A new case of partial trisomy 19q (q13.2→qter) owing to an unusual maternal translocation

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Abstract

A new case of trisomy 19q13.2→qter is described in a male child which was caused by a maternal balanced translocation (13;19)(p13;q13.2). The major clinical features detected in the patient included the following: facial dysmorphism, bilateral coloboma, narrow and hypoplastic nails, cardiac malformations (Fallot's tetralogy), genitourinary and gastrointestinal anomalies, and agenesis of the corpus callosum. A comparison with other reported cases of partial trisomy 19q is presented. A hypothesis is proposed to account for the involvement of p13 regions of different acrocentrics in some cases of familial translocations involving a chromosome 19.

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Phenotypic anomalies resulting from genetic imbalance of chromosome 19 have been observed in very few cases. We report here an additional case of partial trisomy 19q13.2→qter secondary to an unusual maternal translocation (13;19)(p13;q13.2).

Case report

A male child was born at term after a pregnancy complicated by severe polyhydramnios and suspected cerebral malformations. These abnormal clinical signs were discovered after ultrasound was conducted in the late second trimester.

Birth weight was 2100 g (<5th centile), crown-heel length 42 cm (5th centile), and head circumference 33 cm. On clinical examination the following characteristics were observed: receding forehead, broad nose, low set, posteriorly rotated ears, bilateral coloboma, narrow and hypoplastic nails in the hands and feet, bilateral clinodactyly of the fifth finger, hypospadias, and generalised hypotonia. An ultrasound scan of the head showed agenesis of the corpus callosum and echocardiography detected a wide ventricular defect coupled with pulmonary stenosis. The infant died at 10 days of age because of cardiorespiratory failure and necropsy showed Fallot's tetralogy, bilateral hydronephrosis of the kidney, hypoplasia of the gall bladder, and partial agenesis of the corpus callosum.

CYTOGENETICS

Chromosome analysis of the patient's lymphocytes showed an abnormal submetacentric chromosome 13 with additional euchromatic material on the p arm; G banding (fig 1) indicated that it had originated from the 19q or 22q region. Unfortunately a cell line is not available from this patient.

Cytogenetic studies of the parents' lymphocytes detected a maternal balanced translocation between a chromosome 13 and 19. Her karyotype was 46,XX,t(13;19)(p13;q13.2) and thus the aneusomic segment responsible for the malformations in her son could be unequivocally attributed to the 19q13.2→qter region.

Different banding studies were conducted to characterise the derivative chromosomes better. BrdU discontinuous labelling showed no departure from the expected replication pattern of chromosomes.

NOR staining showed considerable silver impregnation on the satellite stalk of the der(13) in all cells examined, but no NOR staining was found on the der(19) and the der(19) was not involved in satellite associations (fig 2).

Discussion

As far as we can determine, only four patients have been previously described with partial trisomy for the long arm of chromosome 19.¹²

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Figure 1 Partial karyotype showing the maternal balanced translocation 46,XX,t(13;19)(p13;q13.2) (A) and chromosome 13 pairs in the affected son (B). The arrows point to the derivative chromosomes. The breakpoints are indicated by bars on the normal ideograms.

Figure 2 Metaphase showing NORs of maternal chromosomes. The arrows indicate the derivative chromosome. Note the der(13) in lateral association with a D chromosome.

The first report¹ concerned trisomy 19q13→qter in two sibs who had the same clinical features including flat facial profile with microcephaly, hypertelorism, ptosis, prominent glabella, a characteristic fish shaped mouth, congenital heart disease, and gastrointestinal anomalies. The abnormal der(22) chromosome in these patients was ascertained to be secondary to a maternal balanced translocation (19;22)(q13;p13).

The second report² concerned the detection of trisomy 19q13.3→qter in two sibs, resulting from an adjacent type 1 segregation of maternal balanced translocation (19;20)(q13.3;pter). Common phenotypic features in these patients included microcephaly, hypertelorism, barrel shaped thorax, diastasis of the rectus muscles, kyphosis, and excess digital arches.

The major clinical features of trisomy 19q13→qter in previously described cases and in the present case are summarised in the table.

Despite the scarcity of published reports and the variable phenotypic expression, some relatively constant features can be recognised in trisomy 19q13→qter including low birth weight and small length and head circumference, craniofacial dysmorphism including eye anomalies, ptosis, low set, posteriorly rotated ears, limb malformations, cardiac defects, and genitourinary anomalies. The neonatal period is marked by feeding difficulties, seizures, and apnoea. Growth is very retarded.

Our case closely resembles those described by Lange and Alfi,¹ with severe malformations including congenital heart defects, gastrointestinal anomalies, and poor prognosis. This suggests that they may share the same aneusomic segment q13.2→qter, despite the fact that the report by Lange and Alfi¹ does not localise the breakpoint precisely in the q13 region.

It is interesting to note the occurrence of a common breakpoint and exchange site in the very distal p13 region of NOR bearing chromosomes (13 and 22) in two out of three familial translocations causing partial trisomy 19q and in a normal male fetus detected at amniocentesis³ with a balanced translocation (15;19)(p13;q13.3).

From a cytogenetic point of view it could be hypothesised that molecular homology between the 19q region and p13 ends of the acrocentrics could 'encourage' chromosomal interchanges. This would be supported by data from molecular cytogenetic studies⁴ that show a large quantity of repeat sequences belonging to the Alu family on the 19q arm and the β satellite family on the p ends of acrocentrics.

In addition it could be that close proximity in the interphase nucleus between the 19q region and the domain occupied by the clusters of acrocentric chromosomes which form a common nucleolus could account for the different acrocentrics in these site specific translocations.

Clinical findings in partial trisomy 19q: comparison of the aneusomic segments in previous reports and in the present patient.

	Lange and Alfi ¹	Schmid ²	Present case
Aneusomic segment	q13-qter	q13.3-qter	q13.2-qter
No of cases	2	2	1
<i>Clinical characteristics</i>			
<i>General</i>			
Birth weight	2240 g (mean)	2240 g (mean)	2100 g
Crown-heel length at birth	41.25 cm (mean)	41.25 cm (mean)	42 cm
Head circumference at birth	31 cm (mean)	31 cm (mean)	33 cm
Postnatal growth retardation	+	+	NA
Death before 2 years	+	—	+
Seizures	+	+	+
<i>Craniofacial</i>			
Receding forehead	—	—	+
Ptosis	+	+	—
Low set, posteriorly rotated ears	+	+	+
Hypertelorism	+	+	—
<i>Limbs</i>			
Hand malformations	+	+	+
<i>Internal malformations</i>			
Congenital heart disease	+	—	+
Genitourinary defects	+	+	+
Gastrointestinal defects	+	—	+
Other malformations	Fish shaped mouth, prominence of the glabella	Barrel shaped thorax, kyphosis, excess of digital arches	Bilateral coloboma, agenesis of corpus callosum

NA = not assessed

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- 3 Shaham M, Pletcher BA, Potter JA, Raymond D, Shah HO. A familiar chromosomal rearrangement with an unusual breakpoint distal to the satellite stalk of chromosome 15. *Abstracts of the Annual Meeting of the American Society of Human Genetics*, October 1989: 0413, A106.
- 4 Holmquist GP. Chromosome bands, their chromatic flavors and their functional features. *Am J Hum Genet* 1992;51:17-37.