Recurrent early pregnancy loss due to trisomy 21.

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Introduction
Numerical chromosomal aberration is the most common cause of early pregnancy loss. Incidence of this aberration is reported to be between 30 and 80%\(^1,2\). While studies lay emphasis on chromosomal aberrations, very few reports are available on their causing consecutive recurrent early pregnancy losses (REPL)\(^3-5\). We report identical chromosomal aberration observed in two consecutive early pregnancy losses of the same couple.

Case report
Couple B had conceived three times during 4 years of married life. First one was a spontaneous conception, resulting in an abortion at 5\(^{th}\) weeks.

Second pregnancy was 2 years after the first abortion. This conception was in clomiphene induced cycle. Ultrasonography at 6\(^{th}\) week revealed a fetus with very low cardiac activity. Mother was given chorionic gonadotrophin and micronised natural progesterone. However, at 8\(^{th}\) week ultrasonography revealed a missed abortion. The products of conception were submitted to karyotyping.

The 3\(^{rd}\) pregnancy was after one year. This pregnancy was also after clomiphene citrate stimulation, and was supported by chorionic gonadotrophin and micronised natural progesterone. However, at 8\(^{th}\) week ultrasonography revealed a missed abortion. The products of conception were submitted to karyotyping.

The 3\(^{rd}\) pregnancy was after one year. This pregnancy was also after clomiphene citrate stimulation, and was supported by chorionic gonadotrophin and progesterone vaginal pessaries. Ultrasonography revealed missed abortion at 7\(^{th}\) week of gestation. Fetal pole was not seen on ultrasonography.

Karyotype analysis
Products of conception of this abortus were also submitted to karyotyping.

Her other investigations and related history were not contributory to REPL.

Karyotype analysis
Products of conception from second and third pregnancies were collected aseptically and cultured using routine tissue culture technics. The cells were separated by enzymatic digestion and grown on DMEM F 12 medium supplemented with fetal calf serum. The metaphases were obtained after colchicine treatment followed by fixation. All the metaphases from the tissue of both the abortuses showed 47 XY karyotype. The extra chromosome in both the abortuses was a small acrocentric chromosome which was identified as chromosome 21 (Figures 1 and 2).

Karyotype analysis of both the partners was normal.

Discussion
Two consecutive abortuses of this couple showed numerical chromosomal aberration namely trisomy 21. The earlier preceding abortus was not karyotyped. However a possibility of similar aberration cannot be ruled out. Since, both the fetuses had chromosomal aberration, pregnancy loss could not be avoided even after early progesterone support. Furthermore, continuation of these pregnancies would have produced chromosomally abnormal babies.

Couples with REPL are routinely karyotyped to rule out balance translocations. Of them 2.4% have balanced translocations and remaining show normal karyotype. The cause of REPL remains idiopathic in these couples. Despite having normal karyotype these couples have abortuses with numerical chromosomal aberrations due to nondisjunctions.
Hence, it can be emphasised that in REPL cases it is important to analyse chromosomal patterns of the fetus, for exact diagnosis and for counseling the couple.

This couple had normal karyotype and trisomy 21 was observed in two consecutive abortuses. Similar observations were reported by Brancati et al. and Pergament et al. In both these reports three consecutive pregnancies had triploidy. On the otherhand, Stephenson et al. had found anuplodic pattern of chromosomes in four women. In all of them consecutive pregnancies also had trisomies involving dissimilar chromosomes. Any trisomy or monosomy of similar or dissimilar chromosome is caused by nondisjunction. All the above studies are indicative of the fact that the causative factor in REPL is chromosomal aberrations due to nondisjunction.
Trisomies of nearly all the chromosomes are observed in the first trimester abortuses. Trisomic cells are formed due to nondisjunction either at meiosis or mitosis. Since nondisjunction of the same chromosome took place at least twice in this couple we postulate that there could be some kind of predisposing factor giving rise to nondisjunction leading to CIN in REPL. Karyotype analysis of the fetus is essential for the diagnosis of abortion as well as for monitoring the next pregnancy in REPL.

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Reference