Case reports

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Fetal phenotype in a case of partial trisomy 21 and partial monosomy 22 detected prenatally

SUMMARY Prenatal diagnosis was performed in a woman whose previous pregnancy resulted in a girl with probable Down syndrome who died soon after delivery. The mother was found to be a carrier of a reciprocal balanced translocation between chromosomes 21 and 22, and the fetus was found to have an unbalanced translocation involving chromosomes 21 and 22: 46,XX, -22, +t(21;22)(q22;q11)(21pter→21q22::22q11→22qter). Despite partial monosomy for the proximal segment of 22 and trisomy for proximal 21, the fetus did not have gross external abnormalities, but several internal malformations were found. To our knowledge, this is the first time that this unbalanced karyotype has been described.

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It is well established that Down syndrome results from trisomy of the distal region of the long arm of chromosome 21, while trisomy of its proximal region may produce non-specific effects on the phenotype, such as mild mental retardation, low posterior hairline, and fleshy external ears.^{1–5}

On the other hand, although several cases of monosomy of the distal region of chromosome 22 have been reported,^{6,7} we could not find any reference to monosomy of the proximal region, as has been described in chromosome 21. Therefore, we would like to report a case of proximal partial monosomy 22 (22pter→22q11) associated with proximal partial trisomy 21 (21pter→21q22). This was observed in a fetus with an unbalanced 21;22 translocation, who was detected in the course of prenatal diagnosis in a woman who had previously had a child with Down syndrome.

Case report

A 19-year-old woman in the 18th week of pregnancy was referred for genetic advice because she had previously given birth to a malformed child, who

FIG 1 G banded karyotype of the mother showing a balanced reciprocal translocation between chromosomes 21 and 22.

died soon after delivery and was said to have had features of Down syndrome as well as cleft lip and palate.

Amniocentesis and chromosome studies of the parents were performed simultaneously.

Results

Cytogenetics studies of the parents revealed that the mother had a reciprocal balanced translocation:

46,XX,t(21;22)(q22;q11)(21pter→21q22::22q11→22qter;22pter→22q11::21q22→21qter) (fig 1).

The fetal cells showed a 46,XX complement. All cells showed one abnormally large G group chromosome which corresponded to one of the translocated chromosomes of the mother (21pter→21q22::22q11→22qter) (fig 2). Thus, the fetus was trisomic for the proximal portion of the long arm of chromosome 21 and monosomic for the proximal segment of the long arm of chromosome 22.

FIG 2 G banded karyotype of the fetus, showing an enlarged G group chromosome which corresponds to (21pter→21q22::22q11→22qter)mat.

FIG 3 Fetal phenotype.

The parents were informed of the results of the prenatal diagnosis and the possible effects of this anomaly on the child's phenotype. They decided to terminate the pregnancy at 25 weeks' gestation.

Cytogenetic studies performed on peripheral lymphocytes, as well as kidney and lung fibroblasts, from the fetus confirmed the prenatal diagnosis. Physical examination (fig 3) showed a female fetus which measured 35.8 cm from crown to heel, weighed 900 g, and had a head circumference of 24.5 cm. The following features were found: apparent ocular hypertelorism, wide and prominent nasal bridge, asymmetrical nares, malformed and low set ears, long philtrum, small mouth, craniofacial asymmetry, and oedematous hands with thickened proximal interphalangeal joints. Except for an abnormal thumb placement, radiological examination did not show any other skeletal anomalies.

Anatomopathological studies revealed absence of the left thyroid and cytomegaly of both adrenals. The right ovary could not be found even under microscopical examination. A portion of what was thought to be the left ovary was processed in order to look for meiotic cells, but they could not be found. The remaining organs were apparently normal.

Discussion

The mother is a carrier of a balanced translocation (21;22) who transmitted the normal chromosome 21 and the translocated (21pter→21q22::22q11→

22qter) chromosome, making the fetus partially trisomic for chromosome 21 (from 21pter to 21q22) and partially monosomic for chromosome 22 (from 22pter to 22q11). The unbalanced karyotype was interpreted as the result of an adjacent type II malsegregation of the meiotic maternal quadrivalent MI22,IV(21p11) (fig 4).

Although it was not possible to study the previous child with features of Down syndrome, his phenotype could be explained by an adjacent type I malsegregation at maternal meiosis, giving rise to trisomy of distal 21: 46,XX,der(22),t(21;22)(q22;q11)mat, or a 3:1 malsegregation giving rise to 47,XX,-22,der(22),t(21;22)(q22;q11)mat.

Our case showed significant abnormalities, including agenesis of the left thyroid and probable agenesis of the ovaries. As mental deficiency is the only manifestation of partial trisomy of the heterochromatic region and the short arm of chromosome 21,^{2,5,8} the phenotypic features in our case could be attributed to partial monosomy of chromosome 22 from 22pter to 22q11.

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FIG 4 Quadrivalent configuration in maternal meiosis.