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The value of echogenic foci ('golfballs') in the fetal heart as a marker of chromosomal abnormalities

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ABSTRACT

Objective *The aim of our study was to determine the significance of antenatally detected hyperechogenic foci in the fetal heart.*

Design *Prospective study.*

Subjects and methods *During a 21-month period, 6995 women underwent a sonographic screening investigation. A detailed structural survey was performed on each fetus according to our sonography protocol, including a four-chamber view and an evaluation of the great vessels, as permitted by gestational age. We prospectively identified each fetus with an echogenic intracardiac focus.*

Results *A total of 150 fetuses with this sonographic finding were identified. The incidence rate was 2.15%. In 114 patients (76%), prenatal karyotyping was performed. The aneuploidy rate was 4.4%*

Conclusions *The echogenic intracardiac focus can be easily diagnosed in most cases. This should prompt an extensive search for other 'soft' markers. The presence of an echogenic intracardiac focus as a single soft marker should raise the question of prenatal karyotyping. It might help in the decision-making regarding invasive prenatal testing in cases with an otherwise low risk for chromosomal abnormality. In cases with other markers for chromosomal abnormality (advanced maternal age, sonographic signs, positive serum marker screening), the presence of an echogenic intracardiac focus should be an additional incentive for a chromosomal examination.*

INTRODUCTION

The four-chamber view of the fetal heart represents a fundamental part of the second-trimester ultrasonographic examination and has proved to be an important screening tool in the prenatal identification of congenital heart disease. The increasing use of high-resolution ultrasonography makes it possible to detect small, isolated echogenic foci, so called 'golfballs', in the fetal heart. These structures appear near the papillary muscle and move with the mitral leaflets throughout the cardiac cycle.

Echogenic foci in the fetal heart were first described by Schechter and colleagues in 1987[1]. The histopathological manifestation of this sonographic sign is a mineralization of the papillary muscle[2]. Echogenic foci can be found more often in the left cardiac ventricle, with an incidence between 0.46 and 20%[3,4], and may be associated with chromosomal abnormalities, particularly trisomy 21[2,5–7]. Other reports found no correlation with Down's syndrome; the echogenic foci were considered to be a normal variant in the development of papillary muscles and chordae tendinae[8–10].

This topic is still controversial. We therefore performed a prospective study in order to determine the value of fetal intracardiac echogenic foci as a marker for chromosomal abnormalities.

MATERIALS AND METHODS

During a 21-month period, 6995 women underwent a sonographic screening investigation. The patients were referred from the Department of Obstetrics in our hospital, or from other institutions.

All ultrasound examinations were performed using a Toshiba Sonolayer SSA 270A machine with a 3.5-MHz curved array transducer. A detailed structural survey was performed on each fetus according to our sonography protocol, and included a four-chamber view and an evaluation of the great vessels, as permitted by gestational age. All

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fetuses with suspected or proven abnormalities were excluded from the evaluation.

Between July 1996 and April 1998, we prospectively identified each fetus with an echogenic intracardiac focus. For verification, the focus was required to be seen from two different angles (four-chamber view and long-axis view) and the echogenicity in the region of the papillary muscle had to be comparable to that of bone (Figures 1 and 2). The locations and numbers of these foci were recorded, as were any abnormalities.

When an echogenic intracardiac focus was detected, detailed information and the possibility of karyotypic investigation (amniocentesis or chorionic villus sampling (CVS)) were offered to the parents.

RESULTS

In our patients, an echogenic intracardiac focus was observed in 150 cases (2.15%). The mean gestational age at initial diagnosis was 20.5 weeks (range 15–28 weeks). The mean maternal age was 29.54 years (range 14–44 years). At the time of the initial scan, 29 women were 35 years or older, and 121 women were younger than 35 years.

After informed consent was obtained, 114 (76%) patients underwent prenatal karyotyping. In 58 cases, we performed CVS, in 48 cases amniocentesis, in seven cases both amniocentesis and CVS and one patient underwent cordocentesis. Out of these 114 patients, we found a normal karyotype in 109 cases. Five fetuses were aneuploid, representing 4.4% of the women who underwent an invasive procedure. The positive predictive value of an echogenic intracardiac focus for aneuploidy in all patients was 3% (5/150). Two out of 24 fetuses born to women 35 years or older were aneuploid, while, among the fetuses of younger mothers, three out of 90 were aneuploid. Only one of the five aneuploid fetuses had an echogenic intracardiac focus as the only sonographic marker for chromosomal aberration. The other four aneuploid fetuses showed various sonographic markers, indicating an increased risk for chromosomal abnormalities (Table 1). Among the euploid fetuses, other markers for chromosomal aberration and other anomalies were noted by prenatal testing in 18 cases. These were Potter syndrome ($n = 1$), duodenal stenosis ($n = 1$), fetal ovarian cyst ($n = 1$), cardiac tachyarrhythmia ($n = 1$), cystic adenomatoid malformation of the lung type III and hydrops fetalis ($n = 1$), hyperechogenic bowel ($n = 3$), mild pyelectasis ($n = 4$), unfused amnion and chorion ($n = 3$), choroid plexus cyst ($n = 1$) and an abnormal triple screening test ($n = 2$). The isolated presence of an echogenic intracardiac focus was found in 92 cases; subsequently one chromosomal aneuploidy was detected (1.09%). The combined finding of an echogenic intracardiac focus with other sonographic markers led to the detection of four chromosomal aberrations (22.2%).

The majority of the echogenic foci were located in the left ventricle, in 144 of the 150 fetuses (96%). Only one isolated echogenic focus was found in the right ventricle (0.67%). In five fetuses, the echogenic focus was found in both ventricles (3.4%). In the five cases of aneuploidy, the echogenic focus was found in the left ventricle.

In the 36 cases in which the parents did not agree to an invasive procedure, the fetuses showed no physical features

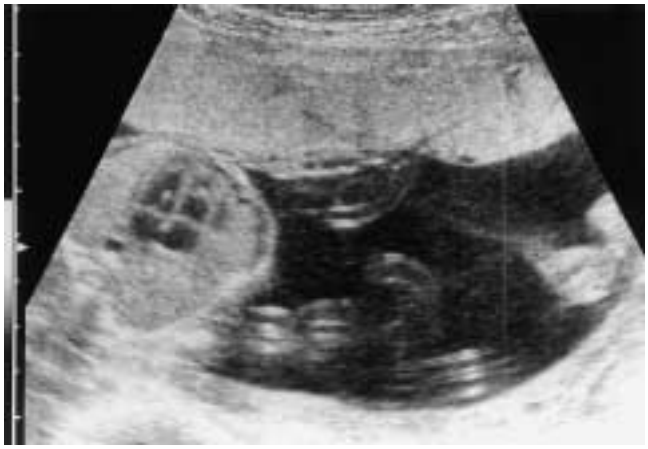

Figure 1 Four-chamber view of the fetal heart; echogenic intracardiac focus in the left ventricle

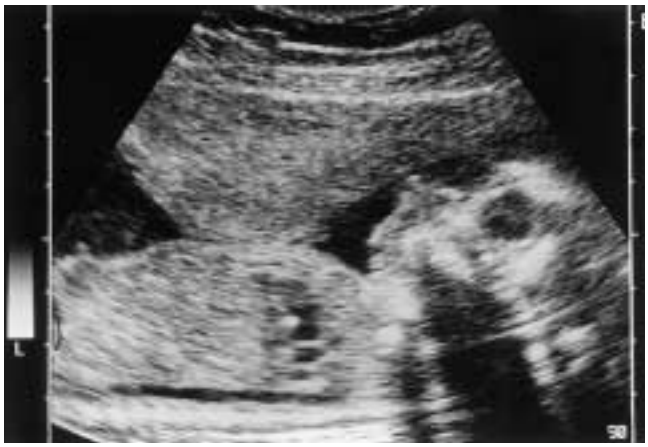

Figure 2 Long-axis view of the fetal heart

Table 1 Aneuploid fetuses with an echogenic intracardiac focus (EIF)

Case	*Procedure*	*Indication for scan*	*Maternal age* (years)	*Gestational age* (weeks)	*Ultrasonographic findings*	*Karyotype*	*EIF location*
1	CVS	advanced maternal age	37	19	mild hydronephrosis	trisomy 21	left
2	AC/CVS	screening	20	23	—	46,XX/45,X0	left
3	AC	advanced maternal age	37	19	VSD	trisomy 21	left
4	CVS	IUGR	34	20	ventriculomegaly	trisomy 13	left
5	AC	?ventriculomegaly	32	20	ventriculomegaly	trisomy 21	left

CVS, chorionic villus sampling; AC, amniocentesis; VSD, ventricular septal defect; IUGR, intrauterine growth restriction

of chromosomal aneuploidy after delivery. (We are aware of the fact that some chromosomal aberrations, for example mosaicism, show a normal phenotype during the perinatal period.)

In 15 cases, serial fetal echocardiographic examinations were performed and in 13 of these cases the echogenic focus in the fetal heart remained unchanged in shape, structure and location until the third trimester. The reason for this small number of follow-up ultrasound examinations is that most of our patients were referred to our unit from other departments for prenatal ultrasound screening or karyotyping exclusively. In two cases, the echogenic intracardiac focus disappeared after initial diagnosis: in one case 4 weeks later, in a second case 9 weeks after the first diagnosis.

CONCLUSIONS

Our study shows that the majority of fetuses with an echogenic lesion in a ventricle of the heart had a normal karyotype. These data support the benign nature of echogenic intracardiac foci. This seems to be a normal variant in the development of papillary muscles and chordae tendinae. Unfortunately, we do not have data about the chromosomal status of the 6845 patients without an echogenic intracardiac focus. In our opinion, it would not be ethically justified to perform prenatal karyotyping in order to determine the baseline aneuploidy rate. Data of postnatally determined chromosomal status would be of some interest, however, to establish the rate of chromosomal abnormalities in fetuses with a normal phenotype (e.g. mosaicism), but, because these data would always be incomplete, this information does not seem to be of great relevance. Furthermore, since our patients have delivered in approximately 20 institutions, it would be impossible for us to collect this information.

Although the echogenic intracardiac focus is a normal variant in most cases, it has been associated with a small risk for aneuploidy according to the reports of other investigators[6,11,12]. Comparable to other sonographic markers (choroid plexus cysts, echogenic bowel, mild hydronephrosis), the echogenic intracardiac focus is not of functional importance for the fetus, especially not associated with a structural cardiac abnormality.

Four of the five fetuses with aneuploidy showed other sonographic markers, indicating an increased risk for chromosomal abnormalities. In only one low-risk case (the mother was younger than 35 years) was the echogenic intracardiac focus the only sonographic sign that led us to offer karyotyping.

When an echogenic intracardiac focus is detected in a fetus, detailed information for the parents about the minimally increased risk for chromosomal abnormalities should be given. In our opinion, the focus can be easily diagnosed in most cases. The prenatal identification of this sonographic sign should initiate transfer of the patient to a prenatal care center.

After detecting an echogenic intracardiac focus, a detailed search for other sonographic signs or abnormalities should be performed. These include especially sonographic signs of trisomy 21 (iliac angle > 90°, short femur and humerus, sandal gap). In agreement with the report of Benacerraf and co-workers[13], the focus should be incorporated into the sonographic scoring index for identifying fetuses with autosomal trisomies.

In our opinion, the finding of an echogenic intracardiac focus should prompt an extensive search for other 'soft' markers. In our study, we found additional markers in four out of five patients with chromosomal abnormalities. The presence of an echogenic intracardiac focus as a single soft marker should raise the question of prenatal karyotyping and might help the decision whether to undertake invasive prenatal testing in cases with otherwise low risk for chromosomal abnormality. In cases where other sonographic markers for chromosomal abnormality are detected, or in cases of advanced maternal age or with a positive serum screening test, the echogenic intracardiac focus should be an additional, important motive for a chromosomal examination.

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