Analyses of 95 First-Trimester Spontaneous Abortions by Chorionic Villus Sampling and Karyotype

CHARLES M. STROM, NORMAN GINSBERG, MICHAEL APPLEBAUM, NADER BOZORGI, MELODY WHITE, MELISSA CAFFARELLI, and YURY VERLINSKY

Submitted: April 23, 1992
Accepted: July 20, 1992

Purpose: Our purpose was to determine the incidence of chromosomal aneuploidy in first-trimester pregnancy losses using chorionic villus sampling (CVS).

Study Design: All patients presenting for CVS with no fetal cardiac activity were offered CVS.

Results: Cytogenetic results were completed in 95 of 96 cases (99%). Eighty-three percent of the karyotypes were aneuploid. The 16 euploid fetuses had no excess of females.

Conclusion: CVS is the most reliable method of determining the karyotype of spontaneously aborted fetuses. The incidence of aneuploidy is much greater than in previous reports that analyzed passed products of conception. CVS should be offered to women who present with first-trimester spontaneous abortions.

KEY WORDS: chorionic villus sampling; karyotype; spontaneous abortions; first trimester.

INTRODUCTION

Approximately 15% of recognized pregnancies spontaneously abort between the 6th and the 28th weeks of gestation (1). Many studies of the cytogenetic findings of spontaneous abortions have been undertaken. In all but three of these studies, tissue culture of products of conception was used to obtain karyotypes. Most such studies have observed an approximately 50% incidence of aneuploidy in samples of combined first- and second-trimester spontaneous abortions. These studies also have revealed an excess of females in euploid fetuses (2–9). Two studies have revealed an excess of euploid male fetuses (10,11). Contamination of the cultures with maternal cells has been proposed as a potential etiology for the excess of females among chromosomally normal spontaneous abortions. Guerneri et al. demonstrated a 76.7% aneuploid rate when analyzing chorionic villi from retained abortions (12).

A recent study applied chorionic villi direct preparation methods to karyotype products of conception after the tissue was passed from the uterus (13). This study also revealed an approximately 50% incidence of aneuploidy (50.1%) and an abnormal sex ratio of 0.71 male:female among euploid fetuses.

Two studies have been reported involving chorionic villus sampling (CVS) of first-trimester spontaneous abortions. In one study (13), 19 patients who presented with blighted ova or spontaneous abortion consented to have CVS performed prior to removal of the products of conception. Unlike all previous studies involving spontaneous abortions, 100% of these karyotypes demonstrated aneuploidy. Since there were no euploid karyotypes, no sex ratio for euploid fetuses was obtained. In a continuation of this study, 24 of 26 fetuses had abnormal karyotypes when analyzed following CVS. Both normal results were male (14).

The present study analyzed 96 first-trimester pregnancies with spontaneous abortions or blighted ova. Karyotypes were completed in all but one case. Aneuploidy was observed in 83% of the cases. Of the 16 euploid fetuses, 9 were male and 7 were female. This study suggests that the excess of females observed in products of conception of spontaneous abortion material is due to karyotyping of maternal cells giving rise to an underestimate of the
true incidence of aneuploidy in spontaneous abortion material.

MATERIALS AND METHODS

In the present study, all women presenting for CVS who were found to have either a spontaneous abortion or a blighted ovum were offered CVS. Ninety-six women consented to the procedure. CVS was accomplished by either the transcervical or the transabdominal approach under real-time ultrasound guidance. Karyotypes were performed using direct and tissue culture methods described previously (15). There is no overlap of patients from this previous study (15) and the current study.

RESULTS

Two thousand eight hundred eighteen consecutive patients presented to the Reproductive Genetics Institute at Illinois Masonic Medical Center for chorionic villi sampling between 9 and 13 weeks of gestation after July, 1988. The indications for CVS are shown in Table I. The majority (92%) of patients was of advanced maternal age, defined as 35 years or older at the estimated date of confinement, although 97 (3.4%) of these patients had an additional indication for CVS. One patient was referred by one of the authors for CVS following an office diagnosis of a spontaneous abortion.

The age distribution of the 2818 patients is shown in Table II. The average age of all patients was 37.1 years of age. All patients had ultrasound examinations prior to the CVS procedure. In 127 (4.5%), no fetal cardiac activity was detected and the diagnosis of spontaneous abortion or blighted ovum was made. Each patient was offered a CVS to determine the fetal karyotype. Ninety-six patients (75%) requested the CVS procedure.

Karyotypes were completed on 95 of the 96 samples (99%). The single failure consisted of an extremely small sample (approximately 2 mg of villi) and microscopic examination of the villi showed severe hydropic changes. Of the 95 successful analysis, 78% were complete for both the direct and the tissue culture results, and in 21% the direct preparations did not yield interpretable results. In one case, results were obtained from the direct preparation only. There were no discrepancies between the direct and the tissue culture results in these 95 spontaneous abortion samples.

The 95 karyotype results are shown in Table III. Normal karyotypes were observed in 16 cases. Of