Abstract

Objective: In this study, the abnormal cytogenetic report of the spontaneous abortion material was presented and it was discussed in the light of the related literature.

Case: A 30 yearold woman had spontaneous pregnancy after 5 years of infertility history and 2 unsuccessful IVF programme. When she was at her 9th gestational week the patient was diagnosed to have a blighted ovum. After surgical curettage, the abortus material was transferred to genetics laboratory in a sterile culture medium and long term tissue cultures were set up in three different flasks.

Conclusion: The cultivation of the abortion material revealed 49,XY,+8,+20,+21 karyotype. We here present the study, as this is the first triple aneuploidy case with this unique chromosomal combination and also aim to remind the probability of the occurrence of different aneuploidies in the same abortion material.

Keywords: Chromosomal abnormalities, spontaneous abortions, triple trisomy.

Triple Autosomal Trisomy Detected in a Spontaneous Abortion Material

Elif Pala¹, Mehmet Erdem², Ahmet Erdem², Meral Yirmibes Karaoguz¹

¹Gazi Universitesi Tip Fakultesi, Tibbi Genetik, Ankara
²Gazi Universitesi Tip Fakultesi, Kadin Hastaliklar ve Dogum, Ankara

Introduction

The majority of spontaneous abortions occur during the first trimester and over 50% of these miscarriages are chromosomally abnormal.4,5 Single trisomies account for >50% of the chromosomal abnormalities.4 Double trisomies have also been associated with early miscarriages. We have previously reported 2 cases of double trisomies, which comprises 0.49% of all products of conceptions karyotyped.5 Triple trisomy is a rare finding with a frequency of 0.05% in spontaneous abortions.6 To our knowledge only
eleven triple trisomy cases detected within spontaneous miscarriages have been reported so far.\textsuperscript{3,6-11} We here present a case of triple trisomy, with a unique combination of chromosomes 8, 20 and 21 (49,XY, +8,+20,+21); the first triple aneuploidy case with this specific karyotype reported in the literature.

**Case Report**

A 30 year-old, primigravid woman, married with a 35 year old man, was referred to our laboratory for karyotyping the products of conception of her miscarriage. Her past history revealed infertility for 5 years. Her husband had normal sperm concentration but low sperm motility in semen analyses. She had multiple unsuccessful intrauterine insemination cycles with gonadotropins and 2 cycles of IVF. The couples had a complete diagnostic workup for recurrent implantation failure including normal karyotype. This pregnancy occurred spontaneously 2 months after her last IVF attempt. She was at her 9th gestational week according to the last menstrual period at admission. Sonographic examination demonstrated a gestational sac with no fetus and a yolk sac and the patient was diagnosed to have a blighted ovum. Once the couple was informed and informed consent was obtained, surgical curettage was performed under general anesthesia. Curettings of the abortus was collected into a sterile culture medium and transferred to genetics laboratory immediately. After getting material into a steril petri dish (60 mm x 15 mm), it was examined microscopically to exclude the maternal decidua. Explants were transferred into three different flasks with a new sterile medium (Bio-Amf-1 medium, Biological Industries) and placed in a 5% CO2 incubator for long-term tissue culture. Two separate primer cell cultures were culvitated for a period shorter than two weeks and seven metaphase spreads were analysed, sixteen metaphase spreads were counted. Chromosome analysis of the abortion material revealed as 49,XY,+8,+20,+21 karyotype. Pathological examination of the placenta did not show any abnormality (Fig. 1).

**Discussion**

Triple trisomy detected in abortion materials is an exceedingly rare finding. Table 1 presents

<table>
<thead>
<tr>
<th>Table 1. Triple trisomies in spontaneous abortion.</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
</tr>
<tr>
<td>----</td>
</tr>
<tr>
<td>Kajii et al. (1980)</td>
</tr>
<tr>
<td>Johnson et al. (1990)</td>
</tr>
<tr>
<td>Petrella et al. (1991)</td>
</tr>
<tr>
<td>Soukup (1992)</td>
</tr>
<tr>
<td>Reddy (1999)</td>
</tr>
<tr>
<td>†Reddy (1999)</td>
</tr>
<tr>
<td>Reddy (1999)</td>
</tr>
<tr>
<td>‡Reddy (1999)</td>
</tr>
<tr>
<td>Hassold et al. (1984)</td>
</tr>
<tr>
<td>Our case</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
</table>

\* For this case the gestational age 18 weeks, others less than 12 weeks. † For this case the material not reported, others chorionic villus.
*In the report by Dejmek(1992) no reported information for two triple trisomy cases, therefore not listed.
the chromosomal combinations of the triple trisomies studied from spontaneous abortions cultivated from villi reported so far, including our case.\(^6\)\(^{11}\) The chromosomes involved in triple trisomies are 2, 5, 8, 11, 12, 14, 15, 16, 18, 20, 21, 22 and sex chromosomes. The present case was structured coincidentally from the union of the most reported trisomies.\(^6\)\(^{10}\) Nine out of ten cases were aborted in the first trimester period and the cytogenetic analyses of the all cases revealed nonmosaic aneuploidies, similar with the present case. The maternal ages of them are ranged from 29 to 46, concordant with our case. Of these cases 4/10 are over 35 years. Maternal first meiotic division errors predominated for all trisomies including double trisomies. It is unclear how three non-disjunction involving three different chromosomes could occur in triple trisomies. There are several mechanisms including; error in maternal meiosis I involving two chromosomes (like double trisomy) and error in maternal meiosis II involving the third chromosome component, might occur. Hassold et al performed molecular studies to investigate the origin of the triple aneuploidy.\(^11\) They demonstrated that, of the 49,XX,+14, +15,+22 karyotype, trisomy 14 had a maternal origin (Meiosis I). However, they couldn’t evaluate the origin of the chromosomes 15 and 22 in their case. Trisomy, due to the non-disjunction in spermatogenesis could be the other reason for the occurrence of the triple aneuploidies. Trisomy 21 had a significantly increased proportion of paternally derived cases by comparison with all other trisomies.\(^10\) The possibility of paternal inheritance of aneuploidies has triggered investigations on numerical chromosome aberrations in human sperm. Sperm chromosome studies using multicolor fluorescence in situ hybridization technique have shown that the frequency of disomy 21 is higher than the frequency of disomy for other autosomes; suggesting that chromosome 21 has tendency to non-disjunction.\(^12\) Compared with the general male population, men with abnormal sperm parameters appear to have an increased frequency of aneuploidy.\(^15\) There are several studies in the literature investigating whether the asthenozoospermia could be associated with sperm aneuploidies.\(^14\)^\(^{15}\) It seems that low sperm motility could be a reason for altered sperm chromosome segregation as evident for aneuploidies, concordant with the relatively low sperm parameters in our case; which might cause the paternal meiotic division errors.

Figure 1. The karyotype of triple trisomy;49,XY,+8,+20,+21.
Conclusion

As a result, except the trisomies of chromosome 13, 18, 20, 21 and gonosomal trisomies, many trisomies are generally lethal and frequently can be detected in spontaneous abortion materials. The rare triple trisomies, similar with this case, can not be alive. The clinicians who are dealing with this aspects must take care of the triple trisomy reports to explain the reason of the abortion material, especially the ones who have abnormal sperm parameters and/or abnormal sperm motility in their obstetric histories.

References


