

First trimester diagnosis of fetal anomalies by transvaginal sonography

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Key words: anencephaly, exencephaly, fetal anomalies, megacystis, transvaginal sonography, transabdominal sonography

Abstract

A prospective sonographic study of fetal anatomy was carried out in 125 pregnancies between 9 and 14 weeks of gestation using both transabdominal and transvaginal scanning. The study included 50 high-risk patients and 75 low risk ones. In 3 cases (2.4%) major fetal anomalies that were missed at transabdominal scanning were diagnosed by transvaginal examination. They included: a case of anencephaly, a case of exencephaly and megacystis and a case of monoamniotic twin pregnancy with twin reverse arterial perfusion sequence. In the first two cases pregnancy was terminated by the end of the first trimester. In the third one intrauterine death in the 14th week of gestation occurred.

The study confirms the superiority of transvaginal ultrasound examination in the first trimester of pregnancy: minimizing some of the technical difficulties of transabdominal scanning, early diagnosis of fetal anomalies and termination of pregnancy by D&C, possibilities for rapid fetal karyotyping if necessary. However high qualification and experience with the examination are required. Some ethical aspects of the early diagnosis of fetal anomalies (possible diagnostic errors, absence of histopathologic confirmation in most of the cases) must be considered too.

Introduction

Antenatal diagnosis of major fetal anomalies by ultrasound has been reported in the early seventies (1). The introduction of real time sonography in the obstetric everyday practice and the accumulation of knowledge for the sonographic appearance of normal and abnormal fetal structures makes possible the antenatal diagnosis of an increasing number of anomalies. Routine second trimester screening for fetal anomalies is performed in most of the developed countries in the world (2). The introduction of high resolution transvaginal probes makes possible the very early diagnosis of fetal anomalies - by the end of the first and the beginning of the second trimester of pregnancy (3,4). With transvaginal scanning normal embryonic fetal structures are visualized early in gestation. Recently the term "sonoembryology" is often used when embryonic structures at different gestational ages are described (5,6).

Organ-age timing charts enhance the assessment of normal and abnormal fetal anatomy (5).

Early diagnosis of anencephaly, spina bifida, abdominal wall defects, amniotic band syndrome, limb, cardiac and urinary tract anomalies have been recently reported in literature (7, 8, 9, 10, 11, 12, 13, 14). Some prospective studies including a significant number of cases also confirm the importance of transvaginal sonography in early pregnancy (15).

Aim of the study

To compare the diagnostic possibilities of first trimester transabdominal and transvaginal sonography regarding early diagnosis of fetal anomalies.

Materials and Methods

A prospective sonographic study of fetal anatomy was carried out in 125 pregnancies ranging from 9 to 14 weeks of gestation (w.g.). Seventy five of the patients were low risk ones. The remaining 50 cases were pregnancies with high risk for fetal anomalies (previous affected child, maternal diabetes, multiple pregnancy, advanced maternal age). The first scanning was performed between 9 and 14 w.g. depending on the patient's referral to our Ultrasound Unit. A transabdominal ultrasound examination was first carried out, followed immediately by a transvaginal one. In the cases of normal transabdominal and transvaginal first scans a second transvaginal scanning in the 14 w.g. and a transabdominal in the 20th w.g. to confirm normal fetal anatomy were performed. In one case with suspicious sonographic finding after the first transvaginal scanning (9 w.g.) the patient was reexamined two weeks later. All pregnancies but the terminated ones were followed up until delivery and normal fetal anatomy was confirmed. The equipment used was Sigma 44 HVCD, and Sigma 1A with 7.5 MHz transvaginal and 3.5 MHz transabdominal sector probes. The sonographic studies were carried out by two experienced operators with the patients' informed consent.

Registration of congenital anomalies and fetal dysmorphology

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Key words: Bulgaria, congenital anomalies, registration

Registration of congenital anomalies (CA) according to EUROCAT criteria and requirements was undertaken in the city of Sofia from the beginning of 1996. The method allows prenatal detection and follow up of fetuses with isolated and multiple congenital anomalies. Over a period of 6 months 5,196 pregnancies came to birth or were terminated for various reasons. 73 families (1.4%) have been registered because of CA in a terminated fetus, newborn baby or an infant under 1 year of age. This report summarizes the results of US testing follow-up and management of 23 pregnancies with increased genetic/environmental risk (9.2) or fetal structural anomalies, detected by ultrasound (12). In the latter group 1 false positive result has been proved and 11 fetuses showed isolated or multiple CA as follows: chromosomal - 3 (45, X0, trisomy 13,

trisomy 18), single gene defects - 3 (Meckel syndrome, polycystic kidney disease, chondrodysplasia punctata), other MCA syndromes - 3 (acardic monozygotic twin monster syndrome, Cantrell syndrome, abdominal wall defect), CHD, isolated major congenital anomalies - 2 (ventriculomegaly). The registration of CA during pregnancy is a powerful method for studying the normal variation of different fetal structures, diagnosis and improvement the medical care of preexisting diseases states in the families, as well as early diagnosis of an increasing number of nonchromosomal, nonmetabolic dysmorphic syndromes. At the time being sensitivity and specificity of the prenatal US testing remains relatively low that needs further debate concerning acceptability and criteria for efficiency of the mass US screening of pregnant women.

Prenatal diagnosis in the Czech Republic

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Key words: Czech Republic, prenatal diagnosis

When we speak about prenatal diagnosis in the Czech Republic, it is necessary to take into account the historical roots and political context in the formation of the health system. As it is generally known, until 1989 all health care in our republic was provided by the state free of charge. The advantages and drawbacks of this situation are familiar to all of us. On one hand it was the availability of health care to all, on the other hand it was the significant financial limitation of

the more expensive procedures and methods, difficult approach to relevant information and the inability to exchange experience with advanced health care systems in the Western Europe.

The first encounters with methods of prenatal diagnosis in the Czech Republic date back to late seventies. Since then they were firmly anchored in the list of health examinations and their spectrum widened similarly as in other countries in

ORIGINAL ARTICLE

Four-quadrant assessment of gestational age-specific values of amniotic fluid volume in uncomplicated pregnancies

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Background. The purpose of this study was to establish a normative scale of amniotic fluid index (AFI) throughout gestation in uncomplicated singleton pregnancies, and to identify the lower and upper limits for each gestational week.

Methods. Four-quadrant assessment of amniotic fluid volume (AFV) was performed prospectively in 750 uncomplicated pregnancies between 16 and 43 weeks. The logarithmic transformations were used to get the data in Gaussian distribution. The means, and the 90%, 95% and 98% confidence intervals at each week of gestation were calculated from polynomial regression equation. Statistical differences in AFI among gestational age groups were tested.

Results. The amniotic fluid index observations from regression equation curve were stratified in week-specific normative curve. The variations between mean AFI of the total population and the means of the preterm, term and postdate pregnancies were statistically significant ($p < 0.0001$). The 90%, 95% and 98% confidence limits about the mean (12.5 cm) were 5.4 to 20.6, 4.2 to 22.3, 1.8 to 25.8 cm, respectively in term gestation. The 5th and 95th percentile serves as lower and upper limits of normal, respectively.

Conclusions. Gestational age-specific values of AFI were established, determining the significant trends of changes in the AFV with gestation. The normogram may have a clinical benefit to accurate, reliable and semiquantitative diagnosis of oligohydramnios and polyhydramnios.

Key words: four-quadrant assessment; amniotic fluid volume; oligohydramnios; polyhydramnios

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The maintenance of the amniotic fluid volume (AFV) within normal limits is important for the fetal well-being. Aberrations in volume either above or below normal are associated with poor perinatal outcome (1, 2, 3). Several reports (4, 5) have indicated with the dye dilution techniques which were quantitative, reproducible and appropriate.

Brace and Wolf (5) have provided a good quantitative characterization of changes in AFV in normal pregnancies. However, these methods are of a limited clinical usefulness for their attendant risks and potential complications.

In this recent ultrasonographic era, a noninvasive, semiquantitative assessment of AFV is possible. Subjective determination of the AFV (6), measurement of a single deepest pocket (SDP) (1–3, 7–9) and two-diameter pocket volumes (10) have been employed. These techniques showed good correlation between 'abnormal AFV' and 'adverse perinatal outcome'; but the definitions for the nor-

Abbreviations:

AFI: amniotic fluid index; AFV: amniotic fluid volume; NST: non-stress test; LSD: least significant difference; SD: standard deviation; SEM: standard error of mean; SE: standard error; SDP: single deepest pocket; CI: confidence interval; ANOVA: analysis of variance.

PRACTICAL APPLICATION OF DOPPLER VELOCIMETRY IN OBSTETRICS

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The rapid development of contemporary science and technology allowed principally new, non-invasive methods for the assessment of fetal well-being to be introduced in practice. One of these methods is Doppler velocimetry^{1,2,3,4}. Nowadays it is widely used in the everyday work of the obstetricians for screening, diagnosis and control of treatment. In the same time it is a powerful tool for research work and for clarifying the unknown pathogenetic mechanisms of the most common, but yet not completely studied complications of pregnancy. Doppler velocimetry is a comparatively new method of investigation in our country. Two opposite tendencies - the under- and the overestimation of the capacity of this method - exist among practitioners. This is the reason a brief review on the problem to be presented to the attention of the audience.

At the present moment Doppler velocimetry has proved to be of particular significance in later gestation, namely after the 20 week⁴. A lot of efforts are devoted to revise the concepts, concerning its importance in early gestation but this is still a problem to be studied and discussed.

Doppler velocimetry is undoubtedly informative and widely applied in practice in the following cases:

I. Screening for the development of preeclampsia and asymmetrical type of IUGR in the second trimester of pregnancy⁴. The method has higher sensitivity and easier application than the well-known tests with angiotensin, beta-blockers, roll-over test and mean arterial pressure.

II. Diagnostic application.

1. The method has particular significance in the diagnosis of distress^{12,14,15,16}. Pathologic sonograms in the feto-placental circulation can be detected a week prior to the changes in the NST. The practical significance of this fact is that a normal Doppler sonogram can reduce the necessity of very frequent records since in this case a sudden deterioration in the fetal condition is not expected. On the other hand pathologic sonograms, combined with still normal NST must keep the obstetrician alert with the possibility of a "sudden" unfavourable outcome. This possibility will be discussed later in the item "Pathologic sonograms and adverse perinatal outcome". It should be noted, that Doppler velocimetry has informative value in those cases in which the fetal distress is caused by vasospasm, but not by other reasons. This is not the case with postterm pregnancy, where the method is unreliable¹⁷.

For the proper assessment of the condition of the fetus the utero-placental and the feto-placental circulation should be studied simultaneously. The findings can be grouped as follows:

I. Normal flow velocity waveforms in both the uterine arteries and the umbilical artery^{4,7}. Fetal distress is not expected to be manifested soon.

II. Pathologic sonograms in the uterine arteries, combined with - normal sonograms in the umbilical artery. This is a common finding in cases with preeclampsia, chronic hypertension and pregnancy, asymmetrical type IUGR. This condition requires active management - treatment of the pregnant woman, frequent assessment of the fetal well-being for early detection of distress, preterm delivery.

III. Normal sonograms of the uterine arteries combined with pathologic findings in the umbilical artery and - or fetal aorta. It is generally accepted that the reason for this condition is in the fetus. It might be a chromosomal abnormality, an intrauterine infection of the fetus or some structural abnormality that has been missed. It must be remembered that such a finding may be occasional and temporary, but if it persists, further investigation is necessary including karyotyping, serologic study and precise second level ultrasonographic examination. The data from the additional tests will determine the obstetric management in any particular case¹⁸.

IV. Pathologic flow velocity waveforms in both the uterine arteries and the feto-placental circulation. This indicates severe fetal distress and the necessity of urgent decision making, so that the unfavourable perinatal outcome would be avoided¹⁹. The time for delivery is determined on the basis



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Clinical Science: case report

Antenatal ultrasound diagnosis of perineal ectopic testis — a case report

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Abstract

Perineal ectopia testis is a rare congenital anomaly with incidence of $< 1\%$ of all cases of undescended testes. We report a case of perineal ectopic testis detected by ultrasound at 38 weeks gestational age presenting as an oval echogenic structure located beneath the male fetal genitals. The diagnosis was confirmed postpartum by clinical examination and karyotyping of the neonate. Orchiopexy was performed 1 year after delivery. © 2001 Elsevier Science Ireland Ltd. All rights reserved.

Keywords: Perineal ectopic testis; Antenatal diagnosis; Ultrasound

1. Introduction

Since perineal ectopia testis was first described by John Hunter in 1786, more than 200 cases have been reported (Campobasso et al., 1993; Dieckmann et al., 1988; Kullendorff et al., 1985; Uchijima et al., 1984). The postnatal diagnosis is relatively easy made by palpation and occasionally by ultrasound (Kullendorff et al., 1985). Our survey of the literature failed to reveal any previous reports of perineal ectopia testis detected antenatally by two-dimensional ultrasound.

2. Case report

A 31-year-old woman, gravida 4, para 2, was referred for evaluation at 38 weeks gestational age because of a preceding cesarean section performed for fetopelvic disproportion. Ultrasound demonstrated a singleton live fetus in cephalic presentation with no gross structural abnormalities. Observation of the perineal fetal region revealed an oval echogenic structure below the normally looking penis and scrotum (Fig. 1). A suspicion of ectopia testis was made, though some genital abnormalities were also discussed. A 3500 g infant was delivered by planned cesarean section performed several days after admission. Examination

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SHORT COMMUNICATION

Introduction of the QF-PCR analysis for the purposes of prenatal diagnosis in Bulgaria—estimation of applicability of 6 STR markers on chromosomes 21 and 18

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Objective The aim of our study was to estimate the observed heterozygosity and informativeness of 6 STR markers on chromosomes 18 and 21 in the Bulgarian population. We have evaluated the applicability of these markers used from other investigators for QF-PCR prenatal diagnosis of the most common autosomal aneuploidies in Bulgaria.

Methods DNA samples ($n = 486$) were extracted from different fetal tissues (amniotic fluid cells, chorionic villus samples, and fetal tissue after abortions). PCR amplifications of 4 STR markers located on chromosome 21 (D21S11, D21S1411, D21S1270, and D21S1440) and 2 on chromosome 18 (D18S535 and D18S51) were performed. They were analysed on an automated sequencer, and the allele dosage ratios were calculated.

Results The results indicate the selected markers as highly informative for our population and suitable for QF-PCR prenatal diagnosis in Bulgaria. All samples with trisomy 21 ($n = 8$), trisomy 18 ($n = 4$) and triploidy ($n = 1$) were correctly detected by our analysis. Thus, no false-negative results were observed.

Conclusion QF-PCR analysis could be an applicable alternative in prenatal and postnatal diagnosis in cases with a strong suspicion for particular autosomal aneuploidies (including chromosomes 21, 18, and 13) in small countries with limited resources like Bulgaria. Copyright © 2004 John Wiley & Sons, Ltd.

KEY WORDS: prenatal diagnosis; QF-PCR; STRs

INTRODUCTION

Prenatal cytogenetic analysis in high-risk pregnancies has been performed routinely since the early 1970s. This analysis detects chromosomal anomalies, but is long-lasting and cost-consuming. With the development of DNA technologies, a new diagnostic method has been proposed since the 1990s—indirect quantitative fluorescent PCR analysis (QF-PCR). It is based on the investigation of highly polymorphic DNA markers (short tandem repeats (STRs)) located on the target chromosomes (Pertl *et al.*, 1996; Adinolfi *et al.*, 1997; Verma *et al.*, 1998). The high accuracy of this technique, its low cost and rapidity have introduced it as a reliable alternative for detection of the most common human aneuploidies such as trisomies 21, 18, and 13, as well as triploidy.

The most frequent autosomal aneuploidy is trisomy 21 (Down syndrome)—approximately 1 affected newborn in 800 live births (Nora *et al.*, 1994). It is associated with variable, but often severe mental retardation,

and sometimes with structural anomalies. Trisomy 18 (Edwards syndrome) is the second common autosomal aneuploidy—it affects 1 of 8000 newborns (Nora *et al.*, 1994) and is characterized by severe multiple malformations and lethal outcome soon after birth.

The allele frequency and the heterozygosity of the STR markers vary among the different ethnic population groups (Sacchetti *et al.*, 1999). In order to minimize the percentage of uninformative results from QF-PCR analysis, the proper choice of markers is important. The aim of our study was to estimate the level of observed heterozygosity (and therefore, informativeness) of four markers, located on chromosome 21 and two markers, located on chromosome 18 for the purposes of the QF-PCR prenatal diagnosis in Bulgaria.

MATERIALS AND METHODS

Biological samples

A total of 486 fetal DNA samples were investigated. Pregnancies ranged from 10 to 34 weeks of gestation (most of them between 16 and 20 weeks). Pregnant women were referred for prenatal diagnosis because of

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