Case Presentation

We report a case of rare familial unbalanced translocation of chromosomes 7 and 12 which was diagnosed prenatally at 20+3 weeks of gestation. Woman’s partner had been tested in the past and found to be a carrier of a balanced translocation. Partner’s brother has an unbalanced form of the translocation with severe learning disability.

The diagnosis of the anomaly was based on two and three-dimensional ultrasound and microarray analysis. Ultrasonographic findings included fetal microcephaly and holoprosencephaly, dysmorphic face and hyper-echogenic bowel. Cytogenetic results from the amniotic fluid showed unbalanced translocation in chromosome 7 and 12 with deletion of an approximately 16.5 Mb and a duplication of 6.1 Mb respectively. Chromosomals analysis confirmed that this result represents an unbalanced translocation product from a translocation between chromosomes 7 and 12. This unbalanced translocation product has been inherited by the balanced translocation in this fetus’ father.

In view of the presentation of this case and strong family history of affected family members the risk of recurrence of an unbalanced translocation for subsequent pregnancies is thought to be 20%.

Discussion

Possible outcomes of subsequent pregnancies include [3]:

a) Entirely normal karyotype.

b) Balanced translocation; people who carry such a balanced rearrangement of their chromosomes are not affected by it. The only time that it is important to them is when they come to have children, when their offspring can inherit what is called an unbalanced form of the translocation.

c) Unbalanced translocation; which may cause miscarriage or handicap.

Prenatal diagnosis would be possible in two forms: pre-implantation genetic diagnosis (PGD) or invasive prenatal diagnostic tests such as chorionic villous sampling (CVS) or amniocentesis. After PGD, successful in vitro fertilisation (IVF) rate is about 35%. This couple did not experience any fertility problems or previous miscarriages. In view of this, for future pregnancies, parents opted for early prenatal testing (CVS) and for termination of pregnancy if an unbalanced type of translocation is diagnosed.

Results

Cytogenetic Investigations:

Parental Karyotyping:

- Woman’s blood: 46 XX
- Partner’s blood: 46, XY, r(7;12)(q34; q24,32)

Male karyotype with a balanced translocation long between arms of chromosomes 7 and 12 with breakpoints 7q34 and 12q24,32.

Fetal amniotic fluid:

- Micro-Array:
  - Fetal amniotic fluid: Arr 7q34q36.3(142,668,576-159,161,648)x1, 12q24.32q24.33(127,708,720-133,777,560)x3

Genome wide array analysis indicated a copy number loss for the long arm of chromosome 7 with breakpoints at 7q34 and 7q36.3 and a copy number gain for the long arm of chromosome 12 with breakpoints at 12q24.32 and 12q24.33. This result is consistent with a deletion of approximately 16.5 Mb and a duplication of 6.1 Mb respectively. Chromosome analysis confirmed that this result represents an unbalanced translocation product from a translocation between chromosomes 7 and 12 (i.e. der (7/t(7;12)(q34; q24,32))pat). This unbalanced translocation product has been inherited by the balanced translocation in this patient’s father.

Deletion of 7q24 and 7q36 is associated with growth retardation, cleft lip and palate and dysmorphic face [1]. This deletion also includes the SHH gene: deletion of the SHH gene is associated with holoprosencephaly. Duplication of the 12q24 is associated with multiple congenital abnormalities [2] including holoprosencephaly, cleft palate and dysmorphic face.

The array analysis result obtained was consistent with XY (male) chromosome complement.

Post-Mortem Report:

The body of fresh male baby was examined (Figure 1), whose measurements are consistent with 20 weeks gestation. The skin showed no maceration. There was microcephaly with alobar holoprosencephaly, the head showed flat occiput; poorly lobated lungs; the face was abnormal: there was hypotelorism, a large nose with a single nostril and a small mouth; the ears were normal. The limbs and digits were normal but there was flexion of elbows and fingers. The trunk (back, chest, heart, abdomen) was normal. The anus and nares were patent. External genitalia were normal male. Umbilical cord attached measured 8x0.7cm and had 3 blood vessels.

Figure 1: Antenatal US images and photograph taken in the neonatal period

![Antenatal US images and photograph taken in the neonatal period](image)

1. Cerebellum
2. Alobar holoprosencephaly
3. Alobar holoprosencephaly
4. Hyper-echogenic bowel
5. Flat occiput
6. Absent nasal bone
7. Single nostril

References:


3) Great Ormond Street Hospital (GOSH), Counselling letter, Genetics Department, 2014