

## Trisomy 22 with 'cat eye' anomaly

**SUMMARY** The case of a 10-month-old girl with an extra G-like chromosome is presented. Quinacrine, trypsin-Giemsa, and reverse banding identified the extra chromosome as no. 22. The phenotype of the patient is unique in that unilateral iris coloboma was observed, unlike the 18 cases of full trisomy 22 already published. This represents the first reported case of full trisomy 22 with this coloboma, or 'cat eye' anomaly, which is usually associated with partial trisomy 22. It is suggested that the use of the term 'cat eye syndrome' be revised. The terms 'partial trisomy 22 syndrome' and 'trisomy 22 syndrome' should be used instead.

Since Schachenmann *et al.* (1965) described the new chromosomal syndrome of trisomy of *partially deleted chromosome 22*, several reports of similar cases have appeared (Bühler *et al.*, 1972). In addition to mental retardation, the most prominent features were atresia ani and coloboma of the iris. Review of the published reports indeed suggests that the iris coloboma, or 'cat eye' anomaly, frequently has been present in cases characterised by the presence of a supernumerary chromosome 22 which had deletion of the distal portion of its long arms and *not* in cases with full trisomy 22. We selected from the reports 18 cases of full trisomy 22 in which identification of the trisomic chromosome was reliably performed by banding techniques. All 18 patients with true trisomy 22 lacked the 'cat eye' anomaly, a sign described in most patients with the partial trisomy 22.

Heretofore, some authors applied the term 'cat eye syndrome' only to cases with partial trisomy 22, while complete trisomy of chromosome 22 was simply designated as 'trisomy 22 syndrome'. We are presenting a report of a patient with full trisomy of chromosome 22 who had unilateral iris coloboma, thus suggesting inconsistency of the above terminology.

### Case report

A 10-month-old Caucasian girl was referred for failure to thrive, muscle hypotonia, and coloboma of the right iris (Fig. 1). She was the first and only child of a 26-year-old mother and a 30-year-old father. Birthweight was 2583.5 g and birth length was 49.5 cm. Examination disclosed a 43.0 cm head circumference and mild frontal bossing. The inner canthal

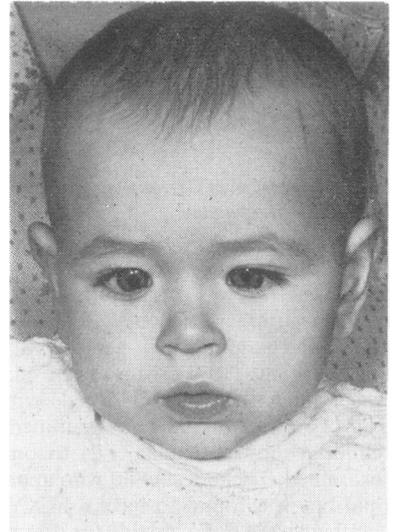


Fig. 1 Patient at 10 months of age. Note the 'cat eye anomaly' and lack of other malformations.

distance of 2.35 cm was normal. Epicanthal folds were present as well as a mild degree of convergent strabismus. A pronounced iris coloboma of the right eye was evident. Auricles were well-formed and preauricular pits were observed bilaterally. The nasal bridge appeared depressed. Palate and mandible were not remarkable and examination of extremities, chest, and abdomen did not show any abnormalities. Dermatoglyphs were within the range of normal; fingerprint patterns consisted of 4 ulnar loops and whorls, the distal palmar triradius was positioned proximally, and palmar flexion creases had normal configuration.

### LABORATORY TESTS

Radiographic examination showed normal skull, chest, and skeletal maturation; the oesophagogram was within normal limits. An EMI (computerized tomogram of the skull) showed evidence of brain atrophy, more prominent on the left, which manifested itself in enlargement of subarachnoid spaces the frontal area and enlargement of the interhemispheric fissure anteriorly. The electroencephalographic evaluation was considered to be unremarkable. The blood tests showed normal levels of chloride, sodium, potassium, calcium, phosphorus, and magnesium. The urine was screened for mucopolysaccharides, ferric chloride, nitroprusside, dinitrophenylhydrazine, and glucose oxidase, with negative results. Amino acid chromatography and serologic analysis was also negative.

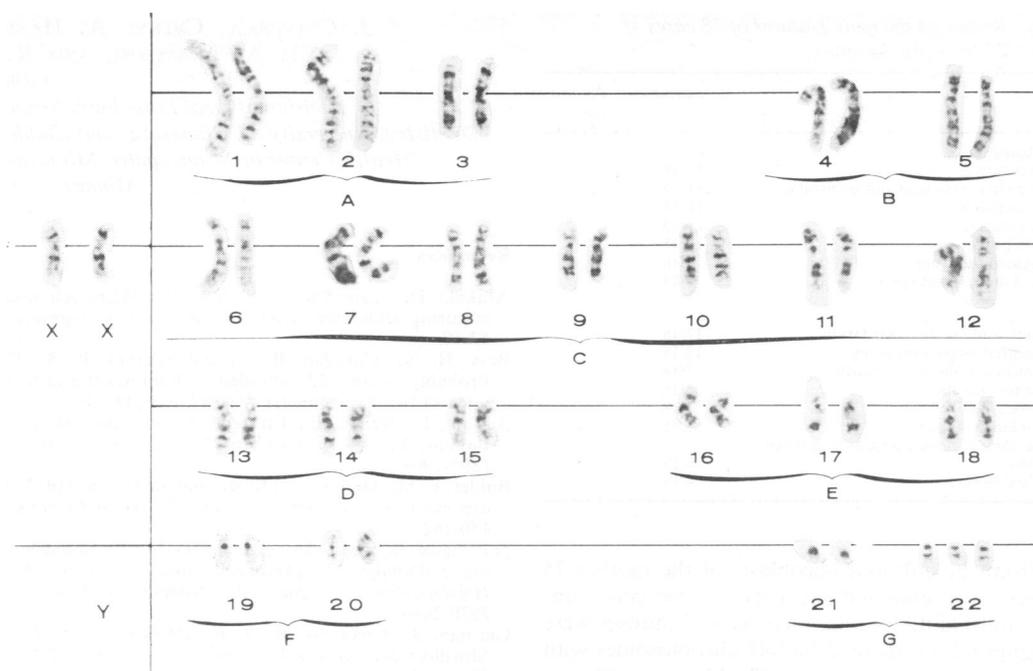


Fig. 2 G-banded karyotype of the patient with trisomy 22.

#### CYTOGENETICS

Chromosomal study was made from peripheral lymphocytes by the modified micromethod of Arakaki and Sparkes (1963) on two occasions. A total of 77 mitoses were examined under the microscope disclosing 47 chromosomes with an additional G-group chromosome (Fig. 2). There was no indication of mosaicism. To identify the supernumerary chromosome, G-, Q-, and R-banding techniques were employed. G-banded slides were prepared by trypsin treatment according to Seabright (1971); Q-banding by quinacrine dihydrochloride staining; and R-banding by the technique of Dutrillaux and Lejeune (1971). Four G-banded karyotypes were constructed, all showing the supernumerary chromosome to be no. 22. No deletion was observed in the G-group or other chromosomes. This finding was substantiated by R- and Q-banding. Further, both parents were analysed for chromosomal mosaicism since according to the review by Zellweger *et al.* (1975), in 4 of 37 families of 47,+22q- and 47,+22 probands, parental mosaicism has been described.

Chromosomal analysis of the patient's father and mother was performed on peripheral blood lymphocytes. Of 50 mitoses counted in the father, 36 contained a normal diploid set of chromosomes, none were hyperdiploid, and 14 had different hypodiploid numbers. However, in analysing the mother's

chromosomes we have encountered an unusual finding. Among 190 mitoses examined, from blood culture, 21 contained an unusual C-group chromosome (Fig. 3) which was identified as number 10 by G- and Q-banding. The distal portion of the long arms of this chromosome appeared deleted, but the fragment was always present in the topographical proximity of the long arms. This incidental observation could not be related to the patient's (trisomy 22) karyotype and it is being reported for the sake of interest. In two cells, which did not contain this abnormal C-group chromosome, trisomy of a G-group chromosome was identified. It was not obvious whether this supernumerary chromosome was 21 or

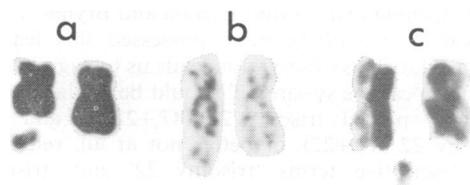


Fig. 3 Chromosome 10 from 11% of mother's mitoses from peripheral lymphocytes showed incomplete deletion of portion of the long arm. (a) Giemsa staining, (b) G-banding, (c) BrdU-induced differential staining of sister chromatids.

Table Review of the main features of 18 cases of trisomy 22 from the literature

|   | Literature | Present case |
|---|------------|--------------|
| <b>Facial features</b>                          |            |              |
| Cleft palate                                    | 13/18      | —            |
| Preauricular skin tags and/or fistulae          | 11/18      | +            |
| Microcephaly                                    | 11/18      | —            |
| Micrognathia                                    | 11/18      | —            |
| Low-set ears                                    | 11/18      | —            |
| Elongated philtrum                              | 4/18       | —            |
| Iris coloboma ('cat eye')                       | 0/18       | +            |
| <b>Other</b>                                    |            |              |
| Growth and mental retardation                   | 17/18      | +            |
| Congenital heart anomalies                      | 13/18      | —            |
| Hypotonia at birth or infancy                   | 7/18       | +            |
| Hip abnormalities                               | 6/18       | —            |
| Failure to thrive                               | 7/18       | +            |
| Low-placed nipples                              | 5/18       | —            |
| Long, slender fingers and/or finger-like thumbs | 6/18       | —            |
| Inguinal hernia                                 | 4/18       | —            |

22. From the cultured fibroblasts of the mother 75 mitoses were analysed. Seventy-six per cent contained normal diploid numbers while 5 mitoses were hyperdiploid. Of these, 2 had 47 chromosomes with supernumerary chromosome 22. Mitoses with unusual chromosomes were not detected.

## Discussion

Despite the fact that our proband has trisomy of total, non-deleted chromosome 22, she is mildly affected. Her normal facial features and lack of anal atresia, congenital heart defect, cleft palate, hip abnormalities, and other skeletal defects make her probably the least severely affected patient with trisomy 22 reported to date. The presence of coloboma of the iris, the so-called 'cat eye anomaly', is another unique finding, since in 18 reported cases of full trisomy 22 reliably identified by banding techniques (Bass *et al.*, 1973; Buffoni *et al.*, 1974; German *et al.*, 1971; Hsu *et al.*, 1971; Omar *et al.*, 1974; Penchaszadeh and Coco, 1975; Perez-Castillo *et al.*, 1975; Punnett *et al.*, 1973; Uchida *et al.*, 1968; Uchida and Brynes, 1976; Zackai *et al.*, 1973), none possessed this feature (see Table). This observation leads us to suggest that the term 'cat eye syndrome' should be applied either to both partial trisomy 22 (47,+22q-) and full trisomy 22 (47,+22), or better not at all, retaining the descriptive terms 'trisomy 22' and 'trisomy 22q-'.

We wish to express our gratitude to Carmen Yasis, Karen D. Kurvnik, and Lynn Davis for their valuable assistance.

J. CERVENKA, CHERYL A. HANSEN,  
R. A. FRANCIOSI, AND R. A. GORLIER

Division of Oral Pathology, School of  
Dentistry, University of Minnesota; and Children's  
Health Center of Minneapolis, Minneapolis,  
Minnesota, USA

## References

- Arakaki, D. T., and Sparkes, R. S. (1963). Microtechnique for culturing leukocytes from whole blood. *Cytogenetics*, **2**, 57-60.
- Bass, H. N., Crandall, B. F., and Sparkes, R. S. (1973). Probably trisomy 22 identified by fluorescent and trypsin-Giemsa banding. *Annales de Génétique*, **16**, 189.
- Buffoni, L., Reboa, E., Tarateta, A., Vianello, M. G., and Banioli, E. (1974). Trisomy 22. *Minerva Pediatrica*, **26**, 1895-1901.
- Bühler, E. M., Meiles, K., Müller, and Stadler, R. (1972). Cat eye syndrome, a partial trisomy 22. *Humangenetik*, **18**, 150-162.
- Dutrillaux, B., and Lejeune, J. (1971). Sur un nouvelle technique d'analyse du caryotype humain. *Comptes Rendus Hebdomadaires des Séances de l'Académie des Sciences*, **271**, 2630-2640.
- German, J., Chaganti, R. S. K., Mirkinson, A. E., and Morillo-Cucci, G. (1971). Trisomy 22. *American Journal of Human Genetics*, **24**, 56a.
- Hsu, L. H. R., Shapiro, L. R., Gertner, M., Lieber, E., and Hirschhorn, K. (1971). Trisomy 22: a clinical entity. *Journal of Pediatrics*, **79**, 12.
- Omar, S. A., Sanger, R. G., and Connell, G. M. (1974). Trisomy 22: a clinically identifiable syndrome. In *Chromosomal and Malformation Syndromes*, pp. 241-244. Ed. by Daniel Bergsma. Stratton Intercontinental, New York.
- Penchaszadeh, V. B., and Coco, R. (1975). Trisomy 22. Two new cases and delineation of the phenotype. *Journal of Medical Genetics*, **12**, 193.
- Perez-Castillo, A., Abrisqueta, J. A., Martin-Lucas, M. A., Goday, G., Del Mazo, J., and Aller, V. (1975). A new contribution to the study of 22 trisomy. *Humangenetik*, **30**, 265-271.
- Punnett, H. H., Kistenmacher, M. L., Toro-Sola, A., and Kohn, G. (1973). Quinacrine fluorescence and Giemsa trisomy 22. *Theoretical and Applied Genetics*, **43**, 134-138.
- Schachenmann, G., Schmid, W., Fraccaro, M., Mannin, A., Tiepelo, L., Perona, G. P., and Sartosi, S. (1965). Chromosomes in coloboma and anal atresia. *Lancet*, **2**, 299.
- Seabright, M. (1971). A rapid banding technique for human chromosomes. *Lancet*, **2**, 971-972.
- Uchida, I. A., and Brynes, E. M. (1976). Confirmation of trisomy 22 with fluorescence banding. *American Journal of Human Genetics*, **28**, 189.
- Zackai, E., Aronson, M., Kohn, G., Moorhead, P., and Mellman, M. (1973). Familial trisomy 22 (abstract). *American Journal of Human Genetics*, **25** (6), 89A.
- Zellweger, H., Ionasescu, V., and Simpson, J. (1975). Trisomy 22. *Journal de Génétique Humaine*, **23**, 65-75.

Requests for reprints to Dr J. Cervenka, Health Sciences Unit A 16-133, University of Minnesota, Minneapolis, Minnesota 55455, U.S.A.