Additional chromosome in a child as a result of a balanced reciprocal translocation t(12;18)(p13;q12) in his mother’s karyotype

In case of a balanced reciprocal translocation the exchange of fragments between two chromosomes does not cause any addition or loss of genetic material in the carrier. However the consequence of this type of chromosome aberration in meiosis is formation of a quadrivalent and production of 20–70% of unbalanced gametes due to disorders in quadrivalent disjunction (Goldman et al. 1993; Oliver-Bonet et al. 2002; Patel et al. 2004; Morel et al. 2004; Kozma et al. 2004). The result of meiotic segregation depends upon several factors, such as morphology of the chromosomes involved, the length of the interstitial and translocated segments, as well as the number and location of chiasmata that determine the quadrivalent orientation (Oliver-Bonet et al. 2002). However, the problem of quadrivalent segregation is still discussed.

In this case report we present a child with an additional chromosome in the karyotype. The karyotypes of the boy and his parents were analyzed by use of a conventional banding technique (GTG) and fluorescence in situ hybridization (FISH). Probes painting whole chromosomes 12 and 18 were used in FISH. Cytogenetic examination of the parents revealed that his mother was carrying balanced reciprocal translocation between chromosomes 12 and 18. Her karyotype was described as 46,XX,t(12;18)(p13;q12). Father’s karyotype was normal, described as 46,XY. The boy’s karyotype was defined as 47,XY,+der(18)t(12;18)(p13;q12). The additional chromosome appeared probably due to 3 : 1 meiotic disjunction of the maternal balanced translocation, known as tertiary trisomy. The mother displayed a normal phenotype and delivered earlier a healthy child. However, the boy with the unbalanced karyotype shows multiple congenital abnormalities.

Key words: FISH, reciprocal translocation, segregation 3 : 1, tertiary trisomy.

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In the course of pregnancy, oligohydramnios was observed. Moreover, perinatal asphyxia was diagnosed. He was subjected to genetic examination due to multiple congenital abnormalities, including dysmorphic face with a broad and high forehead, flat bony face, Gothic palate, low-set poorly modeled ears, narrow palpebral fissures, short nose with a broad bridge, hypertonia, anal atresia, bilateral cryptorchidism. The organs in the abdominal cavity showed the following characteristics: left hydronephrosis, smooth urinary bladder, adrenal glands without changes. In the 10-month-old boy ultrasound and echocardiography showed ventricular system symmetrical. Examination demonstrated also micro pulmonary incompetence, marginal tricuspid as well as mitral incompetence, without leaks in atrias and ventricles of the heart. The aortic arc is left-sided and the circulatory system is competent. The boy had a normal chest and vertebral column. At present, he is 2-year-old. He is 84 cm high and weighs 11.0 kg. So far no anomalies in the nervous system have been observed. The child demonstrates poor psychomotor activity and feeding difficulty.

Blood samples were taken from the proband, both parents and his healthy elder brother. Cytogenetic examination was carried out using standard techniques of peripheral blood lymphocyte culture, according to the method of Arakaki and Sparkes (1963) with minor modifications. The karyotypes were analyzed using the GTG banding technique.

The karyograms were prepared according to the recommendation of the International Standing Committee for Human Cytogenetic Nomenclature (ISCN 1995).

Whole chromosome 12 painting probe as well as whole chromosome 18 painting probe (Qbiogene)
were used according to the manufacturer’s instruction in fluorescence in situ hybridization (FISH).

The mother was found to carry a balanced reciprocal translocation, in which chromosomes 12 and 18 were involved 46,XX,t(12;18) (p13;q12). Chromosome analysis of the proband showed the presence of an additional chromosome in the karyotype. Partial karyograms of the mother and the proband with the unbalanced karyotype are shown in Figure 1A and 1C. The FISH method confirmed that the mother carries a balanced reciprocal translocation between chromosomes 12 and 18 (Figure 1B). Moreover, on the basis of the FISH and GTG findings, the unbalanced karyotype of the proband was described as 47,XY,+der(18)t(12;18)(p13;q12) and interpreted as a result of 3 : 1 segregation of the maternal tetravalent configuration (Figure 1C and 1D). The proband’s father and brother showed the normal karyotype 46,XY (data not shown).

Many carriers with balanced reciprocal translocations exhibit regular phenotypes (Wojda et al. 2003). Several authors described cases of balanced reciprocal translocations associated with mental retardation, behavioral abnormalities, and early mortality (Braddock et al. 2000; Bugge et al. 2000; Santos et al. 2003). In the present case the mother with the translocation t(12;18)(p13;q12) was phenotypically normal.

Segregation of the quadrivalent during meiosis depends on different conditions. The 3 : 1 segregation is preferred when one of the chromosomes (normal or derivative) in the quadrivalent is small. The der(18)t(12;18) is small in comparison to the normal chromosome 12. Thus the presence of an additional small derivative chromosome in the proband’s karyotype can be explained by 3 : 1 segregation. This type of 3 : 1 segregation is known as tertiary trisomy (Patel et al. 2004).

Thus results of this case study provide further information about genotype/phenotype interaction in patients with reciprocal translocations.

REFERENCES


