PARTIAL TRISOMY 9p(p22→pter) FROM A MATERNAL TRANSLOCATION 4q35 AND 9p22

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ABSTRACT

We present clinical and cytogenetic data on a 7-year-old female child with partial trisomy for 9p22→9pter as a result of a maternal balanced reciprocal translocation. Her karyotype was ascertained as 46,XX,dec(4)t(4;9)(q35;p22)mat. The father had a normal karyotype, while the mother had an apparently balanced translocation involving chromosomes 4 and 9 [46,XX,t(4;9)(q35;p22)]. This case will be briefly compared with other published cases of a similar translocation.

Key words: Chromosome 9; Partial trisomy 9p; Maternal translocation

INTRODUCTION

Trisomy 9p is the most common autosomal syndrome after trisomies 21,13 and 18, whose main clinical features include psychomotor retardation, microcephaly and brachycephaly, enophthalmos, antimongoloid eye slant, hypertelorism, abnormal ears, globulous nose, downward slanting mouth, hypoplasia of phalanges and abnormal palmar creases [1]. Here we compare a new case of partial trisomy 9p due to a maternal balanced translocation with similar cases from the literature.

CASE REPORT

A 7-year-old female child was referred to our laboratory for chromosome studies because of her hyperactivity. Her weight was 16 kg (-2.732 SDS) and her height was and 107 cm (-2.762 SDS) at the time of examination. She was the only child and born from consanguineous parents (second degree cousins), at term by natural delivery. Her birth weight was 2600 g (-1.834 SDS). She had developmental delay at all developmental stages including lifting her head, sitting up and speech.

Examination revealed hair growth down to her eyebrow region, an unusually big mouth and normal tongue, protrusion of the forehead bones, protrusion of the left bridge nose, and protrusion of the left upper lip. She also had a mild hearing impairment. She was mentally retarded and needed to attend special school (IQ had not been measured).

CYTOGENETIC STUDY

Cytogenetic analysis of phytohemagglutinin (PHA)-stimulated peripheral blood leukocytes was performed using a standard protocol [2] and additional
PARTIAL TRISOMY 9p(p22→pter) material on the short arm of chromosome 9 was detected in all cells analyzed (Figure 1A). Chromosomal analysis of her father revealed a normal karyotype but that of her mother had an apparently balanced translocation between chromosomes 4 and 9 [46,XX,t(4;9)(q35;p22)] (Figure 1B). The patient’s karyotype was ascertained to be 46,XX,dec(4)(t(4;9)(q35;p22))mat.

Many patients with duplications and trisomies of 9p have been reported. These are summarized in Table 1.

The female patient of Jelin et al. [3] had microcephaly and an incomplete bilateral cleft lip and palate, bilateral single palmar creases, and fifth digit brachydactyly; cytogenetic analysis revealed a partial trisomy 9p21.1→9pter and a deletion of 9p12.1 to 9p11.2. The male patient of Rossi et al. [4] had a partial trisomy of the 9p24 region and presented with oropharyngeal dysphagia and the common clinical signs of trisomy 9p syndrome such as microcephaly, micrognathia, brachycephaly, bulbous nose, down turned oral commissures, malformed ears and feet, and hypotonia.

The six patients of Wang et al. [5] reported a proband with a partial trisomy 9p as a result of a translocation between chromosome 4q35 and 9p22. The cases had mild facial and little finger anomalies and mental retardation. The five patients reported by Temtamy et al. [6] had de novo trisomy/duplication of 9p between regions p21 and p24 and exhibited growth retardation, severe intellectual disability, high broad forehead, low-set ears, hypertelorism with downslanting palpebral fissures, bulbous nose, down turned corners of the mouth, and hand and foot anomalies. A boy with an extra segment of the end of chromosome 9p from a maternally-inherited translocation t(4;9)(q31;p24) had mental retardation, delayed motor development (in holding up head, sitting, walking and speech) and facial dysmorphisms included long slant of palpebral fissures, broad space between the eyes, depressed nasal bridge, a globular nose with small nares and long philtrum [7].

Trisomy 9p has also been reported in adult and even elderly people. For example, Ricart and Pareja [8] reported on a 50-year-old mentally retarded woman with dysmorphic facies, severe cerebral malformations, limb deformities, retarded sexual maturation. Partial trisomy 9p cases have also been reported in prenatal patients. These include a fetus with a duplication of the 9p22.1p24 chromosomal region and many common features of trisomy 9p such as major growth retardation, microcephaly and microretrognathia[9] and a fetus with partial trisomy 9p (9pter→p11.2) who exhibited Dandy-Walker malformation and ventriculomegaly on prenatal ultrasound in the second trimester. In the third case referred to Chen et al. [10], suggested that a dosage effect of genes located on 9pter→p11.2 may be associated with abnormal development of the central nervous system in patients with partial or complete trisomy 9.

In general, the results of Panasiuk et al. [11] on carriers with a breakpoint position at 9p22, at 9p13 and at 9p11.2 showed that reciprocal chromosome translocations involving the short arm of chromosome 9 as a risk factor of unfavorable pregnancy outcomes. There are other reports that confirm facial malformations in trisomy 9p patients[12-22].

From the data presented in Table 1, we suggest investigation of the 9p24 region for genes that could be

Figure 1. A) The karyotype of the patient; the arrow shows the abnormal chromosome 4.
B) The karyotype of the mother; the arrows show the abnormal chromosomes 4 and 9.
### Table 1. Clinical findings of patients with partial trisomy/duplication of 9p

| Region | Sex-Age | Mouth | Nose | Ears | Lips | Eyes | Other Facial Anomalies | Ref. |
|--------|---------|-------|------|------|------|------|------------------------|------|
| 46,XX, dec 4; (4;9)(q35;p22)mat | F-7 | unusually big mouth (macroglossia) | protrusion, left bridge | malformed ears | protrusion, left upper lip down turned | – | protruding frontal bone, hair growth down to the eyebrow region | This |
| Partial trisomy 9p21.1→9pter and a deletion of 9p12.1 to 9p11.2 | F: at birth | bilateral cleft palate | – | – | bilateral cleft lip | – | narrow forehead | 3 |
| 46,XY, der(9)(9;15) (9p24;9q11.1:15q11.15q26),-15 | M: at birth | down turned oral commissures | bulbous nose | malformed ears, low-set ears | – | hypertelorism, bilateral epicanthic fold | – | mild facial anomalies | 4 |
| 46,XY, der(21)(9;21) (9p22.2:21q22.3) pat (six patients/23 member family) | M-F | down turned corners of the mouth | bulbous nose | low-set ears | – | hypertelorism with down-slanting palpebral fissures | high, broad forehead | 6 |
| trisomy/duplication of 9p between regions p21 and p24 (five patients) | M-F | – | nasal bridge, globular nose with small nares | – | long philtrum | long slant of palpebral fissures, broad space between the eyes | – | 7 |
| 46,XY(45)(q31.p24) | M-1 | corners of the mouth | – | low-set ears, cup-like simple ears and down turned | midfacial hypoplasia | bilateral simian palmar creases, epicanthic folds, hypertelorism | – | 8 |
| 47,XX(9p+) | F-25 | – | nasal bridge, globular nose with small nares | – | long philtrum | – | 9 |
| 46,XY, inv dup(9)(p22.1p24) (34-week fetus) | M | – | low-set ears, cup-like simple ears and down turned | midfacial hypoplasia | – | – | 10 |
| 46,XX, der(12)(9;12)(p11.2;p13.3)mat | F-5 | large mouth with down turned corners | – | low-set malformed ears | – | hypertelorism, deep-set and down slanting eyes | – | dysmorphic facies | 12 |
| 47,XX, +9p | F-50 | – | broad base of the nose | – | – | – | 13 |
| [46,XY, dup(9)(p13p24)] | M-3 mths | narrow mouth | a prominent, wide nose with a high nasal bridge | – | short, wide philtrum with thin upper lip | deep-set eyes, small palpebral fissures | midfacial flattening, mild micrognathia | 14 |
| [46,XX, dup(9)(p22p24)] | F-9 | mouth “V” | – | low-set ears | – | inverted convergent strabismus | craniofacial asymmetry | 15 |
| 46,XX, der(13) (9;13)(p11.1;q10) (wcp9+, wcp13+) | F-6 mths | – | low-set ears | – | inverted convergent strabismus | mandibular hypoplasia | 15 |
| 46,XY, add(16)(qter), Ishder(16) t(9;16)(q21.1.q15) (tel16p+/16q+tel9p+/tel) | corner of mouth in “V” | – | low-set ears | thin upper lip | inverted convergent strabismus | – | 16 |
| 47,XX, der(14)(9;14)(p21q13)mat | F: at birth | down turned corners of the mouth | bulbous nose, hypoplastic nares | low-set, malformed ears | thin upper lip | slight epicanthus, slightly downward slanting eyes | – | 16 |
responsible for some of the facial malformations such as those of the nose, mouth and ear, as in our patient, and in many cases with the partial trisomy 9p24. We also suggest that a region in 9p may contain a gene(s) responsible for the common features of partial trisomy/duplication 9p such as antimongoloid eye slant, abnormal ears, a globulous nose and downward-slanting mouth.

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