

Trisomy 16, Cause of First Trimester Abortion

Madam, Trisomy 16 is the most frequent autosomal anomaly seen in early spontaneous abortions, accounting for 15% of all chromosomally abnormal early spontaneous abortions and suggesting a high rate of non-disjunction of this chromosome¹. This trisomy is thought to be lethal in the non-mosaic state and incompatible with full fetal development¹. Deoxyribonucleic studies in aborted conceptuses with trisomy 16 have demonstrated a maternal origin in all cases². There have been cases of confined placental mosaicism, fetal mosaicism and partial trisomy involving chromosome 16 reported in term fetuses. The prenatal detection of trisomy 16 cells is associated with a high probability of fetal death, preterm delivery, intrauterine growth retardation and fetal anomaly³. The various outcomes may reflect the diversity of mechanisms involved in the resolution of this abnormality. As 80% of these patients were ascertained because of the abnormal levels of maternal serum alpha fetoprotein (MSAFP) or maternal serum human chorionic gonadotrophin (MSHCG), the increased use of maternal serum screening should bring much more cases to clinical attention^{4,5} which should be followed by amniocentesis and karyotyping.

We report the results of chromosomal studies conducted on products of conception from a 30 years old primigravida, after a non-consanguineous marriage. The history was unremarkable for any familial illness. Her β HCG performed at 4 weeks showed a level of 479.88 (3-4 weeks range 9-130 IU/L). Mother started bleeding per vaginum at 7 weeks of gestation. Transvaginal ultrasound performed showed a well-defined gestational sac measuring 24 mm compatible with 6 weeks and 5 days of gestation. Since a proper fetal pole was not identified, curettage was performed and histopathology of products of conception revealed necrotic and haemorrhagic decidua along with many chorionic villi covered with unremarkable cytotrophoblastic and syncytiotrophoblastic cells. No evidence of molar change was found. Chromosomal analysis showed trisomy 16.

Disorders associated with chromosome 16 abnormalities include both numerical as well as structural abnormalities. Among the numerical abnormalities, full trisomy 16 is not compatible with life and is the most common chromosomal cause of first trimester abortion. Mosaicism is seen in some but not all of the cells of the affected individual's body. Whereas, a mosaic form confined to the placenta also exist in addition to uniparental disomy of chromosome 16. Structural abnormalities include 16p-, 16q-, 16p+, 16q+, unbalanced translocation, inversion and many other combinations of deletions and/or duplication¹. This wide range of variation leads to a wide variety of outcomes, from no obvious problems to severe physical and mental handicaps, most commonly intrauterine growth retardation, congenital heart disease and developmental delay. The various outcomes may reflect the diversity of mechanisms involved in the resolution of this abnormality³.

Prenatal diagnosis is possible after high-risk results for Down's syndrome and neural tube defects in maternal serum screening⁴. Reported results displayed unusually elevated levels of human chorionic gonadotrophin and raised levels of alpha-fetoprotein values, which are consistent with abnormal placental function in trisomy 16 mosaicism⁴. Serial ultrasound evaluation to detect any late onset growth retardation and fetal echocardiography may be indicated for patients with extraordinary high levels of HCG, especially if MSAFP is also elevated.

The increased use of maternal serum screening should bring more cases to clinical attention. In cases with increased risk for both Down's syndrome and NTD, fetal karyotyping should preferably be done on placental biopsy, especially when ultrasound in the absence of anomalies demonstrates early IUGR. Presence of high levels of trisomic cells in the placenta alone consistently produces a more variable inhibition of fetal growth, which may also, in cases, be associated with late pregnancy loss.

Finally, it is to emphasize the importance of prenatal serum screening and cytogenetics analysis of the first spontaneous abortion. More than 50% of spontaneous abortions have an abnormal karyotype. The cytogenetic evaluation of reproductive losses is carried out by culture of the products of conception sent to the laboratory after evacuation. Today a woman is considered a 'habitual aborter' when she has had 3 or more miscarriages. The lack of information increases prenatal distress for the uncertainty it creates about the outcome of next pregnancy. Furthermore, if we establish that a couple must be studied only after their third abortion, we will not only have lost a chance to know the cause of previous miscarriages, which would allow us to select the additional studies they should undergo, but also to identify couples with high risk of having children with chromosomal disease because of parental chromosomal aberrations.

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References

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