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Triple Autosomal Trisomy Detected in a Spontaneous Abortion Material

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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 unsuccesful 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 culvitation 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 probabilty of the occurence of different aneuploidies in the same abortion material.

Keywords: Chromosomal abnormalities, spontaneous abortions, triple trisomy.

Spontan abortus materyalinde belirlenen üçlü otozomal trizomi

Amaç: Bu çalışmada spontan abortus ile sonlanan gebelik materyalinden yapılan sitogenetik çalışmada belirlenen anomalili karyotip ve bunun literatür bilgileri ışığında tartışması sunulmaktadır.

Olgu: 30 yaşındaki olgunun 5 yıllık infertilite öyküsünün ardından, 2 başarısız IVF denemesi sonrası spontan gebeliği oluşmuştu. Gebelik 9. haftasında boş kese (blighted ovum) olarak değerlendirildi ve ailenin onamı ile kürete edildi. Gebelik materyali uygun doku kültürü medyumu içerisinde laboratuvarımıza ulaştırıldı ve üç ayrı flaskta uzun dönem doku kültürü yapıldı.

Sonuç: Uzun dönem doku kültürü sonrası fetüste 49,XY,+8,+20,+21 karyotipi belirlenmiştir. Bu olgu, üçlü (triple) anöploidide ilk defa bu üç kromozomal kombinasyonun birlikte olması ve abort materyalinden yapılan sitogenetik çalışmada birden fazla kromozomun anöploidisinin eşlik edebileceğini göstermesi açısından anlamlıdır.

Anahtar Sözcükler: Kromozomal anomaliler, spontan abortus, üçlü trizomi

Introduction

The majority of spontaneous abortions occur during the first trimester and over 50% of these miscarriages are chromosomally abnormal.[1-3] 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

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eleven triple trisomy cases detected within spontaneous miscarriages have been reported so far.[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 unsuccesful 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 pregnacy occured 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. Curretings 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 1. Triple trisomies in spontaneous abortion.

	2	5	8	11	12	14	15	16	18	20	21	22	X/Y
Kajii *et al.* (1980)	+	+	+										
Johnson *et al.* (1990)									+		+	+	
Petrella *et al.* (1991)	+		+	+									
Soukup (1992)		+						+		+			
Reddy (1999)									+		+		+
†Reddy (1999)							+			+			+
Reddy (1999)	+		+		+								
Reddy (1999)										+	+	+	
‡Hassold *et al.* (1984)						+	+						+
Our case			+							+	+		
Total	3	2	4	1	1	1	2	1	2	4	4	2	3

† 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.*

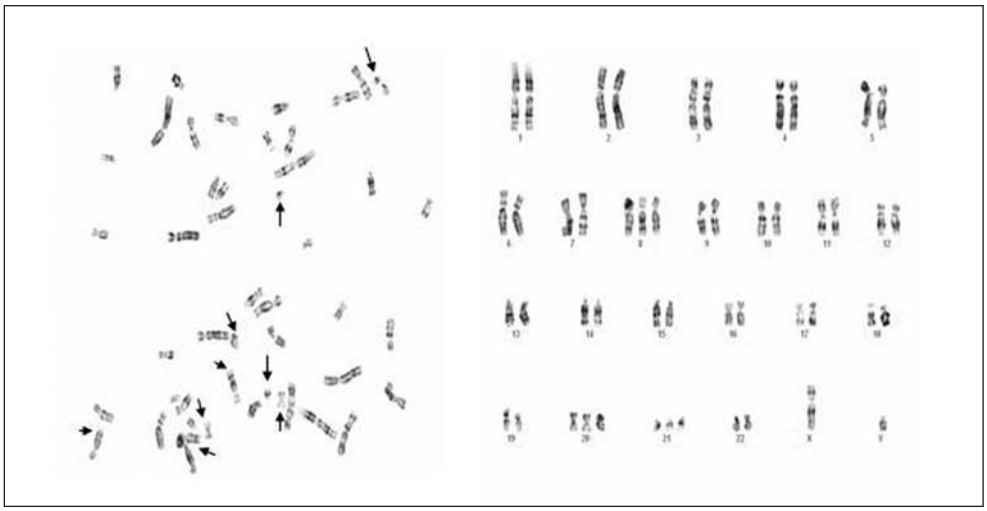

Figure 1. The karyotype of triple trisomy;49,XY,+8,+20,+21.

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 triosomies 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 meisosis 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 (Meisosis 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 occurence 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 parametres appear to have an increased frequency of aneuploidy.[13] 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 divison errors.

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

1. Karaoguz MY, Nas T, Konac E, Ince D, Pala E, Menevse S. Is cytogenetic diagnosis of 46,XX karyotype spontaneous abortion specimens erroneous? Fluorescence in situ hybridization as a confirmatory technique. *J Obstet Gynaecol Res* 2005; 31: 508-13.
2. Ford JH, Wilkin HZ, Thomas P, McCarthy CA. 14-year cytogenetic study of spontaneous abortion: Clinical applications of testing. *Aust NZJ Obstet Gynaecol* 1996; 36: 314-18.
3. Dejmek J, Vojtassak J, Malova J. Cytogenetic analysis of 1508 spontaneous abortions originating from South Slovakia. *Eur J Obstet Gynecol Reprod Biol* 1992; 46: 129–36.
4. Nagaishi M, Yamamoto T, Iinuma K, Shimomura K, Berend SA, Knops J. Chromosomal abnormalities identified in 347 spontaneous abortions collected in Japan. *J Obstet Gynaecol Res* 2004; 30: 237-41.
5. Korucuoglu U, Erdem M, Pala E, Karaoguz MY, Erdem A, Biri A. Double aneuploidy in spontaneous miscarriages: Two case reports and review of the literature. *Fetal Diagn Ther* 2008; 24: 106-10.
6. Reddy K S. Triple aneuploidy in spontaneous abortions. *Clin Genet* 1999; 56: 103-4.
7. Kajii T, Ferrier A, Nikawa N, Takahara H, Ohama K, Avirachan S. Anatomic and chromosomal anomalies in 639 spontaneous abortuses. *Hum Genet* 1980; 55: 87-98.
8. Johnson MP, Drugan A, Koppitch FC, Uhlmann WR, Evans M I. Postmortem chrorionic villus sampling is a better method for cytogenetic evaluation of early fetal loss than culture of abortus material. *Am J Obstet Gynecol* 1990; 163: 1505-10.
9. Petrella M J, Hirschhorn K, German J.Triple autosomal trisomy in a pregnancy at risk for Bloom's syndrome. *Am J Med Genet* 1991; 40: 316-318.
10. Soukup S W. Triple trisomy in a spontaneous abortion. *Hum Genet* 1992; 88: 363.
11. Hassold T, Chiu D, Yamane J. Parental origin of autosomal trisomies. *Ann Hum Genet* 1984; 48: 129-44.
12. Egozcue J, Blanco J, Vidal F. Chromosome studies in human sperm nuclei using fluorescence in situ hybridization (FISH). *Hum Reprod Update* 1997; 3: 441-52.
13. Colombero L, Hariprashad JJ, Tsai MC, Rosenwaks Z, Palermo GD. Incidence of sperm aneuploidy in relation to semen characteristics and assisted reproductive outcome. *Fertil Steril* 1999; 72: 90-6.
14. Rives N, Mousset-Simeon N, Mazurier S, Mace B. Primary flagellar abnormality is associated with an increased rate of spermatozoa aneuploidy. *J Androl* 2005; 26: 61-9.
15. Collodel G, Capitani S, Bacetti B, Pammolli A, Moretti E. Sperm aneuploidies and low progressive motility. *Hum Reprod* 2007; 22: 1893-8.