Repetitive Pregnancy Loss in inv(22)(p13q12) Carrier

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Introduction

The pericentric inversions are estimated to occur in frequency of 0.12–0.7%, and most commonly discovered in chromosome 1, 9, 16 and Y. Pericentric inversions are usually benign and do not cause any phenotypic effects. However, those inversions can cause an abnormal pregnancy or abnormal offspring by production of recombinant unbalanced gametes. The present report describes a case of pericentric inversion 22 in a female experiencing repetitive pregnancy loss and fetal hydrops, which may have been caused by unbalanced recombinant derived from maternal inv(22)(p13q22).

Case Report

A 37-year-old female underwent an amniocentesis at 15 weeks gestation due to fetal hydrops that was detected in an ultrasonograph examination. This was the fifth pregnancy for her. The patient had previously experienced three times spontaneous abortions at an early gestational age. After abortions, karyotyping analysis had been performed for patient and her husband. Findings had been unremarkable. Subsequently, another pregnancy ended in the successful delivery of a healthy and full-term baby. That baby was healthy (body weight 3,520 g, height 50 cm, and body circumference 35 cm) and didn’t show any abnormal findings. This time pregnancy, amniotic karyotyping analysis revealed an abnormally large p arm of chromosome 22 (22p+), which was suspected to be a derivative chromosome (Fig. 1A). Based on this finding, the previous parental karyotyping data was reviewed again. The review uncovered a chromosome 22 abnormality that was suspected to be an inversion 22 in the maternal karyotype.

Key Words: Recombinant, inv(2), Partial trisomy 22, Repetitive pregnancy loss
Fluorescence in situ hybridization (FISH) analysis was performed to confirm inv(22). The analysis utilized DiGeorge/VCFS region-specific probes (Vysis, Downers, USA) which consist of a TUPLE1 (22q11.2) probe labeled with SpectrumOrange and an ARSA (22q13) probe labeled with SpectrumGreen. One orange and one green signal were evident on normal chromosome 22, whereas one orange and two green signals were found on abnormal chromosome 22 in fetal metaphase cells (Fig. 2A). In the maternal FISH analysis, one orange signal and one green signal were found on both chromosome 22, but each signal was located on each arm of inverted chromosome 22, compared to the location of all signals on only one arm of normal chromosome 22 (Fig. 2B). Therefore, the karyotype of fetus was established as 46,XX,rec(22)dup(22q)inv(22)(p13q12)mat and a maternal karyotype as 46,XX,inv(22)(p13q12).

Discussion

In our knowledge, only eight cases about inv(22) have been reported in the literature. Most of the cases were of liveborn patients who displayed a partial trisomy of 22q due to rec(22) derived from a parental inv(22) carrier. The eight cases shared a similar phenotype such as mental retardation, growth retardation, cleft lip/palate, micrognathia and microcephaly, which have been found in other types of partial trisomy 22 syndrome. In one case, partial monosomy of 22q was derived from a familial inv(22)(p11q12)\(^5\). That patient also revealed some abnormalities, such as mental retardation and dysmorphic phenotypes. In some of the eight cases, the inv(22) carrier parents experienced abnormal pregnancy histories that included repetitive pregnancy loss; whether this is consistent with all the cases is unknown, since not all the reports described the pregnancy history. In our case, the patient experienced repetitive pregnancy loss at early gestational ages and a fetal hydrops. Although the karyotyping analysis was not performed following the unsuccessful pregnancies, partial trisomy 22q or partial monosomy 22q due to recombination might be the main cause of pregnancy loss.

Interestingly, about five of the eight previous inv(22) cases were Hispanics from Mexico. This has led to a suggestion of a "founder effect" and the possibility that rec(22) derived from inv(22) might be a hidden cause of mental retardation in Hispanic people\(^3\). The latter study also suggested that the cause of underestimation of rec(22) is due to the difficulties in detecting rec(22) through conventional karyotyping analysis. Detection of rec(22) is somewhat difficult due to small size and morphologic similarities with normal variant 22 having

![Fig. 1. Karyotyping of fetus (A) and mother (B). Arrowed chromosome 22 in each karyogram represents a rec(22)dup(22q)inv(22)(p12q12) and an inv(22)(p13q12) in fetus and mother, respectively.](image-url)
Identification of inv(22) is similarly difficult. Chromosome 22 is very small in size and bright color in conventional staining method, so it is easy to be overlooked. Although the present patient did successfully give birth to a healthy baby, there was a possibility that the patient experienced another spontaneous abortion without notice because of the missed diagnosis. Therefore, care should be taken in detection of small chromosomal changes like 22 and the possibility of inv (22) as well as rec(22) should be recognized in the examination of infertility cases or prenatal tests. Moreover, additional molecular tests like FISH might be helpful for confirmation of suspected cases.

The present study reports a case of inv(22) (p13q12) carrier who experienced repetitive pregnancy loss and fetal hydrops due to rec(22)dup(22q)inv(22) (p13q12) mat. Careful attention should be paid during examination of chromosome 22 to the probability of inv(22) or rec (22), because detection of such abnormalities can be easily overlooked due to small size and confusing morphology.

References

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