MULTIPLE CONGENITAL ANOMALIES IN ASSOCIATION WITH SUPERNUMERARY CHROMOSOME 47 INHERITED FROM A MATERNAL BALANCED TRANSLOCATION

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Abstract: Tertiary trisomy is uncommon and may arise only when one of the derivatives is small and, in the abnormal individual with karyotype 47, exists as a supernumerary derivative chromosome (+der). We describe a case of 47, XY, +der(9)t(5;9)(q33.1;q13)mat. The patient (a 1-day-old male) presented with multiple congenital anomalies including microcephaly, wide fontanelles and sutures, microphthalmia, deep-set eyes, short palpebral fissures, bulbous nose, wide nasal bridge, high arched palate, low-set and posteriorly rotated ears, micrognathia, short neck, ptosis, patent ductus arteriosus, hypoplastic external genitalia, cryptorchidism, inguinal hernia, flexion contractures of joints, short stature, clenched hands, rocker-bottom feet, simian crease, distal mottling of the skin, nail hypoplasia, hypoplasia of bones and hydrocephalus. The supernumerary derivative chromosome resulted from a meiotic recombination of a maternal balanced translocation, t(5;9) (q33.1; q13), suggesting that 3:1 disjunction in the oocyte occurred.

A supernumerary chromosome inherited from a parental balanced translocation leading to a trisomy syndrome is a rare condition. Trisomy syndrome occurs when a viable trisomic combination results from movements of chromosomes to daughter cells in a 3:1 tertiary segregation. We describe a case in which the mother had a balanced translocation t(5;9). From 3:1 segregation at meiosis, the son inherited normal 5 and 9 plus the derivative chromosome 9, resulting in a tertiary trisomy distal 5q and 9p. The proband had typical craniofacial anomalies and other anomalies of central nervous, cardiac, genitourinary, and musculoskeletal systems.

Case Report

This 1-day-old male was delivered normally at Chung Shan Medical University Hospital after an uneventful 36 weeks' gestation but had multiple congenital anomalies (Fig. 1). He was the first baby of healthy, non-consanguineous parents aged 36 and 35 years at the time of birth. The family history was unremarkable, except for a maternal cousin with mental retardation.

At birth, he was small (birth weight 2,050 g, below the 10th centile; birth length 40 cm, below the 3rd centile), had microcephaly (head circumference 30.5 cm, 10th centile), wide fontanelles and sutures, microphthalmia, ptosis, deep-set eyes, short palpebral fissures, bulbous nose and wide nasal bridge, micrognathia, and short neck. The palate was highly arched and ears were low set and posteriorly rotated. Chest roentgenogram showed a normal rib cage. Echocardiography showed patent ductus arteriosus with no other cardiac anomalies. Hand roentgenogram showed hypoplasia of the middle phalanges. Magnetic resonance imaging of the brain showed hydrocephalus, and poor myelination. Renal ultrasound was normal. He also had hypoplastic external genitalia, cryptorchidism, and bilateral inguinal hernia. Neurologic assessment showed generalized marked hypotonia. Flexion contractures of multiple joints, bilateral...
simian crease, rocker-bottom feet, and nail hypoplasia were also noted.

Because of multiple congenital anomalies, frequent respiratory distress, intermittent cyanosis, and poor weight gain, he was admitted to our neonatal intensive care unit for treatment. On the 66th day of hospitalization, he developed labored breathing and bradycardia and died.

Cytogenetic analyses of the proband and his parents were performed on peripheral blood lymphocytes, which were cultured with phytohemagglutinin for 72 hours, and G-banded with trypsin using Wright’s stain. The karyotype of the proband was 47, XY, +der(9)t(5;9)(q33.1;q13)mat. The father’s karyotype was normal. Chromosome analysis of the mother showed 46, XX, t(5;9)(q33.1;q13) (Fig. 2).

**Fig. 1.** The patient at age 1 month. Note low-set ears, flexion contracture of multiple joints, bilateral clenched hands, and bilateral rocker-bottom feet.

**Fig. 2.** A) Partial karyotype of the proband (upper panel) and his mother (lower panel). B) Idiogram shows the rearrangement in the patient (upper panel) and his mother (lower panel).

**Discussion**

Tertiary trisomy is uncommon and may arise only when one of the derivatives is small and exists as a supernumerary derivative chromosome (+der) in the abnormal individual with karyotype 47. Viable trisomic combinations result from movements of chromosomes to daughter cells in a 3:1 tertiary segregation. The presence of der(9) (the 47th chromosome) does not restrict intrauterine development, and a pregnancy could continue to term, with the child having trisomy for the derived segment, 5q33.1→qter and the segment 9 pter→q13.

Trisomy 9 syndrome is an uncommon disorder, with less than 40 delivered infants analyzed and reported in the literature. This syndrome is characterized by bulbous nose, microphthalmia, dislocated limbs, and other anomalies of central nervous, cardiac, genitourinary, and skeletal systems. Trisomy 9 is marked by severe mortality and morbidity. Shorter life span and more severe anomalies are found in the complete trisomy form. Mean life span is less than 3 weeks. (range, 10 min to 107 d) [1, 2]. Mean survival age of mosaic infants is approximately 1 year; the oldest survivor was 9 years of age at the time of his death [1, 2].

Trisomy 9p has been well described in more than 150 cases [3–5]. The phenotype is therefore well delineated and includes typical facial and limb anomalies [4–6]. The typical facial phenotype includes microcephaly, enophthalmos, hypertelorism, antimongoloid slant of palpebral fissures, broad nasal root with bulbous nasal tip, down-turned corner of the mouth, and anomalous ears. Skeletal anomalies are often seen in this syndrome. The middle phalanx of the fifth finger is the most commonly affected site (50%) [7]. This condition is associated with hypotonia later in life, which is also common in trisomy 9p patients [7]. Most trisomy 9p cases arise from meiotic segregation of balanced parental translocated chromosomes [4, 6].

The distal 5q trisomy genotype has been associated with clinical signs that include growth and mental retardation, eczema, craniofacial anomalies, and malformations of heart, lungs, abdomen, limbs, and genitalia [8]. Distal 5q trisomy can be divided into two groups, with duplication of segment 5q31-qter or 5q34-qter. The larger duplication is thought to be associated with a more severe set of clinical signs of distal 5q trisomy. However, this classification system has been disputed due to the identification of a patient who exhibited the more severe clinical phenotype with duplication of the chromosome segment 5q35-qter [9].

Parental balanced translocation involving chromosome 9 and other chromosomes leading to trisomy 9p has been reported. Balanced translocation (9;22) resulting in trisomy 9p has been described in at least five cases [3, 10–13]. Half of the derivative chromosome 9 was composed of heterochromatin: the centromeric and heterochromatic region of the long arm of chromosome 9 associated with the short arm and satellites of chromosome 22. The probability of 3:1 segregation was then very likely since trisomy 9p is viable and trisomy for the heterochromatic regions (9p and 22p) does not lead to any abnormal phenotype. A partial duplica-
tion of chromosome 5 (q31_qter) was observed in an infant with congenital malformations and dysmorphic features resulting from a normal mother and a balanced translocation father, 46, XY, t(5;9)(q31;p24) [14]. To our knowledge, this is the first report of a maternal balanced translocation t(5;9) (q33.1; q13) leading to trisomy 9 pter → q13 and trisomy 5q33.1 → qter.

References