Second-trimester nasal bone hypoplasia/aplasia associated with cleidocranial dysplasia

A 26-year-old primigravid woman was referred at 20 weeks' gestation for genetic amniocentesis because of the absence of nasal bone ossification. Her husband was 41 years old. The parents involved in this pregnancy were unrelated and healthy. There was no family history of congenital malformations. Ultrasonography at 20 weeks' gestation revealed a fetus with absence of the nasal bone (Figure 1a). The amniotic fluid volume was normal. The fetal head and abdominal circumference measurements were consistent with the dates, but the long bones were at the 10th centile in length. The fetal anatomy appeared normal. No clavicular study was made. Genetic amniocentesis revealed a karyotype of 46,XX. Mild shortness of the femur and absence of a nasal bone were noted during the follow-up sonographic examinations at 22 and 31 weeks' gestation. A female baby was delivered at 36 weeks' gestation with a birth weight of 2406 g, a length of 46 cm, and Apgar scores of 8 and 8 at 1 and 5 min respectively. The infant postnatally manifested a typical appearance of cleidocranial dysplasia with bilateral absence of clavicles, large fontanelles with wide sutures, hypomineralization of the skull, brachycephaly, a flat occiput, midfacial hypoplasia, a depressed nasal bridge (Figure 1b), and slight frontal bossing. The parents were not affected with this disorder.

Cleidocranial dysplasia (OMIM 119 600), an autosomal dominant skeletal disease, is caused by heterozygous mutations in the *RUNX2* gene, which is responsible for an osteoblastic-specific transcription factor (Lee *et al*., 1997; Mundlos *et al*., 1997). Cleidocranial dysplasia is characterized by hypoplastic/aplastic clavicles, a brachycephalic skull, delayed closure of fontanelles, midfacial hypoplasia with a low nasal bridge, slight to moderate shortness of stature, delayed eruption of permanent teeth, multiple supernumerary teeth, and other skeletal abnormalities (Jones, 1997). Prenatal diagnosis of cleidocranial dysplasia has been possible in several reports (Hamner *et al*., 1994; Bowerman, 1995; Hassan *et al*., 1997; Stewart *et al*., 2000; Paladini *et al*., 2000). Of these, most were detected with a positive family history on the basis of sonographic identification of clavicular abnormalities. Other potentially detectable findings on prenatal ultrasound include a brachycephalic skull with hypomineralization, midfacial hypoplasia, frontal bossing, generalized immaturity of ossification, abnormal hands, cleft palate, micrognathia, and hypoplastic iliac wings. The present case shows that the associated midfacial hypoplasia may present as second-trimester nasal bone hypoplasia/aplasia during routine prenatal fetal nasal bone evaluation, which has been applied widely to improve the performance of ultrasound screening for Down syndrome (Cicero *et al*., 2001; Cuckle, 2001; Bromley *et al*., 2002; Lee *et al*., 2003). In this regard, nasal bone hypoplasia/aplasia serves as a valuable marker for cleidocranial dysplasia in addition to clavicles and may thus lead to early detection of affected fetuses with a negative family history. We suggest that prenatal observation of nasal hypoplasia/aplasia in chromosomally normal fetuses should prompt a careful search for skeletal dysplasias and a thorough investigation of the clavicles.

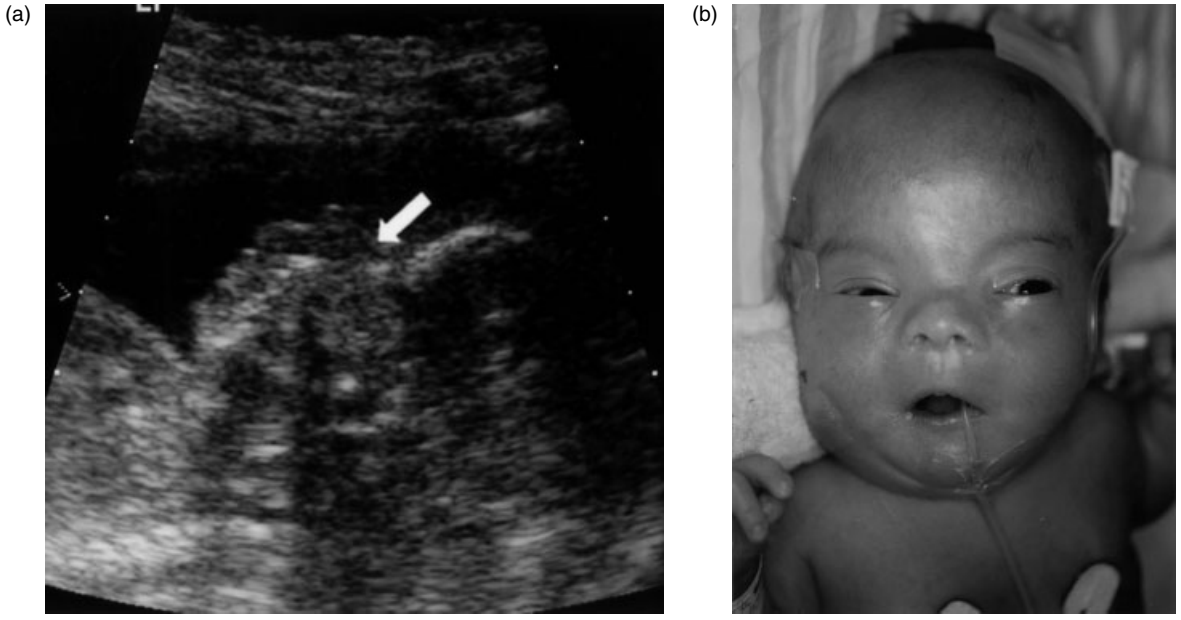

Figure 1—(a) An ultrasound picture in midline sagittal view showing the absence of a nasal bone (arrow). (b) The face of the neonate showing a depressed nasal bridge

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