Absent nasal bone

Society for Maternal-Fetal Medicine; Beryl R. Benacerraf, MD; Bryann Bromley, MD; Angie C. Jelin, MD

Introduction

In euploid fetuses, nasal bone length increases with advancing gestational age.[1-4] Absent nasal bone in any trimester is a marker for fetal aneuploidy, most notably trisomy 21, although this has also been described in fetuses with trisomies 18 and 13, sex chromosome abnormalities, and other rarer aneuploidies.[1,2,5-8] Reported rates of absent nasal bone among fetuses with trisomy 21 vary widely; however, approximately 36% of fetuses with trisomy 21 will have an absent nasal bone, compared with 0.5% of euploid fetuses.[9] The influence of ethnicity on nasal bone appearance in the second trimester is controversial but may influence screening test performance. Nasal bone length has been reported for many different ethic groups and appears to be notably shorter in some groups, especially fetuses of Afro-Caribbean ancestry.[2,10,11]

Definition

The nasal bone is considered absent when it is not visualized on a midsagittal view of the profile; nasal bone hypoplasia occurs when the nasal bone appears short or hypoechoic. Criteria for defining nasal bone hypoplasia have not been uniform, and the significance of this finding is controversial.[1,2,12,13]

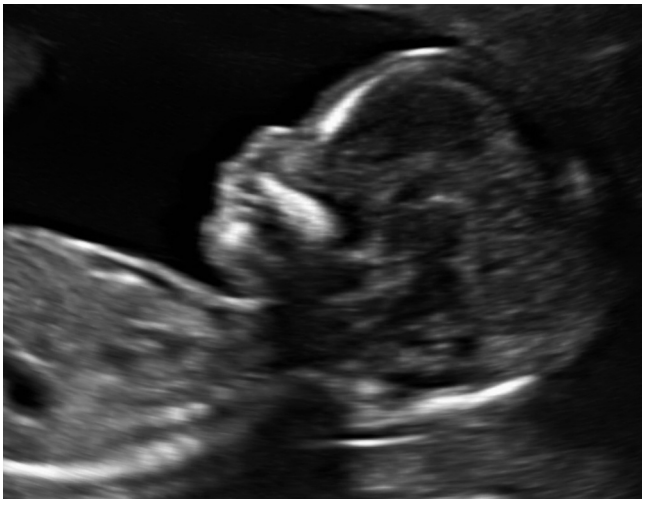
Ultrasound Findings

In the second trimester, a true midsagittal view of the fetal profile is obtained and magnified to fill the majority of the image space. The nasal bone appears as an echogenic linear structure below the skin edge. The optimal angle of insonation is 45 degrees to the longitudinal axis of the fetal nasal bone. If the angle of insonation is 0 or 180 degrees, the nasal bone may appear artificially absent. The presence or absence of the nasal bone may be determined at the time of the 11- to 14-week ultrasound examination and used as part of the risk assessment for aneuploidy (Figure).[14,15]

Associated Abnormalities

The identification of an absent nasal bone during the second-trimester anatomy scan should prompt a detailed anatomic assessment of the fetus to look for other structural anomalies and markers of aneuploidy. An absent nasal bone may occur as an isolated finding in fetuses who are euploid or aneuploid. This finding may be associated with other described markers for trisomy 21, such as a thickened nuchal fold and hyperechoic bowel, as well as with structural abnormalities that are associated with aneuploidy, including congenital heart defects.[1,16] The nasal bone may be absent in various craniofacial anomalies, such as frontonasal dysplasia, midface hypoplasia, or arrhinia. An absent nasal bone is also associated with several genetic and chromosomal syndromes.

FIGURE
Midsagittal view of a second-trimester fetus



The midsagittal view shows the correct angle of insonation that is required to determine the presence or absence of the fetal nasal bone. This second-semester fetus has no echogenic line under the nasal bridge and therefore has an absent nasal bone.

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Differential Diagnosis

Differential diagnosis will depend largely on associated markers and structural anomalies. An absent nasal bone is associated with an increased risk of aneuploidy, most notably trisomy 21.[17] The likelihood ratio for aneuploidy will vary depending on the presence of other sonographic markers, structural abnormalities, and ethnicity.[10,16]

The significance of an absent nasal bone can be estimated with the use of Bayes' theorem and likelihood ratios, although ethnicity-specific risks are not well-defined. In a metaanalysis of second-trimester sonographic markers, the pooled estimates of positive and negative likelihood ratios of absent nasal bone for trisomy 21 were 66.75 (95% confidence interval, 40.62–109.69) and 0.71 (95% confidence interval, 0.65–0.78).[16] In another recent metaanalysis, the pooled estimates of positive and negative likelihood ratios for trisomy 21 were 40.08 (95% confidence interval, 18.10–88.76) and 0.71 (95% confidence interval, 0.64–0.79).[9]

Genetic Evaluation

Evaluation of an absent nasal bone is dependent in part on the gestational age at detection. If noted at the time of first-trimester screening with an otherwise normal ultrasound image, this finding should be incorporated into the

first-trimester screening, and the patient should be counseled based on those results. An absent nasal bone at the time of a second-trimester anatomy screen is primarily important as a risk factor for Down syndrome, and counseling should incorporate results of any testing for aneuploidy that has been performed. Given the high likelihood ratio and specificity of this finding for Down syndrome, diagnostic testing with amniocentesis or screening with cell-free DNA should be offered. In the setting of low-risk cell-free DNA or normal fetal diagnostic testing results (karyotype or chromosomal microarray analysis [CMA]), an isolated absent nasal bone most commonly represents a normal variant. Chromosomal microarray analysis should be offered in the presence of additional anomalies that are not consistent with aneuploidy or if the prenatal karyotype is normal. If there are additional anomalies, consanguinity, or a family history of a specific condition, gene panel testing or exome sequencing is sometimes useful because CMA does not detect single-gene (Mendelian) disorders. If exome sequencing is pursued, appropriate pretest and posttest genetic counseling by a provider who is experienced in the complexities of genomic sequencing is recommended.[18]

Pregnancy and Delivery Management

A detailed ultrasound examination is recommended. A fetal echocardiogram should be performed in the setting of associated findings. Referrals to additional specialists should be based on additional sonographic findings and genetic testing results. Pregnancy termination is an option that should be discussed with all patients in whom a fetal anomaly is detected, although an isolated absent nasal bone in the second trimester is most often associated with a normal outcome. Antenatal monitoring is dependent on the presence of associated anomalies and the underlying diagnosis. Mode of delivery should be based on the usual obstetric indications, and site of delivery should be based primarily on other abnormalities or syndromic diagnosis.

Prognosis

Prognosis is dependent on the presence of associated anomalies and underlying cause. Support groups for parents of patients with trisomy 21 are available, and patients can be referred if a diagnosis is suspected or confirmed. As an isolated finding in euploid fetuses, a normal outcome is anticipated.[5]

Summary

An absent fetal nasal bone is associated primarily with an increased risk of aneuploidy. A detailed ultrasound examination should be performed to exclude other structural anomalies or markers of aneuploidy. Genetic counseling is recommended. As an isolated finding in a euploid fetus, a favorable outcome is anticipated. In the setting of other anomalies, the outcome will depend on the underlying cause.

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