A prenatal tertiary trisomy resulting from balanced maternal 8; 9 translocation

Annenin dengeli 8; 9 translokasyonu sonucu oluşan prenatal tersiyer trizomi

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Abstract

An additional derivative chromosome 8 was found in the cytogenetic analyses of the chorionic villus biopsy specimen of a balanced reciprocal translocation carrier mother. This was a 3:1 segregation of the unbalanced product of the balanced maternal 8:9 translocation. The chromosomes of the carrier of the balanced reciprocal translocation pair with their matching homologous segments at meiosis I, a quadrivalent figure is formed and chromosomes segregate from this configuration. Increased nuchal tranaslucency was also determined on fetal sonography at the 13rd week of gestation. The final karyotype was 47,X Y,+der(8)t(8;9)(q11.2;p22) mat, and the parents were informed about this tertiary trisomy. After genetic counseling, the parents decided to terminate the pregnancy. The presented case is a reminder of the probability of the unbalanced products of the 3:1 segregation, rather than the common 2:2 segregation.

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Key words: Derivative chromosome 8, nuchal translucency, reciprocal translocation, tertiary trisomy, 3:1 segregation

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Özet

Dengeli resiprokal translokasyon taşıyıcısı annenin, koryon villüs biyopsi materyalinden yapılan sitogenetik analizinde, ek olarak derivatif 8. kromozom belirlenmiştir. Bu dengesiz durum, 8. ve 9. kromozomlar arasında dengeli resiprokal translokasyon içeren annenin, 3:1 gamet ayrışımından kaynaklanmaktadır. Resiprokal dengeli translokasyon taşıyıcılarının kromozomları, mayoz 1'de homologları ile eşleşebilmek için quadrivalen yapıyı oluşturmakta ve buradan kromozomların segregasyonu sözkonusu olmaktadır. Gebeliğin 13. haftasında yapılan fetal ultrasonografide ayrıca nukkal kalınlık artışı saptanmıştır. Fetüsün karyotipi 47,XY,+der(8)t(8;9)(q11.2;p22) mat olarak rapor edilmiş ve tersiyer trizomi hakkında aileye bilgi verilmiştir. Aile genetik danışmanlık sonrası gebeliğini sonlandırmaya karar vermiştir. Burada sunulan olgu, resiprokal translokasyon taşıyıcılarının dengesiz gamet oluşumunda 2:2 segregasyonun yanısıra, daha az oranda da olsa 3:1 segregasyon olasılığının da olduğunu hatırlatması açısından önemlidir. (J Turkish-German Gynecol Assoc 2011; 12: 183-5)

Anahtar kelimeler: Derivatif 8. kromozom, nukkal kalınlık, resiprokal translokasyon, tersiyer trizomi, 3:1 segregasyon

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Introduction

Reciprocal translocations are structural chromosomal abnormalities commonly seen in humans, with a frequency of 1:500. The phenotype of the balanced translocation carriers is usually normal; however, they have significant risks of unbalanced progeny or spontaneous abortion (1-3). At meiosis I, the translocated chromosomes pair with their matching homologous at a quadrivalent formation and imbalanced gametes result from the disjunction of these chromosomes for the segregation models i.e. adjacent 1, adjacent 2, 3:1, 4:0 (1, 2).

Offspring of carriers often have 46 chromosomes, including one of the derivative chromosome, so are partially trisomic and partially monosomic for the translocated chromosomes. Nevertheless, a karyotype with 47 or 45 chromosomes due to 3:1 segregation is often complicated by the presence of two partial trisomies or regular and partial monosomies; namely tertiary trisomy/monosomy and interchange trisomy/monosomy. Here, we presented a prenatal tertiary trisomic case with the partial trisomy 8p (and also including a tiny part of 8q; 8q11.2) and the partial trisomy 9p due to 3:1 segregation derived from balanced maternal 8;9 translocation.

Case Report

A 33 year old balanced reciprocal translocation carrier, was referred to us at the 14th week of her third gestation for prenatal cytogenetic analyses. The parent was informed and then signed the informed consent for the invasive prenatal sampling and cultivation of the chorionic villus biopsy specimen. Her first pregnancy had ended with spontaneous abortion at the 7th week and they had a 2-year-old healthy boy from the second pregnancy. Chromosome analyses of the parent had been performed in our laboratory after the first pregnancy and the mother was diagnosed as a balanced reciprocal translocation carrier [t(8;9)(q11.2;p22)] (Figure 1). In this progeny at the 13rd week of gestation, a thickened nuchal fold (10 mm) was also found on fetal sonography. G-banding

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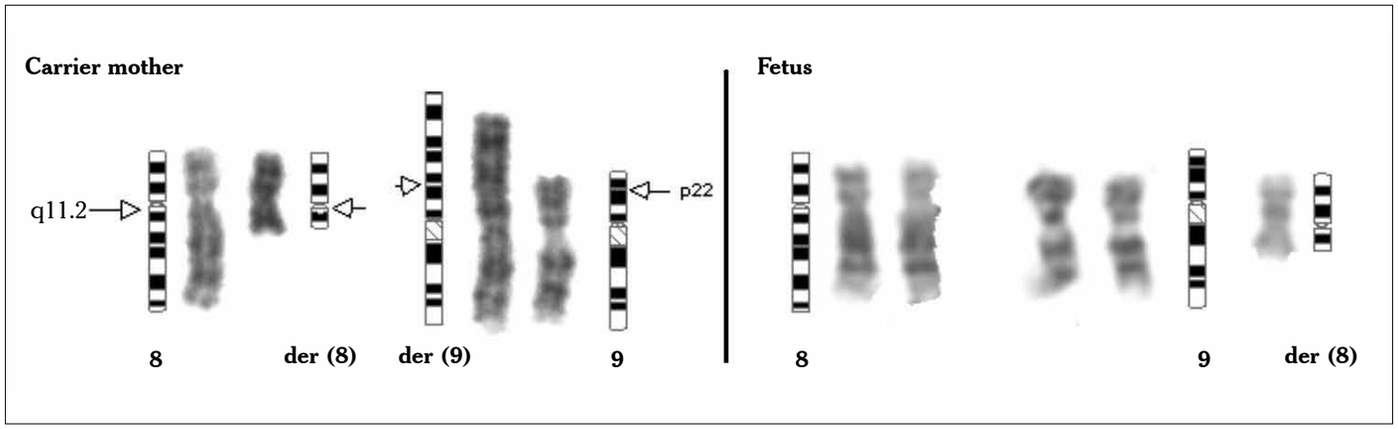

Figure 1. GTG banded partial karyotype and ideogram of carrier mother (left) and the imbalance fetus (right). The arrows indicate the breakpoints

for short-term and long-term tissue cultures and Fluorescence *in situ* hybridization (FISH) technique were performed on the chorionic villus biopsy specimen. FISH was informative for the common aneuploidies but not for the reciprocal translocation because of the lack of the specific probes for the chromosomal rearrangement. We could not obtain a qualified chromosome from short-term tissue culture and the long-term tissue culture result was 47,XY,+der(8)t(8;9)(q11.2;p22)mat (Figure 1). Breakpoints of the derivative chromosome involved the same bands; 8q11.2 and 9p22, as the mother. This was a tertiary trisomy for the whole short arm and a small part of the long arm of the chromosome 8 (8pter→8q11.2) and the partial short arm of the chromosome 9 (9pter→9p22) resulting from the 3:1 segregation of the balanced maternal 8;9 translocation.

The pregnancy was terminated in the 15th week of gestation at another center. We could not evaluate the physical properties, but only learnt from the information obtained from the mother that the fetus had frontal bossing and hypertrichosis.

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Discussion

Balanced reciprocal translocations are usually harmless rearrangements for the carriers, but the derivative chromosomes and their matching homologous form a quadrivalent figure at meiosis I and 2:2, 3:1, and 4:0 segregation models yield mostly unbalanced gametes. The rates of segregant distributions are not a significant distinction in each sex, except the 3:1 category and a predisposition for 3:1 segregation in oogenesis can be confirmed (4-7). The factor for the possibility of segregant models produced by Daniel A (1979), is the percentage of the total haploid autosomal lentgh (HAL) (8). As a viability conceptus, if one of the translocated or derivative chromosomes is small, similar to our case, 3:1 segregation is more likely than the other segregation models (9, 10).

The living patients with tertiary trisomy are mostly reported for chromosome 9p (11, 12). The distal half of the short arm of chromosome 9p (9pter-9p21), approximately the same segment as our case (9pter-9p22) (Figure 1), is responsible for the major clinical features of the syndrome; growth and mental retardation, ear anomalies, hypertelorism etc. (12). The reported cases with trisomy 8p, are generally results of the inversion duplication and of the reciprocal translocations, and their clinical features are hypotonia, neonatal feeding problems, mental retardation, brain and orthopedic abnormalities and specific facial features (13, 14). As far as we know, there is no report which met all the criteria of the translocated segments of our case. A case of trisomy 8p12-pter, quite similar to our case (trisomy 8q11.2-pter) resulting from 8;15 balanced maternal translocation, had similar findings of the other trisomy 8, however, since our case was detected prenatally, we could not evaluate the clinical findings except for the increased nuchal translucency on fetal sonography (14). Nuchal translucency thickness shows an increased risk for trisomies 13, 18 and 21, this also may be true for other regular trisomies and/or tertiary trisomies as well (15). This information can be helpful in genetic counseling and for decision making. The recurrence risk of unbalanced infants is the second important parameter for the reciprocal translocation carriers and their proceeding gestations. The risk from 3:1 disjunction is similar to that for other imbalanced offspring; only the abortion rate for 3:1 disjunction is higher than others (2).

In conclusion, in the couples with chromosomal rearrangement and/or with abnormal fetal sonography findings, cytogenetic analyses and chromosome specific FISH paintings should be performed in the prenatal period. While providing genetic counseling, not only the unbalanced gametes due to 2:2 segregation but also the risk of unbalanced progenies from 3:1 disjunction should be considered and pre-implantation genetic diagnosis could be suggested.

Conflict of interest

No conflict of interest was declared by the authors.

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