Ultrasound Detection of Fetal Aneuploidy in Patients With Elevated Maternal Serum Alpha-Fetoprotein

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Increasing confidence in the ability of high-resolution ultrasound to detect neural tube and ventral wall defects has enabled us to offer a revised risk estimate to the patient with an elevated maternal serum alpha-fetoprotein (MSAFP) level, such that amniocentesis may not be necessary. Recent authors have suggested that a reduced emphasis on follow-up amniocentesis fails to consider an increased risk for chromosomal anomalies in pregnancies with an elevated MSAFP, and that amniocentesis should still be performed. We reviewed our ultrasound findings from patients who underwent amniocentesis for evaluation of an elevated MSAFP and who had a karyotype prepared from the amniotic fluid sample. Four abnormal karyotypes were detected among 313 amniocenteses, and three of these were correctly predicted based on an abnormal ultrasound. The risk of an unexpected fetal aneuploidy after a normal consultative ultrasound in our series was one in 310. This is comparable to the risk of detecting abnormal chromosomes in the fetus of a 32-year-old woman, an age at which amniocentesis is not routinely offered. *(Obstet Gynecol 77:897, 1991)*

Maternal serum alpha-fetoprotein (MSAFP) screening for the prenatal diagnosis of open neural tube and abdominal wall defects has gained wide clinical acceptance. After detection of an elevated MSAFP, defined as greater than 2.0 multiples of the median (MOM), most programs employ a repeat sample to confirm the initial result. If the second test is elevated, an ultrasound examination is recommended to look for gross anomalies, multiple gestation, fetal death, errors in the estimated gestational age, or obvious placental hematomas. Those patients whose elevated values are followed by a normal ultrasound are offered an amniocentesis to measure amniotic fluid AFP and acetylcholinesterase to detect small open neural tube defects that may not have been detected on the initial sonogram.

Recently it has been suggested that high-resolution sonography performed by experienced personnel has become accurate enough to allow a revised estimate of the risk of detecting a major anomaly by amniocentesis when the sonogram is normal.[1,2] With such a revised risk estimate, Richards et al[1] have shown that over 60% of patients with a normal ultrasound will elect to decline an amniocentesis. Other investigators have cautioned that a normal ultrasound does not reduce the need for amniocentesis.[3]

In support of the continued use of amniocentesis when the MSAFP screen is elevated, several authors have reported an increased incidence of abnormal karyotypes among such pregnancies.[4,5] However, none of these reports addressed the ultrasound detection of fetal anomalies before amniocentesis. Autosomal aneuploidy syndromes such as trisomy 13, trisomy 18, triploidy, and occasionally Turner syndrome frequently present characteristic features that may allow prenatal diagnosis by ultrasound.[6–8] This study was therefore conducted to determine the chance of finding an unexpected fetal chromosome anomaly after a normal consultative ultrasound in patients with elevated MSAFP.

Materials and Methods

During the period April 1985 through April 1990 at the Brigham and Women's Hospital obstetric care facility,

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The opinions expressed in this manuscript are those of the authors and not necessarily those of the United States Air Force or the Department of Defense.

0029-7844/91/$3.50

and September 1985 through April 1990 at the Harvard Community Health Plan prenatal clinics, 313 consecutive patients underwent an amniocentesis for evaluation of elevated MSAFP, defined in our center as being equal to or greater than 2 MOM. Karyotype was performed on each of the amniotic fluid specimens. After obtaining approval by the committees for the protection of human subjects, we reviewed records from the genetics departments from each service and correlated them with the findings of the ultrasound examination performed at the time of amniocentesis between 16–24 weeks' gestation. All examinations were performed by a single expert sonologist (BRB) using an Acuson 128 (Mountain View, CA) ultrasound system with 3.5-MHz transducers.

Results

Four abnormal karyotypes were discovered among 313 patients who underwent amniocentesis for evaluation of elevated MSAFP. Three of four were predicted correctly at the time of the ultrasound examination on the basis of characteristic morphologic features of known fetal aneuploidy syndromes. Two fetuses had cranial abnormalities (Figure 1), neural tube defects, omphaloceles, clubbed feet (Figure 2), and other stigmata of trisomy 18.[6] The findings in both fetuses were confirmed by karyotype. Another patient was found to have a twin gestation, explaining the elevated MSAFP, but one of the fetuses had a large nuchal fold, duodenal atresia (Figure 3), and a complete atrioventricular canal of the heart (Figure 4) suggestive of trisomy 21.[9] An amniocentesis confirmed the diagnosis. The fourth abnormal karyotype was a sex chromosome mosaic, 45,X/47,XXX, which was not predicted by ultrasound at the time of amniocentesis. The patient elected termination of the pregnancy based on the abnormal karyotype.

Discussion

The rate of abnormal fetal karyotypes among women with elevated MSAFP in our study was 1.3%. This compares favorably with that reported from other series, ranging from 0.8–1.4%.[3–5,10–12] Without consideration of the ultrasound results, the chances of finding an abnormal fetal karyotype in this series are comparable to those of a woman aged 39 undergoing an amniocentesis for advanced maternal age.[13]

With attention to the ultrasonographic characteristics of known fetal aneuploidy syndromes, three of four abnormal karyotypes were successfully predicted. Thus, the number of unexpected abnormal karyotypes after a normal ultrasound in this series was one in 310 (0.3%). This is comparable to the chance of detecting abnormal chromosomes in the fetus of a 32-year-old woman, an age at which genetic amniocentesis is not routinely offered.[13]

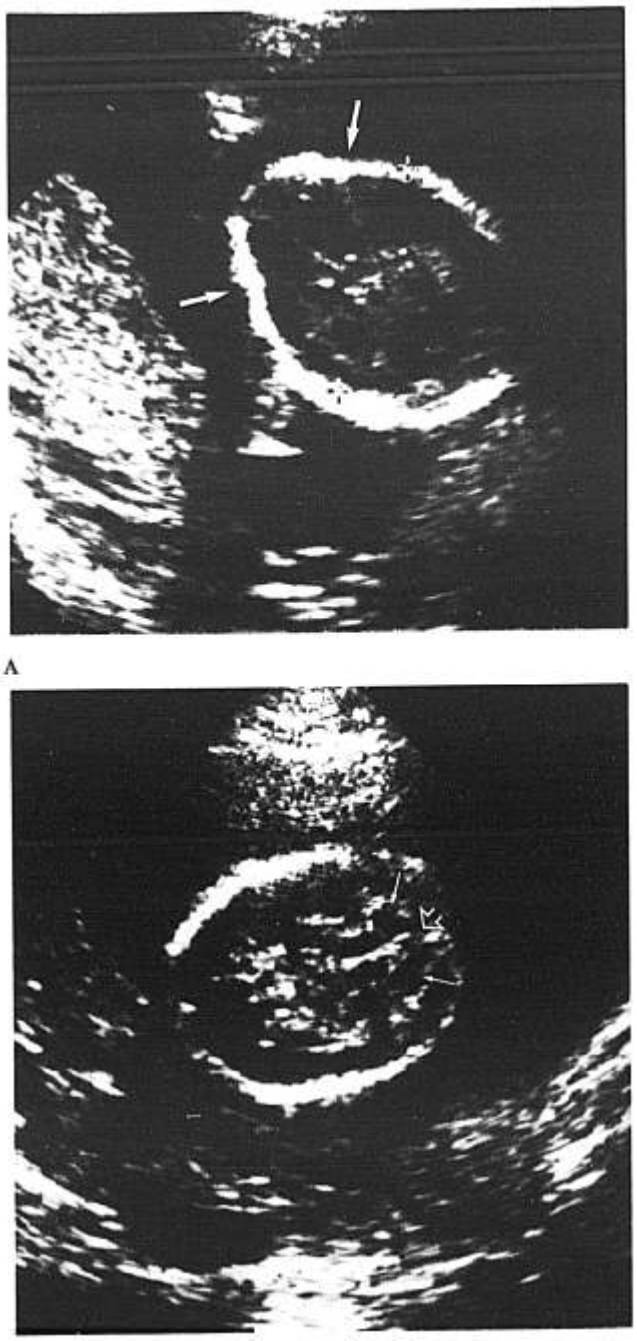

Figure 1. A) Transverse view of the fetal head showing the "lemon" sign, or compression of the frontal bones (*arrows*), in one of the fetuses with trisomy 18 and a neural tube defect. B) Transverse view of the posterior fossa showing compression of the cerebellar hemispheres (*small arrows*) and obliteration of the cisterna magna (*open arrow*) consistent with the "banana" sign in the same fetus.

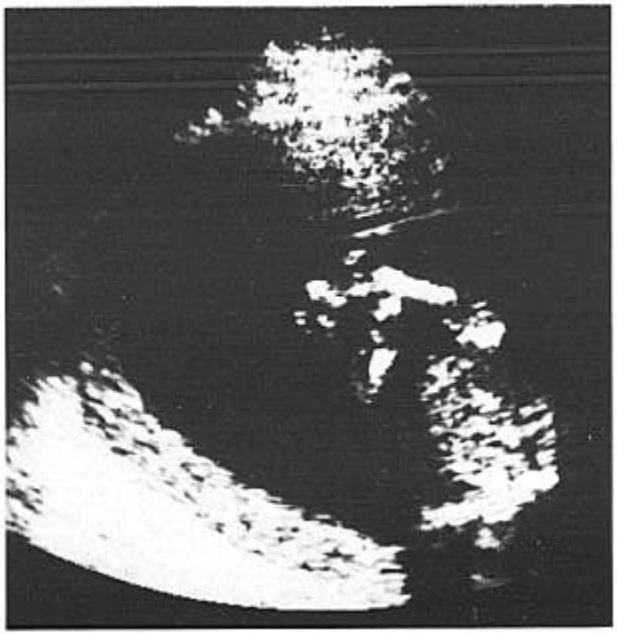

Figure 2. Longitudinal view of the fetal leg showing a clubfoot in one of the fetuses with trisomy 18.

The published sensitivities of ultrasound for the detection of trisomies 13 and 18 at our institution are 100 and 80%, respectively.[6] The most recognizable sonographic features of trisomy 13 include holoprosencephaly and associated midline facial abnormalities, polydactyly, congenital heart disease, omphalocele,

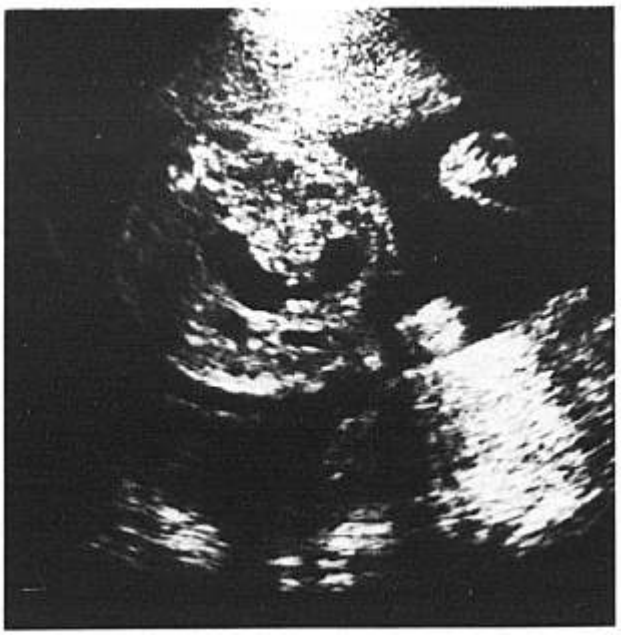

Figure 3. Transverse view of the fetal abdomen showing a "double bubble" sign consistent with duodenal atresia in the fetus with Down syndrome.

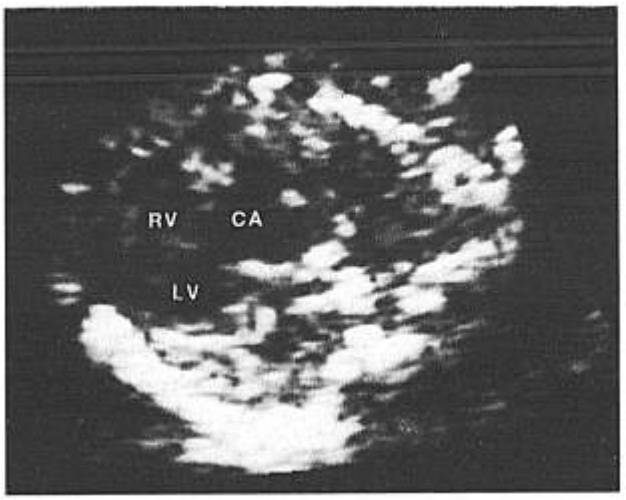

Figure 4. Transverse view of the fetal chest showing a complete atrioventricular canal of the heart in the fetus with Down syndrome. CA = common atrium; RV = right ventricle; LV = left ventricle.

and polycystic kidneys.[6] Features commonly associated with trisomy 18 include clenched fists with overlapping index fingers, limb reduction abnormalities, rocker-bottom or clubfeet, congenital heart disease, diaphragmatic hernias, intrauterine growth retardation, and hydramnios.[6] Although the sensitivity of ultrasound for the detection of triploidy has not been published in a large series, Pircon et al[7] detected sonographic abnormalities in five of seven fetuses (70%) later diagnosed with this syndrome. Triploid fetuses characteristically demonstrate early intrauterine growth retardation, cephalocorporal disproportion with relative macrocephaly, oligohydramnios, and placental abnormalities.[7,14–16] Ultrasound findings in Turner syndrome may include cystic hygromas, hydrothoraces, and nonimmune hydrops.[8,17] Although some authors have reported an increased incidence of sex chromosome abnormalities in patients with a high MSAFP, the prenatal ultrasound diagnosis of these syndromes has not been described with the exception of Turner syndrome.[11,18] As we found only one such case in 313 amniocenteses, a larger series would be needed to fully address this issue.

Amniocentesis is usually performed for detection of aneuploidy when the MSAFP is low.[19] Although some investigators have found an increased incidence of chromosomal defects when the MSAFP is elevated, one might expect that these fetuses have either an abdominal wall or neural tube defect associated with their aneuploidy.[4,5,12] Two of the four fetuses with abnormal chromosomes in this series had trisomy 18 with open neural tube defects, hence the elevation in MSAFP. The fetus with Down syndrome was one of a

twin gestation. In this case, twin gestation was presumed to be the explanation for the elevated MSAFP. We conclude that the elevation of MSAFP that accompanies some aneuploidy syndromes may be secondary to associated anomalies such as abdominal wall and open neural tube defects.

In a recent report from our institution, Nadel et al[2] showed that when the MSAFP level was between 2.5–4.0 MOM and a consultative ultrasound was normal, the risk for a neural tube or abdominal wall anomaly was 0.01–0.15%. Previous reports have suggested that these patients still require amniocentesis because of an increased risk for chromosome anomalies, and have implied that fetal karyotyping may still be required.[4,5] Our data suggest that if a high-resolution ultrasound examination is normal and shows no evidence of a known aneuploidy syndrome, the couple should be reassured that the risk of an unexpected significant chromosomal anomaly is equivalent to that of a 32-year-old woman, for whom current standard obstetric recommendations do not offer genetic amniocentesis.

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Received August 29, 1990.
Received in revised form December 24, 1990.
Accepted December 26, 1990.