Reciprocal translocations are relatively common chromosomal structural rearrangements in humans, with a population frequency rate of 1 per 673 to 1 per 1000. Although carriers of balanced translocations generally have a normal phenotype, their reproductive potential is uncertain. They may produce unbalanced gametes during meiotic segregation of their abnormal chromosomes, which could lead to an increased risk of infertility, spontaneous recurrent abortions, or children with birth defects.

Prenatal diagnosis is effective in detecting unbalanced rearrangements resulting from a balanced rearrangement in one of the parents. Of the 4 possible segregation patterns of most translocations, 2 may produce unbalanced gametes with segmental aneusomies of the chromosomes involved in the rearrangement. This possibility makes follow-up genetic counseling challenging, due to concerns about abnormal outcomes after birth.

This report describes a family with a reciprocal and balanced translocation between chromosome 9 and 13 in the mother, for whom prenatal diagnosis had been performed in 2 of her 4 pregnancies. We compared the genetic and clinical findings from the prenatal diagnoses and postnatal follow-up with previous cases to evaluate the compound...
effect of the segmental aneusomies. The decision of the couple regarding each of the pregnancies is also described herein, highlighting the difficulty in decision making despite genetic counseling.

Clinical History

A South Indian couple of a 33-year-old man and a 25-year-old woman who presented with no family history of miscarriages was referred to our fetomaternal unit for prenatal diagnosis and genetic counseling because of significant ultrasound markers in her third pregnancy. The prenatal sonographic study of her first fetus had showed holoprosencephaly; this pregnancy was terminated at the 20th week. The next pregnancy resulted in spontaneous abortion at 2.5 months. Unfortunately, chromosomal analysis was not performed for these first 2 pregnancies.

For the third pregnancy, ultrasound at 13 weeks, 4 days’ gestation detected an alobar holoprosencephaly and increased nuchal thickness of 4.1 mm. On the advice of their healthcare team, the parents underwent chorionic villus sampling, which revealed a partial deletion in the terminal region of the long arm of chromosome 13. In view of these findings, parental karyotyping was strongly recommended to establish the origin of the aberration. After genetic counseling, the couple chose to terminate the third pregnancy. Induction of labor was accomplished, and a stillborn infant weighing 16.94 g was delivered and was sent for autopsy. The autopsy examination confirmed fetal hydrops, nuchal edema, indeterminate genitalia, oligodactyly of the right foot, holoprosencephaly, and an asymmetric fused horseshoe kidney with anterior ureter.

After 1 year, the couple approached us with their fourth pregnancy. Ultrasound monitoring found a single umbilical artery with unilateral renal agenesis. Amniocentesis was performed at 20 weeks’ gestation, and chromosomal analysis of the cultured amniocytes revealed a derivative chromosome 9 resulting in a partial trisomy 13. After genetic counseling, the couple made an informed decision to continue the pregnancy. A full-term female infant was delivered by lower-segment caesarean section and had a birth weight of 3.1 kg. The infant had microphthalmia, a single umbilical artery, and genitourinary tract and gastrointestinal tract anomalies. Ultrasonographic imaging of the abdomen revealed the absence of a right kidney, although the echocardiography and neurosonography results were normal. Immediately after birth, the infant was admitted to the neonatal intensive care unit (NICU) for observation and phototherapy for jaundice, unrelated to the chromosomal condition. On the sixth day, the infant was readmitted to the NICU for aspiration pneumonitis; she died on her 52nd day in the hospital.

Cytogenetic Study

Chorionic villus sampling and amniocentesis were performed and processed for conventional cytogenetic analysis using standard protocols. Chromosomes subjected to Giemsa staining after trypsin treatment and analyzed on the CytoVision karyotyping platform (Leica Biosystems Nussloch GmbH, Nussloch, Germany) in fetus A from the third terminated pregnancy showed a partial deletion in the terminal region of the long arm of chromosome 13 designated as 46,XY,del(13)(q33) (Image 1A) and a derivative chromosome 9 resulting in a partial trisomy 13 designated as 46,XX,der(9)t(9;13)(p24;q33) (Image 1B) according to the reference guide An International System for Human Cytogenetic Nomenclature (ISCN2009). Image 1C depicts a balanced translocation 46,XX,t(9;13)(p24;q33) harbored by the female proband.

We performed a conventional cytogenetic study of the couple, who are nonconsanguineous, on peripheral blood phytohemagglutinin (PHA)–stimulated 72-hour lymphocyte culture using GTG (G-bands by trypsin using Giemsa staining) banding. The father had the normal karyotype 46,XY. The mother was found to be a carrier of balanced reciprocal translocation between chromosome 9 and 13 with karyotype 46,XX,t(9;13)(p24;q33). Karyotyping for the parents and sister of the female proband revealed that her
mother was a carrier of the same balanced translocation but had no history of recurrent abortions. Also, the sister of the female proband had a normal karyotype.

### Discussion

In our case report, we described the prenatal diagnosis of a partial monosomy 13 in one pregnancy and partial trisomy 13 in another pregnancy, both of which resulted from the abnormal chromosome segregation of a maternal reciprocal translocation. The most noticeable prenatal finding was alobar holoprosencephaly in the first and third pregnancies. We were not able to perform a chromosomal study of the first 2 fetuses conceived by the couple, and so genotype-phenotype correlation was not possible. However, because the ultrasound findings of the first pregnancy were similar to those of the third pregnancy, we hypothesize that partial monosomy 13 had recurred in the third pregnancy.

The autopsy findings for the fetus with partial monosomy 13, from the third pregnancy, revealed fetal hydrops, nuchal edema, indeterminate genitalia, oligodactyly, holoprosencephaly, and fused kidneys. A similar report of a fetus with partial trisomy 7p and partial monosomy 13q at 24 weeks’ gestation revealed microcephaly, an irregular-shaped skull, nuchal edema, and Dandy-Walker malformation.

At birth, partial monosomy 13 usually is apparent because of the features of low birth weight, craniofacial abnormalities, genital malformations, oligodactyly, and varying degrees of intellectual disabilities. Because there was available evidence for the abnormal phenotype in a previous case report, the concerns of the couple were addressed adequately and conformed to the nondirective norm during the genetic counseling session. The couple then made an informed decision to terminate the pregnancy based on their social and economic situation.

However, in their fourth pregnancy, the fetus was detected to carry partial trisomy 13. Despite the abnormal ultrasound findings, abnormal chromosome findings, and available information on the postnatal prognosis, the couple chose to continue the pregnancy. The genetic counselors and medical team respected that decision, and the pregnancy continued with careful monitoring of fetal viability.

However, the infant girl died of postnatal complications by the second month, and her autopsy revealed microphthalmia and the absence of a right kidney. Our findings are in accordance with those of previous reports of prenatal and postnatal diagnosis of trisomy 13, which included single umbilical artery and genitourinary-tract and gastrointestinal-tract anomalies. Moreover, partial trisomy 13, like trisomy 13, is not considered to be compatible with long-term postnatal survival.

Further examination of the pedigree and chromosomal analysis of multiple family members revealed that the translocation was hereditary in the maternal line. The only difference between the female proband and similar case individuals was that there were no reports of infertility, miscarriages, or abnormal offspring in her reproductive history. She had 1 other biological child who was chromosomally normal. These findings reflect the complexity of chromosome segregation, in which a chromosome rearrangement can go undetected in successive generations but subsequently appear in a family, resulting in multiple consequences.

In view of the consecutive abnormal pregnancies mentioned in this case report, we strongly recommend prenatal diagnosis for all individuals with balanced chromosome rearrangement. With the development of preimplantation genetic diagnosis (PGD) for chromosomal rearrangement, new data concerning segregation modes in female translocation carriers are emerging. In vitro fertilization (IVF) with PGD is currently being offered to carriers of balanced translocations to increase their chances of conceiving, to decrease their probability of miscarriages, and to avoid abortions.

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### References


