Apparent Monosomy of a G Autosome in a Jamaican Infant

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Monosomy of an autosome is widely thought to be lethal (Patau, 1963). Deficiencies due to deletions of chromosomes 18 and 5 are well documented (de Grouchy, Lamy, Thieffry, Arthuis, and Salmon, 1963; Lejeune, Lafourcade, Berger, Vialatte, Boeswillwald, Seringe, and Turpin, 1963), and reciprocal translocations which can arise in a carrier person and result in unbalanced offspring with duplications/deficiencies are also described (Clarke, Stevenson, Davies, and Williams, 1964; Uchida, Wang, Laxdal, Zaleski, and Duncan, 1964; Cowie, Kahn, and O'Reilly, 1965). Lejeune, Berger, Réthoré, Archambault, Jérôme, Thieffry, Aicardi, Broyer, Lafourcade, Cruveiller, and Turpin (1964) have also described a case in which they postulate mosaicism involving monosomy of chromosome 21 with a partial monosomy of 21.

Case Report

We here describe a patient whose karyotypes are suggestive of monosomy of an autosome of the G group, though mosaicism cannot be excluded, as only one tissue was examined.

Clinical Data. The only child of a mother aged 18 and a father in the early thirties, was first seen at the Children's Hospital, Kingston, on September 12, 1965 at the age of 1 year. The main complaints were of failure to thrive, intermittent fevers, and vomiting and diarrhoea of 6 weeks' duration.

She was born at home in a country district of Jamaica after a medically unsupervised full-term pregnancy and normal delivery. The birthweight was not known. There was no family history of any malformation. Since birth it had been noted that the thumbs were always held drawn across the palms. Apart from this, the mother claimed that the child had developed normally until the onset of this illness. However, the infant had never attempted to crawl or stand, but had been sitting with support since the age of 6 months. On examination at the age of 1 year, she weighed 9 lb. 11 oz. (4393 g.) and was marasmic and dehydrated with oedema of the

lower limbs. The head circumference was 17.5 in. (44 cm.). The external abnormalities noted were eyes with an antimongoloid slant, large low-set floppy ears, a small receding chin, a high-arched palate, and prominence of the occiput (Fig. 1). The thumbs were held flexed, but the fingers, though slightly flexed, did not overlap. The palmar creases appeared abnormal with two transverse creases, the distal one being more transverse than normal. There was prominent anterior bulging of the thoracic cage more marked on the right. The tone in the lower limbs was slightly increased and they were held partially flexed at the hips and knees. There was also difficulty in abducting the legs at the hips. The external genitalia were normal, and no abnormalities were detected in the cardiovascular system, the eyes, or the ears. The clinical diagnosis was marasmic malnutrition superimposed on a possible chromosomal abnormality, which superficially resembled 18 trisomy.

FIG. 1. Clinical features of patient at 1 year.

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Fig. 2. Karyotype of patient.

Laboratory investigations included the following: Hb 9.0 g.; total proteins 4.4 g., albumin 1.8, globulin 2.6. VDRL, stool cultures, and tuberculin test were negative. Radiographs of skull and skeletal survey were reported as normal. Unfortunately blood group studies were not performed, as the significance of the diagnosis was not perceived until too late.

The infant did not respond to the usual therapy for malnutrition and she died of bronchopneumonia 11 days after admission.

At necropsy (Dr. C. F. Hutchinson) no further congenital abnormalities were discovered, except that the right kidney appeared slightly abnormal in shape. The lungs showed severe bronchopneumonia, and the liver revealed fatty change seen in malnutrition. Histological examination confirmed the two latter pathological findings and revealed no further abnormalities.

Cytogenetic Examination. Peripheral blood was taken from both the patient and her mother. Short-term lymphocyte cultures were performed by the method of Arakaki and Sparkes (1963). In the infant, the mitotic rate was poor but 26 metaphases of good quality were counted and analysed. Karyograms were made from 5 cells. Three cells containing only 44 chromosomes were presumed broken. The remaining 23 cells all contained only 45 chromosomes with a chromosome missing from the group 21-21 (Fig. 2). In some of the cells, one chromosome 16 appeared larger than its homologue. This finding also appeared in some of the mother's cells. Otherwise it was possible to pair well the remaining chromosomes, and in no cell was a fragment or any morphological indication of a translocation seen.

The mother, in an analysis of 30 cells, showed 46 chromosomes in all cells, and apart from the finding of chromosome 16, no other abnormalities were detected

(Fig. 3). Unfortunately the patient's father could not be traced.

Discussion

It was thought that by examining the parents of the patient, a balanced translocation would be uncovered which would satisfactorily explain what appears, on the face of it, to be monosomy of chromosome 21 or 22. In the absence of the father, one can only conjecture on the interpretation of the findings. We can make three possible suggestions.

(i) An unbalanced translocation of part of the missing G autosome resulting in an undetectable increase in size of another chromosome. This could have arisen in the early divisions of the zygote, in one of the parents as a single event in one of the gonia, or as an event that resulted in gonosomal mosaicism or the formation of a parent carrier of a translocation for which the parent was balanced. It was felt that the increase in size of the No. 16 chromosome seen in some of the cells of the infant and her mother probably represented the normal range of variation for chromosome 16. If the mother had a balanced translocation involving a G chromosome and chromosome 16, the distribution of the remainder of the chromosomes in the karyotype would have been altered or one of the G chromosomes would have been reduced in size.

(ii) Mosaicism, undetected in our patient because of examination of an insufficient number of cells and only one tissue. This could be of the type described by Lejeune *et al.* (1964) in which a monosomy G line existed with a line containing a small fragment which was concluded by the

FIG. 3. Karyotype of mother.

authors to be either a ring chromosome or a small part of chromosome 21. They felt that the high proportion of cells without the fragment was due to selection through mitotic instability. Our patient resembles clinically the description given by Lejeune *et al.*, though no photographs were shown. They also compared their patient's anomalies with the stigmata of trisomy 21 and commented that the contrast in the clinical features recalled those of the haplo IV and triplo IV states seen in *Drosophila*.

(iii) The final possibility is complete monosomy for a G autosome (which has not, to the authors' knowledge, yet been reported in either living individuals or spontaneous abortions). We are, therefore, reluctant to conclude that the findings in this patient indicate complete monosomy, but feel that there is almost certainly loss of some material from chromosomes 21 and 22 likely to result in the physical abnormalities described above. Of the suggestions we have made, alternative (ii) appears to be the most likely explanation.

Summary

A child with an abnormal phenotype, who died of malnutrition and bronchopneumonia, is reported. Examination of the chromosomes of the peripheral blood showed loss of some material from chromosome 21 or 22, and suggested a possible monosomy of a G autosome. Unbalanced and reciprocal

translocation, as well as mosaicism, were also considered.

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