Supernumerary small ring chromosome

SUMMARY A supernumerary small ring chromosome was found in 30% of cultured peripheral leucocytes and 50% of skin fibroblasts in a 6-year-old boy with mild mental retardation and midline cleft palate. The extra chromosome appeared to carry a densely staining region on Giemsa banding. The banding patterns of the remaining 46 chromosomes were normal. C banding indicated that the ring chromosome contained mainly centromeric constitutive heterochromatin.

Chromosome analysis of both parents showed normal karyotypes by both conventional and banding techniques; thus the origin of the ring chromosome could not be determined.

Supernumerary small chromosomes have occasionally been reported, appearing mainly as metacentric (Borgaonkar et al., 1971; Abbo and Zellweger, 1970; Froiland et al., 1963; Gamstorp et al., 1966), or acrocentric chromosomes (Latta et al., 1971). Some of the cases were associated with congenital malformations and others with normal phenotypes (Ellis et al., 1962; Nielsen and Rasmussen, 1975).

Mosaicism for an extra small ring chromosome (46,XY/47,XY,+r), was reported in a 10-year-old boy with cheilo-palato-gnathoschisis and mental retardation (Hoo et al., 1974). We report another patient with mild retardation, midline cleft palate, and mosaicism of 46,XY/47,XY,+r. The similarity of the clinical findings to the previously reported patient is of interest.

Case report

This patient (100468) was born at term after a normal pregnancy to a 24-year-old mother and a 31-year-old father. The mother had been treated with iodine for a 'goitre' until about 2 years before this conception. She was on no treatment before and during the pregnancy. The baby weighed 3400 g at birth and was considered as a normal newborn except for the midline cleft palate. The mother first became concerned about the child's development at 9 months of age when she noted that he had a big head and generalized hypotonia. He could not distinguish her from other people. He began sitting at 1½ years,

References


Requests for reprints to Professor Charles J. Epstein, Department of Pediatrics, School of Medicine, University of California, San Francisco, California 94143, USA.

1This work was supported by Grants GM-19443, HD-02552 from the U.S.P.H.S. and from the National Foundation (C-155).
walking at 2½ years, and did not talk until the age of 4, when the cleft palate was repaired. Thyroid studies performed at that time were normal.

At 6 years of age the physical examination showed a hyperactive boy. Height was 109 cm, weight 20·5 kg (3rd centile), and head circumference 51 cm (50th centile for age). His skin was dry. There was a repaired midline cleft palate, an umbilical hernia, and his left testicle was not palpable in the scrotum or inguinal region. His fingers were short and tapering. The rest of the physical examination was not remarkable. Dermatoglyphs were also within normal limits.

Cytogenetic studies

Chromosome analysis was performed on cultured leucocytes and skin fibroblasts. The peripheral leucocytes showed a mosaicism of 46,XY/47,XY, +r, with 30% of the 50 cells examined showing an extra small ring chromosome (Fig. 1). The cultured skin fibroblasts disclosed the same type of mosaicism with 50% of 50 cells showing 47,XX,+r. The extra chromosome had a ring shape by conventional Q-banding (Breg, 1972) (Fig. 2) and G-banding techniques (Hirschhorn et al., 1973). With G-banding, a densely staining region was seen in this ring chromosome (Fig. 3). The G-banding as well as Q-banding patterns of the remaining 46 chromosomes were completely normal. The C banding (Salamanca and Armendares, 1974) showed that the ring chromosome consisted mainly of centromeric constitutive heterochromatin (Fig. 4).

Peripheral leucocyte cultures of both parents revealed a normal chromosomal constitution by both conventional and G-banding techniques.

Discussion

Similar clinical findings associated with mosaicism for an extra small ring chromosome in 2 patients raises the possibility that the ring chromosome is
Identical in origin. However this origin was not identifiable in either of these cases of unbalanced autosomal aberration.

Autosomal ring formation was discussed in detail by Hecht (1969) and later by Hecht and Vlietinck (1973). Their basic question dealt with the possibility of correlation of consistent clinical syndromes with ring chromosomes. The prediction was made that each patient with a ring derived from a particular autosome might show a different phenotype. They explain phenotypic variability by: (a) location and length of deletion; (b) number of cell lines found, or the formation of mosaicism because of the tendency of ring chromosomes to missegregate; and (c) similar looking rings that originate from different chromosomes. It may be even more complex to explain a supernumerary mosaic ring chromosome, the origin of which is unknown. Extra small ring chromosomes can be considered partial trisomies, with the clinical features depending on the chromosome of origin. The clinical features of our patient and the one reported by Hoo et al. (1974) include mental retardation and cleft palate. This combination has been found in patients with complete trisomies 13 (Smith, 1976) or 22 (Hsu et al., 1971), or partial trisomies of 1q (Norwood and Hoehn, 1974), 7q (Alfi et al., 1973) or 11p (Sanchez et al., 1974), as well as the syndrome of partial deletion of 4p—(Hirschhorn et al., 1975).
It is, therefore, likely that rings formed from segments of these chromosomes would result in some similar clinical findings. Such similarity of findings in patients with ring chromosomes may therefore be the result of a combination of abnormalities common to two different trisomies or to ring formation from the same chromosomes.

We wish to thank Mrs S. Paciuc and Mrs S. Cristian for their excellent technical assistance.

S. Kaffe, H. J. Kim, L. Y. F. Hsu, C. B. Brill, and K. Hirschhorn
The Division of Medical Genetics, Department of Pediatrics, Mount Sinai School of Medicine, Fifth Avenue and 100th Street, New York, New York 10029, U.S.A.

References


Hsu, L. Y. F., Shapiro, L. R., Gertner, M., Lieber, E., and
Case reports


Requests for reprints to Dr. S. Kaffe, Division of Medical Genetics, Department of Pediatrics, Mount Sinai School of Medicine, Fifth Avenue and 100th Street, New York, N.Y. 10029, U.S.A.

Ring chromosome 8 in a boy with multiple congenital abnormalities and mental retardation

SUMMARY A ring chromosome 8 was found in peripheral blood cells in a boy, whose chromosomes were studied because of multiple congenital anomalies. Examination of skin cells revealed a 46,XY/46,XY,8r pattern. Application of several banding techniques suggested a duplication of the most distal bands of both arms in the ring. The terminal end of 8q appeared to have been retained as could be shown by R-banding.

The anaesthesia and surgery the mother underwent in the first month of her pregnancy is considered as a possible cause of the chromosome abnormality.

Ring chromosomes derived from unidentified C chromosomes have been reported in several cases.

After the development of the banding techniques the possibility of identifying the origin of C ring chromosomes led to the publication of reports of 4 patients with a ring chromosome 6 (Moore et al., 1973; Van den Berghe et al., 1974; Fried et al., 1975; Wurster-Hill and Hoefnagel, 1975), 2 patients with a ring chromosome 7 (Zackai and Breg 1973), 1 patient with a ring chromosome 8 (Pfeiffer and Lenard, 1973), and 5 patients with a ring chromosome 9 (Kistenmacher and Punnett, 1970; Jacobsen et al., 1973; Fraisse et al., 1974; Zdansky et al., 1975; Nakajima et al., 1976). In the case of Kistenmacher and Punnett the identification was based on morphology and study of the exchange pattern induced by mitomycin C.

In this paper a ring chromosome 8 is described in a patient who was studied because of multiple congenital abnormalities.

Case report

The propositus (born 13 October 1967) is the first of two children. At birth his mother was 25 and his father was 28 years old. There were no abortions or stillbirths. Unaware of her pregnancy the mother underwent an appendectomy on account of chronic appendicitis on the 18th day of her last menstrual cycle (premedication: 0.5 mg atropine, 25 mg promethazine, 20 mg pantofo; narcotics: thiopen-thone-sodium, suxamethonium-chloride, nitrous oxide, and fluorohane).

Gestation was uneventful and ended 13 days after term. Birthweight was 2770 g, length 47 cm. Feeding was very difficult in the neonatal period.

At 1 ½ years of age the boy suffered from feverish convulsions. When he was 2 years old he was operated on for bilateral hernia inguinalis. Because of an impending dislocation of the right hip, he was treated with a stretch bandage at the age of 2 ½ years. He suffered from recurrent infections of the upper respiratory tract. Psychomotor development was very retarded.

At the age of 5 ½/12 years the boy was admitted to our institution. Physical examination at that time disclosed the following (Fig. 1A and B): dwarfism, dolichocephaly, prominent occiput, asymmetry of the viscerocranium, bilateral strabismus convergens alternans, bilateral epicantid folds, asymmetric ears, tight upper lip, thin lips, gothic palate, asymmetry of the upper dental arch, micrognathia, pectus excavatum, scapulae alatae, wide-spaced areolae mammae, long thorax, bilateral inguinal scars from herniotomy, sacral dimples, and dimples dorsal of the elbows, camptodactyly of both fifth fingers, hyptonia, and cutis marmorata.

The electroencephalogram was normal. Ophthalmological examination revealed a distinct bilateral hypermetropia and minor astigmatism of the right eye, which seems to be affected by amblyopia.

X-ray examination revealed that the right caput femoris was located laterally in the acetabulum and that the right femur was adducted, the right side
Supernumerary small ring chromosome.

S Kaffe, H J Kim, L Y Hsu, C B Brill and K Hirschhorn

doi: 10.1136/jmg.14.6.447

Updated information and services can be found at:
http://jmg.bmj.com/content/14/6/447

These include:

**Email alerting service**
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/