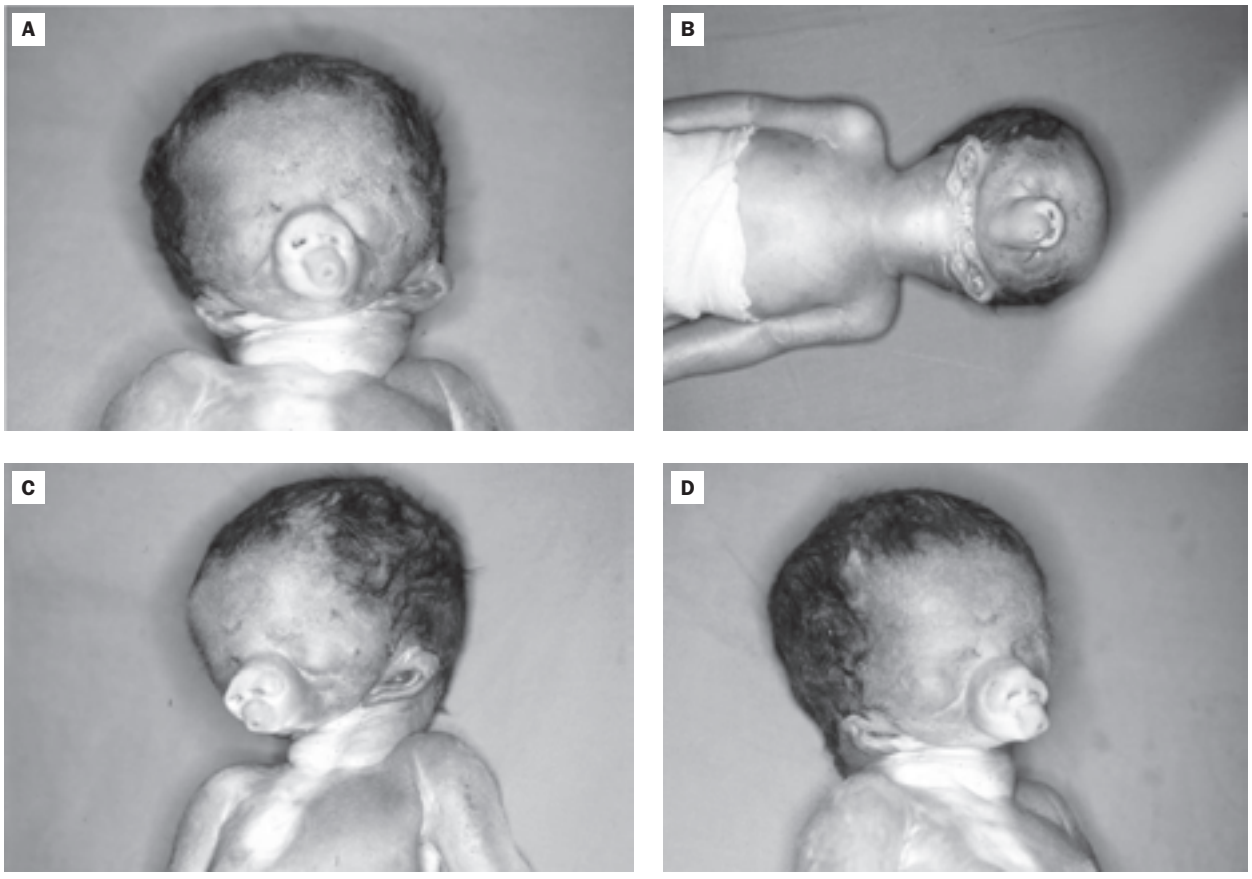

Figure 3. Fetus showing the nose–mouth fusion and the symmetrically low-set ears almost fused together in the midline: (A, B) frontal view; (C, D) lateral view.

anomalies including midline proboscis, absence of mandible, small protruding mouth without an opening, absence of tongue, and simple soft ears that were extremely low-set and located near the midline of the neck (Figure 3). The placenta and the umbilical cord were normal in appearance. Autopsy revealed extremely hypoplastic oral cavity and airway with normal developed orbital contents, central nervous system and other organs.

Discussion

Otocephaly, a defect in the ventral portion of the first branchial arch, is a rare lethal syndrome.[8,9] Evidence from human experience and various animal models suggest that otocephaly is the result of heterogeneous developmental defects. Both genetic and environmental factors have an impact on the formation of otocephaly.[8,9] Teratogenic effects of several agents such as strepnigrin antibiotics and Trypan blue have been reported.[2] It is suspected that theophylline could be a cause of neural crest cells forming otocephaly.[10]

Prenatal diagnosis of otocephaly is extremely rare and usually very difficult. More than 80 cases of otocephaly have been reported to date.[5] The estimated prevalence is of less than 1 in 70,000.[9] The majority of the cases were usually found incidentally after other anomalies such as holoprosencephaly, encephalocele, situs invertus totalis or renal defects were identified.[7,11,12] Three-dimensional ultrasound has been used to distinguish craniofacial features successfully at the mid-trimester of pregnancy.[6] Magnetic resonance imaging also provides precise assessment of fetal facial and ocular abnormalities.[5]

Mice heterozygous for the Otx2 mutation provide new insights into the genetic pathogenesis of human otocephaly.[13] Otx2 genetic modifier loci Otmf18 and Otmf2 located on chromosomes 18 and 2, respectively, were found to correlate with human otocephaly phenotype. This suggests that candidate genes located at these 2 loci may contribute to human agnathia–holoprosencephaly complex diseases.

Although otocephaly is a lethal syndrome and few affected babies can survive after birth, there have been 2 reports on the successful management of otocephalic

babies after birth.[14,15] Clearly, babies surviving from otocephaly pose a significant challenge for reconstructive and rehabilitative specialists. The immediate concern of securing the airway required a tracheostomy at birth because it was not possible to place an oral or a nasal endotracheal tube. However, because the majority of otocephaly babies are stillborn, the value of reconstructing the mandible remains unclear.

In conclusion, otocephaly is a rare and lethal malformation. Prenatal diagnosis should depend on ultrasound analysis (2D or 3D). The sonographic findings include extreme micrognathia, the presence of ears on the front and lateral aspect of the neck, as well as accessory findings such as polyhydramnios and holoprosencephaly. In the face of polyhydramnios, otocephaly is one of the possible fetal anomalies.

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