A CASE OF TRISOMY 8

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A case of 8 trisomy syndrome, identified on the basis of the heat denaturation technique, has been detected in a patient with mental retardation, congenital malformations, and peculiar ocular anomalies. This observation confirms that, even without evidence of mosaicism, this chromosome does not seriously upset the viability of cells and could be less deleterious to the individual than trisomy 13, 18, or 21.

The mental development is not too much impaired and the skeletal abnormalities are mild, as compared to those found in previously reported cases. On the other hand, the cardiovascular system is involved and the ocular lesions are complex. They include prominent eyes, epicanthus, hypertelorism, antimongoloid slant of palpebral fissures, ectopia of lacrimal point, megalocornea, enlarged iridocorneal angle, subatrophic papilla, tortuosities of retinal vessels, absence of deep perception.

The employ of the new techniques for the identification of individual chromosomes has now made possible the characterization of certain gross chromosome abnormalities more precisely. This is particularly true for the C group chromosomes in man, which cannot be distinguished solely on morphological grounds.

Extra C autosomes, both with or without mosaicism, have been detected in spontaneous abortions (Boué and Boué 1969), in a variety of disorders (De la Chapelle et al. 1970, Hellström et al. 1971), in a female with primary amenorrhoea (Jacobs et al. 1961), in apparently healthy females who gave birth to malformed children (Smith 1964, Stolte et al. 1964), or who had missed abortions (Caspersson et al. 1972), and in malformed and or mentally retarded subjects (Pfeiffer et al. 1962, El-Alfi et al. 1963, Stalder et al. 1963, Coryell et al. 1964, Wolf and Reinwein 1965, Jalbert et al. 1966, Kerr and Rashad 1966, Longo and Maccani 1966, Schutt 1966, Bargman et al. 1967, Gustavson et al. 1967, Monnet et al. 1967, Frezza et al. 1968, Higurashi et al. 1969, Lejeune et al. 1969, Oikawa et al. 1969, Juberg et al. 1970, Emberger et al. 1970, Moore and Engel 1970, Eys et al. 1970, Riccardi et al. 1970).

The great variation in the clinical pictures in these cases could be the result of several factors, including diverse degree of mosaicism and differences in involved tissues (Gustavson et al. 1967, Caspersson et al. 1972), or the involvement of different C autosomes. Even if the first two hypotheses are actually difficult to test, it is possible to point out that complete trisomy of any of the C group autosome appears to be a very infrequent occurrence, there being only five reported cases at the present time (Jalbert et al. 1966, Lejeune et al. 1969, Juberg et al. 1970, Caspersson et al. 1972: two cases). The second hypothesis has been recently proved by the identification of different C autosomes' involvement in few of these cases: at least two

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clinically recognizable syndromes have been isolated: the trisomy for chromosome number 8 (De Grouchy et al. 1971, Laurent et al. 1971, Malpuech et al. 1972, Maceck et al. 1972, Caspersson et al. 1972), and the trisomy for chromosome number 9 (Haslam et al. 1973, Feingold and Atkins 1973).

The present paper concerns an additional observation of the trisomy 8 syndrome, occurring in a boy with mental retardation, several congenital malformations, and peculiar ocular anomalies.

CASE REPORT

G.M., a 9 year-old male, was the third child of a 38 year-old mother and a 43 year-old father. The union was nonconsanguineous. The first pregnancy of the mother ended in spontaneous abortion at the second month. One older brother is obese and shows a severe hypogonadism.

Gestation was full term; pregnancy and delivery were normal; birth weight was 3200 g. He was able to seat unsupported at 8 months, and began to walk at 2 years. Mental retardation and impaired speech were detected since early childhood.

At the age of 8 he was admitted to a Clinic, because of conjunctivitis; at that time a diagnosis of bilateral glaucoma, malformation of papilla, and optical nerves atrophia, had been posed.

The patient was referred to us for cytogenetic investigations at the age of 9, because of mental retardation and congenital malformations (Fig. 1). At that time he was 132 cm high; the head circumference was 53 cm; and he weighed 24 Kg.

The physical examination reveals a flat occiput, prominent eyes with mild epicanthus at left; antimongoloid slant of palpebral fissures; internal ectopia of the right lacrimal point (15 mm); ocular hypertelorism (interpupillar distance, 5.5 cm). Additional ocular findings include a megalocornea (diameter, 13 mm), with an enlarged iridocorneal angle and a normal ophthalmotonus, subatrophic papilla, and tortuosities of retinal vessels (Fig. 2). Ultrasonic biometry showed longitudinal diameter 27 μ sec and transversal diameter 30 μ sec. Thus, the eyeball appears to be too short and large. These findings can explain the irregularities of the retinal vessels. At an attentive orthoptic examination the patient is orthophoric, but the deep perception is lacking. Visual activity is 5/10 with correction of the hypermetropic astigmatism.

The ears are low-set, large and slightly malformed, with a large concha; the nasal bridge is prominent, the nostrils small. The mouth is large, with a thick and everted lower lip; the palate is flat; several anomalies in dental alignment and morphology are present. The neck is short. On the thorax, which presents a first-degree pectus excavatum, there are two atrophic additional nipples.

Cardiac examination revealed an harsh murmur; electrocardiogram, phonocardiogram, polycardiogram, and telecardiogram investigations, suggested a mild coarctation of the aorta. This possibility will be investigated further when he is older.

The testes are descended, of normal consistency; the phallus is normal.

The hands show bilateral clinodactyly; the dermatoglyphic pattern is normal.

Radiological investigations have detected 13 pairs of ribs, a dysplastic pelvis with hypotrophy of iliac wings, proximal pseudoepiphyses in the second metacarpal bones and incomplete distal pseudoepiphyses in the first. Distal pseudoepiphyses are also present in the second phalangeal bones of the 5th fingers.

The patient is attending a shool for mentally handicapped children. At the age of 9 his I.Q. is 49 (Stanford-Binet). His articulation is poor; he is a quiet, smiling boy, with no evidence of antisocial behaviour. Last electroencephalographic analysis showed a significant depression in the cerebral electrogenesis.

Repeated chromosome studies on separate blood cultures showed a chromosome constitution of 47, XY,+ C. There was no evidence of mosaicism and no late replicating C group chromosome was found after four hours labelling with tritiated thymidine. Cells from buccal mucosa were sex-chromatin negative and no peripheral blood drumsticks were found. On the basis of the heat denaturation technique (Dutrillaux and Lejeune 1971) the extra chromosome was interpreted as a number 8, with no evidence of structural rearrangements (Fig. 3).

The parents and brothers had normal karyotypes in cells from lymphocyte cultures.

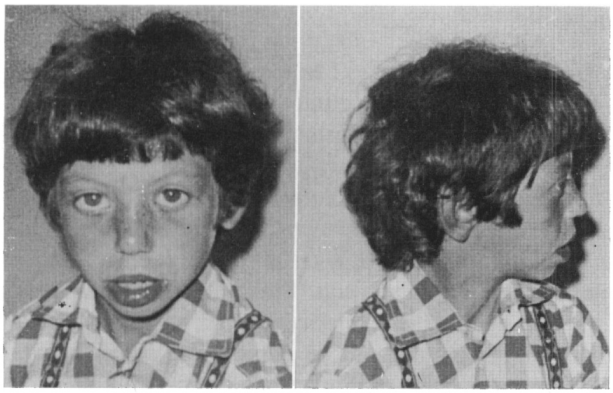

Fig. 1. The propositus.

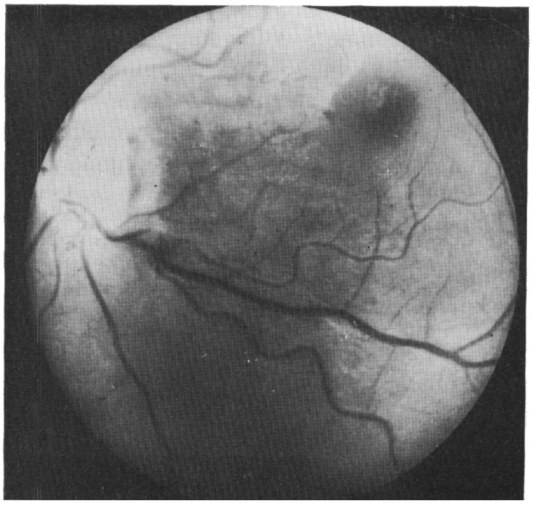

Fig. 2. Subatrophic papilla and tortuosities of retinal vessels.

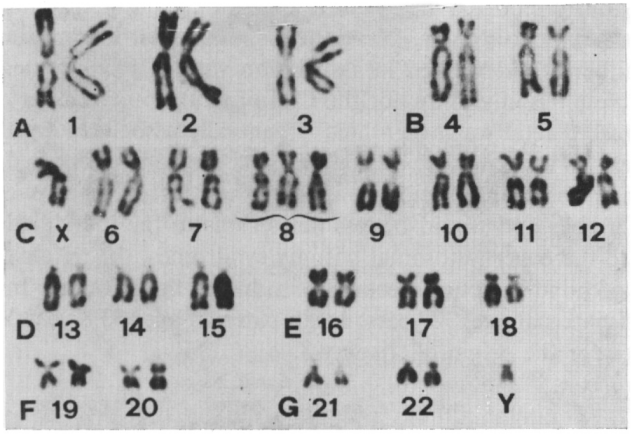

Fig. 3. Karyotype of a heat-denaturated cell.

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DISCUSSION

It has been suggested that several of the patients carrying C trisomies, studied before the advent of the new identification techniques, show a similar clinical picture (Lejeune et al. 1969). In this group of subjects there is a high frequency of osteoarticular lesions, receding jaw, frontal bossing, occasionally associated to macrocephaly, low-set ears, short neck, abnormally long trunk. Less common findings include ocular hypertelorism and congenital cardiovascular defects. Most of the patients are suffering from mental retardation.

However, a more attentive review of the literature shows a rather wide variation in the clinical picture. In this group there are apparently normal subjects (Stolte et al. 1964); patients with hematological disorders (De la Chapelle et al. 1970); patients with mild retardation and congenital malformations (Riccardi et al. 1970), and, more commonly, severe mental retardation, malformations of the central nervous system, genitourinary tract, and skeleton.

Since most cases in the literature have had a 46/47,+ C mosaicism, the clinical variations could be due to differences in the proportion of abnormal cells in various tissues, even if the extra chromosome was the same. This hypothesis can be proved when comparing the few reported cases in which the supernumerary chromosome has been identified by means of the new techniques.

With the exception of one female patient reported by Caspersson et al. (1972), who had a normal mental and physical development and no obvious malformations, the subjects with proved 8 trisomy syndrome display a large variety in the clinical picture. The more constant signs include mental retardation, only rarely amounting to severe subnormality (Laurent et al. 1971), strabismus, in at least three subjects, low-set and malformed ears, protruding lips, dental defects, short neck, clinodactyly, occasionally associated to Marfan-like deformities of fingers, multiple skeletal and articular defects, which become more evident in older patients. In newborn babies it appears to be a rather constant anomaly the stuffed appearance of palms and soles. The internal abnormalities include agenesis of the corpus callosum and hydronephrosis (in at least two subjects), and the abnormalities of the great vessels at their origin in the three cases with no evidence of mosaicism.

The present observation of trisomy 8 displays several points of interest. It confirms that, even without evidence of mosaicism, the mental development is not too much impaired; on the other hand, the cardiovascular system is involved. The skeletal abnormalities are mild, as compared to those observed in previously reported patients; it does not exclude that joint defects will become appreciable when the patient is older. Nevertheless, the ocular lesions are complex and include several defects hitherto undescribed in association with this syndrome.

It has been suggested that the complete trisomy of any of the C-group autosome is a very infrequent occurrence, because of increased fetal wastage, which is generally associated with the trisomy of large autosomes (Kuliev 1971): however, on the basis of previously reported cases of trisomy 8, and according to the present observation, it appears that this chromosome does not seriously upset the viability of cells and would be less deleterious to the individual than trisomy 13, 18, or 21. Similarly to the other autosomal trisomy syndromes, the trisomy of chromosome 8 could be the result of nondisjunction occurring in one of the parents. In fact, an increase of parental age (mean maternal age, 32 years; mean paternal age, 33.8 years) might also be of etiological significance for the origin of trisomy 8.

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