Comparison of ultrasonographic findings in spontaneous abortions with normal and abnormal karyotypes

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To determine whether ultrasonographic findings can predict the karyotype of spontaneous abortions, 137 pregnancies (54 spontaneous, 83 assisted ovulatory cycles) that subsequently aborted and had chromosome analysis performed on the products of conception were studied ultrasonographically. Transvaginal ultrasound was performed using an Acuson 128XP/10 with 7.5 MHz probe. The numbers of empty gestational sacs, small and normal for gestational size, embryonic poles and embryos with documented cardiac activity were calculated. The frequency of each of these findings in pregnancies with normal and abnormal karyotypes was compared. Of the 137 spontaneous abortions, 51 had normal chromosome analyses and 86 had abnormal karyotypes (68 aneuploidies and 18 polyploidies). Ultrasonographic findings in the 51 karyotypically normal pregnancies included 16 (31%) with empty gestational sacs, and 35 (69%) with embryonic poles, of which 24 (69%) were at least 1 week smaller than expected for gestational age and 11 (31%) were the expected size. Embryonic cardiac activity was documented in 22 (63%) which 24 (69%) were at least 1 week smaller than expected gestational sacs, and 35 (69%) with embryonic poles, of which 19 (54%) were at least 1 week smaller than expected gestational age, and 50 (79%) embryos lost after documentation of embryonic cardiac activity. No differences in the frequency of ultrasonographic findings of empty gestational sacs, small embryonic pole and embryonic cardiac activity were observed between karyotypically normal and abnormal spontaneous abortions. Ultrasonographic findings cannot predict the karyotype of spontaneous abortions.

Key words: chromosomal analysis/embryonic cardiac activity/empty gestational sac/spontaneous abortion/transvaginal ultrasonography

Introduction

Recent advances in ultrasonographic technology have allowed documentation of early (day 24–56 from last menstrual period) embryonic growth and development (Britten et al. 1994; Coulam et al., 1996). Nomograms for the mean and 95th percentile of gestational sac diameter, embryonic pole length and embryonic heart rate from 24 to 56 days from last menstrual period (LMP) in pregnancies with subsequent successful outcome have been published (Britten et al. 1994; Coulam et al., 1996). Smaller than expected gestational sac sizes and embryonic pole lengths as well as delayed appearance of embryonic cardiac activity have been shown to be predictive of early pregnancy loss (Bromley et al., 1991; Nazari et al., 1991; Dickey et al., 1992; Goldstein, 1992; Frates et al., 1993). Approximately 50–60% of all first trimester spontaneous aborti have chromosomal abnormalities (Boué et al., 1975; Stern et al., 1996). Several studies have shown an embryonic or fetal length <50th percentile for the expected gestational age among pregnancies that subsequently aborted (Bessho et al., 1995; Brambati and Lanzani, 1987). However, one study (Bessho et al., 1995) reported no difference between the measured and expected crown–rump ratio when concepti from spontaneous abortions with abnormal karyotypes were compared with normal karyotypes. To determine whether other specific ultrasonographic findings can predict the karyotype of spontaneous abortions, 137 pregnancies that subsequently aborted and had chromosome analysis performed on the products of conception were studied.

Materials and methods

The study population consisted of 137 pregnancies that terminated in first trimester abortions between January 1, 1994 and August 21, 1995, had chromosomal analysis performed on the products of conception and had ultrasonographic examination prior to spontaneous abortion. Fifty-four pregnancies occurred in spontaneously ovulating cycles in women with a history of recurrent spontaneous abortion. All women had a history of regular menstrual cycles and the gestational ages were calculated from the onset of the last menstrual period (LMP). The remaining 83 pregnancies occurred in ovarian stimulation cycles. Forty-eight pregnancies resulted from in-vitro fertilization (IVF) and embryo transfer and 35 pregnancies occurred after stimulation with follicle stimulating hormone (FSH) and intrauterine insemination (IUI) of spermatozoa. Multiple follicular development was induced using the gonadotrophin-releasing hormone analogue (GnRHa) leuprolide acetate (Lupron; TAP Pharmaceuticals, Chicago, IL, USA) plus FSH (Metrodin; Serono, Inc., Randolph, MA, USA) in women undergoing IVF. Follicular development was monitored by serial hormone and ultrasonographic measurements (Coulam et al., 1994a,b). Follicles were aspirated under transvaginal ultrasound guidance 34–36 h after injection of 10 000 units of human chorionic gonadotrophin (HCG) (Profasi; Serono, Inc.). For women undergoing IUI, ovarian stimulation was achieved with gonadotrophins (FSH or HMG, Metrodin or Pergonal; Serono, Inc.). Follicular...
development and HCG administration were identical to IVF cycles (Coulam et al., 1994a,b). The days of insemination and embryo transfer were used to calculate the gestational age of pregnancy. Women with irregular menses were not included in this study if the date of conception was not clearly documented.

Embryonic tissue was obtained from each woman by uterine curettage after informed consent. The tissue was processed and analysed using standard G-banding cytogenetic techniques with both short- and long-term cultures (ISCN, 1981).

Transvaginal ultrasonograms were performed using Acuson 128XP/10 (Acuson Computer Imaging, Mountain View, CA, USA) with a 5–7.5 MHz transvaginal transducer. Both B-mode and simultaneous B- and M-modes were utilized. Gestational sacs were measured in longitudinal and transverse views and their diameters averaged. Embryonic poles were measured in the anterior to posterior dimension. Embryonic heart rates were calculated from frozen M-mode images with electronic calipers. Gestational sac diameters and embryonic pole lengths were compared with expected measurements based upon the LMP or upon their relationship to each other (Coulam et al., 1996). An empty sac was defined as a chorionic sac with no identifiable embryonic pole. A small for dates embryonic pole was defined as an embryo measuring <5th percentile for expected size based upon LMP or gestational sac diameter (Coulam et al., 1996). Embryonic cardiac activity was measured prior to diagnosis of pregnancy loss between 5 and 8 weeks of gestation while the embryo was still viable.

The frequency of empty gestational sacs, smaller than expected embryonic pole length and lack of demonstration of embryonic cardiac activity between 5 and 8 weeks of gestation was determined for pregnancies with normal and abnormal karyotypes. The results were compared using $\chi^2$ analysis with Fisher’s exact probability test. A difference of $P < 0.05$ was considered significant.

**Results**

The mean age of the women experiencing spontaneous abortions was 36.3 ± 4.4 years (range 26–46). The mean gestational age at which uterine curettage was performed was 8.1 ± 1.8 weeks. The distribution of gestational age at the time of uterine curettage is shown in Figure 1.

Table I compares the frequency of chromosomal abnormalities among aborti from assisted and spontaneous ovulatory cycles. No significant differences in the frequency of normal and abnormal karyotypes nor aneuploidy nor polyploidy is observed when assisted and spontaneous ovulatory cycles are compared. The distribution of chromosomal abnormalities among aborti from assisted and spontaneous ovulatory cycles are shown in Figure 2; no striking differences are seen.

**Discussion**

Ultrasonographic findings of pregnancies ending in spontaneous abortion did not predict their karyotype. The frequency
Ultrasonography in normal and abnormal abortions

Figure 2. Distribution of chromosomal abnormalities among 137 spontaneous abortions occurring after 83 assisted and 54 spontaneous ovulatory cycles.

Table II. Frequency of normal and abnormal chromosomal analyses among 137 spontaneous abortions, showing frequencies of ultrasonographic findings of empty gestational sac, small embryonic pole length and presence of embryonic cardiac activity

<table>
<thead>
<tr>
<th>Ultrasonographic findings</th>
<th>Chromosomal analysis</th>
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<tr>
<td></td>
<td>Normal n (%)</td>
</tr>
<tr>
<td>Empty sac</td>
<td>39</td>
</tr>
<tr>
<td>Embryonic pole</td>
<td>98</td>
</tr>
<tr>
<td>Small</td>
<td>66</td>
</tr>
<tr>
<td>Normal</td>
<td>32</td>
</tr>
<tr>
<td>Embryonic cardiac activity</td>
<td>72</td>
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</tbody>
</table>

*Normal versus polyploidy P = 0.02; aneuploidy versus polyploidy P < 0.00001.

of empty gestational sacs, small embryonic poles and presence of embryonic cardiac activity prior to pregnancy loss was the same when chromosomally abnormal concepti were compared with normal concepti. The prevalence of empty gestational sacs (~30%), smaller than expected embryonic poles (~50%) and pregnancy loss after documentation of embryonic cardiac activity (53%) are the same as those previously reported in women experiencing repeated spontaneous abortion (Coulam et al., 1994a). In this study, no differences in ultrasonic findings during the first trimester of pregnancy in women who aborted were seen when pregnancies in women with a history of recurrent spontaneous abortion were compared with women with no previous history of abortion. The frequency of chromosomal abnormalities for the ultrasonographic findings of empty gestational sac (59%), smaller than expected embryonic pole, (64%) and pregnancy loss after demonstration of embryonic cardiac activity (69%) is the same as the frequency of chromosomal abnormalities among spontaneous abortions previously reported (Boué et al., 1975; Stern et al., 1996).

An association between morphology and chromosomal anomalies of aborti has been reported (Ohama 1983; Boué et al., 1996). It followed that chromosomally abnormal embryos resulting in first trimester spontaneous abortion might show morphological changes detected by ultrasound. However, there are few data which relate the cytogenetic and ultrasonographic findings for these embryos (Sorokin et al., 1991; Bessho et al., 1995). Empty gestational sacs have been associated with a high prevalence of chromosomal abnormalities (Bessho et al., 1995). Three reports studied the relationship between chromosomal anomalies of abortuses and ultrasonographically measured embryonic pole length in viable embryos which subsequently aborted (Brambati and Lanzani, 1987; Dickey et al., 1994; Bessho et al., 1995). All three studies reported an embryonic pole length in karyotypically abnormal embryos <50th percentile for normal expected at the age of gestation (Brambati and Lanzani, 1987; Dickey et al., 1994; Bessho et al., 1995). One study (Dickey et al., 1994) showed the embryonic pole lengths of aborti with abnormal karyotypes were smaller than those with normal karyotypes that delivered and of abnormal embryos that subsequently aborted. Thus, the literature suggests that: (i) a difference between embryonic pole lengths exists when pregnancies producing live births (normal) are compared to pregnancies ending in spontaneous abortion (abnormal); (ii) no difference in embryonic pole lengths is observed when spontaneous abortions with normal and abnormal karyotypes are compared; and (iii) pregnancies bearing live births of aneuploidic infants are associated with growth retardation (Benacerraf et al., 1994). Taken together, these observations suggest that growth retardation via intrinsic (abnormal karyotype) or extrinsic (normal karyotype) mechanisms is associated with pregnancy loss. Data are accumulating...
which support the concept that immunological events are associated with extrinsic mechanisms involved in growth retardation (Roussev et al., 1993) and pregnancy loss (Coulam et al., 1995; Clark and Coulam, 1996). Although small-for-date viable embryos determined by the ultrasonographic measurement of embryonic pole lengths are at subsequent risk of demise (Brambati and Lanzani, 1987; Bessho et al., 1995), their karyotype cannot be predicted based upon embryonic size. The mechanisms, either intrinsic or extrinsic, by which embryos stop their growth remain unknown.

While spontaneous abortions after establishment of fetal cardiac activity are infrequent (5% of all pregnancies) (Check et al., 1985), chromosomal abnormalities among such pregnancies have been documented (Bessho et al., 1995). In a previous study on spontaneous abortions (Stern and Coulam 1992), 50% occurred after documentation of embryonic cardiac activity. This figure of 50% is similar to the 53% obtained in the present study. Nevertheless, when chromosomal analyses were compared in this group of concepti, significantly more were normal (31%) or aneuploid (67%) than polyploid (3%). However, there was no significant difference between the frequencies of normal and aneuploid analyses. Thus ultrasonographic findings early in pregnancy cannot predict the karyotype of spontaneous abortions.

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References

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