De novo partial trisomy 15q (proximal type)

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Summary This report describes a retarded girl with strabismus, high arched palate, antimongoloid slant, low set ears, hearing loss, micrognathia, short neck, and an anteriorly displaced anus. She was found to have a de novo partial trisomy of the proximal part of the long arm of chromosome 15.

De novo partial trisomy of the proximal part of the long arm of chromosome 15 has been described in nine patients.1−8 We present the clinical and cytogenetic findings in an infant with partial trisomy of the proximal part of the long arm of chromosome 15.

Case report

The proband was the first child of healthy young parents. Delivery was induced at 42 weeks after a normal pregnancy. Birth weight was 2800 g and length 47 cm. Directly after birth the child showed typical dysmorphic signs, such as a broad nose with a bifid tip, narrow nostrils, telecanthus, blepharophimosis, bilateral absence of the middle phalanx of the fifth finger, abnormal palmar creases, and an anteriorly displaced anus. Respiratory distress required oxygen and extra suction of the respiratory tract. Respiration was impaired and a nasal stridor was present. A blood sample was taken for chromosome analysis. She was discharged at the age of two weeks.

In the first months frequent upper respiratory tract infections caused adenohypertrophy. In spite of adenotomy, the girl was admitted to hospital several times elsewhere because of decompensatio cordis. At the age of eight months she was seen by a cardiologist and echocardiography revealed right ventricular hypertrophy but no primary cardiac abnormality. The right ventricular hypertrophy was thought to be caused by recurrent respiratory tract infections. These infections and the narrow nostrils, as well as tube feeding, contributed to upper airway obstruction.

At the age of 15 months she was admitted to our hospital for another adenotomy and uvulectomy. Examination showed a cyanotic, dyspnoeic infant with impaired inspiration. Length was 68 cm (below the 3rd centile), weight 6590 g, and head circumference 45 cm (15th centile). The head was symmetrical. In addition to the findings at birth (telecanthus and blepharophimosis), the eyes showed a strabismus convergens, bilateral ptosis, slight antimongoloid slant, and inverse epicantus (fig 1). There was hypoplasia of the peripheral frontal part.

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of both irides (at this age a minor dysmorphic sign). As was noticed earlier, the nose was broad, with a bifid tip and narrow nostrils (especially on the right side). She had a small mouth with a long philtrum. The palate was high arched and retro- and micrognathia were present. The ears were low set and posteriorly rotated. The neck was broad. She had a low thoracic kyphosis. The finger anomalies were present as described at birth. No syndactyly was noticed. The anus was displaced anteriorly. Repeated cardiological evaluation, including auscultation, ECG, and echocardiography, confirmed the presence of a cor pulmonale and the absence of a primary cardiac abnormality. Developmental age was approximately five to six months.

**ADDITIONAL INVESTIGATIONS**

Blood gas analysis showed respiratory acidosis, which improved after adenotony and uvulectomy. Examination of serum electrolytes, liver function, haematology, lactate, pyruvate, protein spectrum, CK, and thyroid functions showed normal values. Urinary excretion of amino acids, mucopolysaccharides, oligosaccharides, and organic acids showed no abnormalities. EEG was within normal limits for age. Hearing test showed no response to stimuli and there was almost no brainstem evoked response, in accordance with severe hearing loss.

**CYTOGENETIC STUDIES**

The karyotype of the proband was initially interpreted as 47,XX,+ marker chromosome (lymphocyte culture). By using prophase chromosomes and distamycin A/DAPI staining, this extra chromosome was shown to contain the short arm, centromere, and proximal part of the long arm of chromosome 15, though the distal part of the long arm of this extra chromosome could not be identified with certainty (fig 2). The parents had normal karyotypes, and there was no doubt about paternity.

**GENE MARKER STUDY**

Hexosaminidase A activity was studied in the parents and proband because of the gene localisation on chromosome 15 (q22→q25-1). Since normal levels of the enzyme were detected in the proband, involvement of band 15q22→q25-1 is unlikely.

**Discussion**

Partial trisomy of the proximal part of the long arm of chromosome 15 can arise either from a balanced parental translocation, as a result of parental mosaicism, or de novo. Previously reported balanced parental translocations resulted in either partial monosomy, or partial trisomy for different
autosomes,\textsuperscript{7} 13–15 17–19 In these cases a distinct karyotype/phenotype correlation is hard to determine, as the involvement of another autosome may dominate the phenotype.

In the nine well documented de novo cases which have been described, extra unidentified chromosomal material derived from another D or G chromosome was present in two cases.\textsuperscript{3,5} In one case the other extra autosome could be identified as number 22.\textsuperscript{7} The case described by Parker and Alfi\textsuperscript{8} and one of the two cases described by Crandall et al\textsuperscript{7} have been reinterpreted as resulting from an inverted duplication of the proximal part of chromosome 15\textsuperscript{8,23} and represent in fact partial tetrasomy 15. In the four remaining patients,\textsuperscript{7,8} nothing was mentioned about other chromosomes. However, in none of these presumed genuine partial proximal trisomy 15q cases was DA/DAPI staining performed. The marker chromosome in our patient consisted at least of the proximal part of chromosome 15 (as confirmed with DA/DAPI staining) and could be compared with these four patients.

The rather non-specific clinical findings in partial proximal trisomy 15q include severe mental retardation, slight microcephaly, strabismus, high arched or fissured palate, low set ears, and finger and toe anomalies.\textsuperscript{22} Sooner or later in life seizures have been noted in almost 50% of the patients.\textsuperscript{8} Our patient shares some of these characteristics, such as mental retardation, strabismus, high arched palate, and low set ears. However, the short neck, antimongoloid slant, micrognathia, and hearing loss seen in our patient are features of the more characteristic phenotype of partial distal trisomy 15q.\textsuperscript{22} The anteriorly displaced anus, which was present in our patient, was described in one other case, the only known liveborn patient with complete trisomy 15q.\textsuperscript{22} These observations led us to speculate that the distal part of the long arm of the marker chromosome in our case could be derived from the distal part of chromosome 15q. Though this hypothesis is not contradicted by our cytogenetic findings, involvement of band q22→q25.1 is unlikely because of the normal hexosaminidase A activities in the proband and her parents.

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