- ² Bridge J, Sanger W, Mosher G, *et al.* Partial duplication of distal 17q. *Am J Med Genet* 1985;22:229–35.
- ³ Gallien JU, Neu RL, Wynn RJ, Steinberg-Warren N, Bannerman RM. An infant with duplication of 17q21→17qter. *Am J Med Genet* 1981;8:111–5.
- ⁴ Orye E, Van Bever H. De novo distal trisomy 17q. *Ann Genet (Paris)* 1985;28:61–2.
- ⁵ Fryns JP, Parloir C, Van den Berghe H. Partial trisomy 17q. Karyotype 46.XY,der[21],t[17:21][q22:p13]. *Hum Genet* 1979;49:361–4.
- ⁶ Parcheta B, Skawinski W, Wisniewski L, Piontek E, Gutkowska A, Wermenski K. A new case of partial trisomy of 17 long arm. Densitometric analysis of aberrations. *Eur J Pediatr* 1985;143:314–6.
- ⁷ Therman E. *Human chromosomes*. New York: Springer-Verlag, 1986:211–3.
- ⁸ Schwartz S, Schwartz MF, Panny SR, Peterson CJ, Waters E, Cohen MM. Inherited X-chromosome inverted tandem duplication in a male traced to a grandparental mitotic error. *Am J Hum Genet* 1986;38:741–50.
- ⁹ Mules EH, Stamberg J. Reproductive outcomes of paracentric inversion carriers: report of a liveborn dicentric recombinant and literature review. *Hum Genet* 1984;67:126–31.
- ¹⁰ Taylor KM, Franke U, Brown MG, George DL, Kaufhold M. Inverted tandem [“mirror”] duplications in human chromosomes: inv dup 8p, 4q, 22q. *Am J Med Genet* 1977;1:3–19.
- ¹¹ Vogel W, Back E, Imm W. Serial duplication of 10[q11→q22] in a patient with minor congenital malformations. *Clin Genet* 1978;13:159–63.
- ¹² Van Dyke DL, Miller MJ, Weiss L. The origin of inverted tandem duplications, and phenotypic effects of tandem duplication of the X-chromosome long arm. *Am J Med Genet* 1983;15:441–50.

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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 decompensation of the heart. 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 strabismus convergens, bilateral ptosis, slight antimongoloid slant, and inverse epicanthus (fig 1). There was hypoplasia of the peripheral frontal part

Received for publication 23 March 1987.

Revised version accepted for publication 1 April 1987.

FIG 1 The proband at 15 months.

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 adenotomy 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 inter-

FIG 2 Partial karyotype of the proband. (a) DA/DAPI staining. (b) Acridine orange staining. (c) G banding after basic fuchsin staining.

preted as 47,XX,+ marker chromosome (lymphocyte culture). By using prophase chromosomes and distamycin A/DAPI staining,⁹ 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).¹⁰ 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,¹¹⁻¹⁵ as a result of parental mosaicism,¹⁶ or de novo.¹⁻⁸ Previously reported balanced parental translocations resulted in either partial monosomy,¹¹ or partial trisomy for different

autosomes.^{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.^{3 5} In one case the other extra autosome could be identified as number 22.⁷ The case described by Parker and Alf² and one of the two cases described by Crandall *et al*³ have been reinterpreted as resulting from an inverted duplication of the proximal part of chromosome 15^{20 21} and represent in fact partial tetrasomy 15. In the four remaining patients,^{1 4 6 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.²² Sooner or later in life seizures have been noted in almost 50% of the patients.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.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 15.²³ 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.

We wish to thank Professor E de Boer for performing brainstem evoked response analysis, Mrs M E A M Overbeeke-Melkert for cytogenetic work, Mrs C v d Berg for typing the manuscript, and the parents of the proband for their permission to publish this case.

References

- Magenis RE, Overton KM, Reiss JA, MacFarlane JP, Hecht F. Partial trisomy 15. *Lancet*, 1972;ii:1365-6.
- Parker CE, Alf OS. Partial trisomy of chromosome 15. *Lancet* 1972;i:1250.
- Crandall BF, Muller HM, Bass HN. Partial trisomy of chromosome number 15 identified by trypsin-Giemsa banding. *Am J Ment Defic* 1973;77:571-8.
- Howard PN, Stoddard GR, Yarbrough KM. Partial trisomy 15 and Giemsa banding. *Am J Hum Genet* 1974;26:41A.
- Watson EJ, Gordon RR. A case of partial trisomy 15. *J Med Genet* 1974;11:400-2.
- Centerwall WR, Morris JP. Partial D15 trisomy. *Hum Hered* 1975;25:442-52.
- Pfeiffer RA, Kessel E. Partial trisomy 15ql. *Hum Genet* 1976;33:77-83.
- Taysi K, Devivo DC, Sekhon GS. Partial trisomy 15 and intractable seizures. *Acta Paediatr Scand* 1979;68:445-7.
- Schweizer D, Ambos P, Anderle M. Modification of DAPI banding on human chromosomes by prestaining with a DNA binding oligopeptide antibiotic, distamycin A. *Exp Cell Res* 1978;111:327-32.
- McKusick VA. The human gene map 1 December 1984. *Clin Genet* 1985;27:207-39.
- Rethoré M, Dutrillaux B, Lejcune J. Translocation 46,XX,(15;21) (q13;q22.1) chez la mère de deux enfants atteints de trisomie 15 et de monosomie 21 partielles. *Ann Genet (Paris)* 1973;16:271-5.
- Breg WR, Schreck RR, Miller OJ. Familial partial trisomy 15: identification of a deleted no 15 confirmed by anti-5-methylcytosine antibody binding. *Am J Hum Genet* 1974;26:17A.
- Bannister DL, Engel E. A G-like trisomy with a major 15 proximal supernumerary component derived from a D/E balanced maternal interchange. *J Pediatr* 1975;86:916-7.
- Cohen MM, Ornoy A, Rosenmann A, Kohn G. An inherited translocation t(4;15)(p16;q22) leading to two cases of partial trisomy 15. *Ann Genet (Paris)* 1975;18:99-103.
- Castel Y, Rivière D, Boucly JY, Toudic L. Trisomy 15q partielle par translocation maternelle t(7;15)(q35;q14). *Ann Genet (Paris)* 1976;19:75-9.
- Power MM, Barry RG, Cannon DE, Masterson JG. Familial partial trisomy 15. *Ann Genet (Paris)* 1977;20:159-65.
- Geneix A, Jaffray JY, Malet P, Foulon E, Jalbert J, Crost P. A new case of partial trisomy 15q-. *Hum Genet* 1979;51:335-8.
- Wang H, Hunter AGW. A supernumerary G-like chromosome originating from a maternal 13;15 translocation in a nondysmorphic, retarded girl. *Clin Genet* 1979;15:273-7.
- Anneren G, Gusavson KH. A boy with proximal trisomy 15 and a male foetus with distal trisomy 15 due to a familial 13p;15q translocation. *Clin Genet* 1982;22:16-21.
- Schreck RR, Breg WR, Erlanger BF, Miller OJ. Preferential derivation of abnormal human G-group-like chromosomes from chromosome 15. *Hum Genet* 1977;36:1-12.
- Wisniewski L, Hassold T, Heffelfinger J, Higgins JV. Cytogenetic and clinical studies in five cases of inv dup (15). *Hum Genet* 1979;50:259-70.
- de Grouchy J, Turleau C. *Clinical atlas of human chromosomes*. New York: John Wiley, 1984:260-8.
- Coldwell S, Fitzgerald B, Semmens JM, Ede R, Bateman C. A case of trisomy 15. *J Med Genet* 1981;18:146-8.

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