As is true for the great majority of patients described, they were sporadic; no other affected members being known in their families. Only four instances of familial cases are known to us. Consanguinity, however, has been found in three out of 19 families in which it was sought, a strong evidence in favour of recessive genes being implicated in the aetiology of this disease. Cell culture investigations support this conclusion (Danes, 1971). The concordance in the manifestation of this condition in our pair of monozygotic twins is another indication that it could be due to genetic factors. Accepting this hypothesis, the probability of obtaining the extreme segregation ratio observed in our sibship (one affected zygote in 14) is 8.4%. In accordance with previous observations (cf., Macnamara et al., 1970; de Busk, 1972) the chromosomes of our patients showed no detectable abnormalities.

Several authors stressed that the ears of persons with this disease tend to protrude and that the lobes are frequently absent. Our patients, in addition, have very wide external canals that permit the observation of the tympanic membrane without special light. This exaggerated diameter of the auditory external canals was also present in de Busk’s case 60 (1972) and probably should be considered as a possible sign in future descriptions of this condition.

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21 Monosomy in a retarded female infant*

Summary. A 20-month-old female infant with complete monosomy 21 is described. She has marked mental and physical retardation, antimongoloid slant, low set ears, micrognathia, syndactyly of the toes, and cardiac abnormalities. Karyotypes of fibroblasts and lymphocytes, examined with Giemsa banding, quinacrine banding, and reversed banding techniques revealed no evidence of translocation.

The application of chromosome banding techniques in cases of apparent complete G monosomy has revealed that most have a translocation involving chromosomes No. 21 or No. 22, or mosaicism with one 45, –21 cell line (Wyandt et al., 1971; Cooksley, Firouz-Abadi, and Wallace, 1973; Richmond, MacArthur, and Hunter, 1973). One case has been reported in which absence of one chromosome 21 has been documented by banding techniques (Gripenberg, Elving, and Gripenberg, 1972). We report here a case of apparent monosomy 21 in a 20-month-old female infant.

Case report

The patient, a 20-month-old female, was the first child of a 23-year-old mother and a 25-year-old father. The parents are not related. A paternal uncle is reported to be retarded.

The child was born at 38 weeks’ gestation following a pregnancy complicated by emotional and social problems in an unwed mother for whom there was no prenatal care. Delivery was normal and the baby weighed 1900 g and had a length of 46 cm. She had several generalized seizures during the first few days of life which were interpreted as secondary to hypoglycaemia and responded to therapy with glucose. At 3 weeks of age, evaluation of failure to thrive revealed absence of a G-group chromosome. Subsequently the child continued to show reduced growth.

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tarded growth and development and had several respiratory infections. She was first evaluated at Yale-New Haven Hospital at 15 months of age, and was digitalized with a presumptive diagnosis of mitral and tricuspid valvular insufficiency. Growth and development remain markedly retarded. At 20 months her height was 70 cm and weight 5.7 kg. She sat alone at 1 year and at 20 months could pull to standing but could not walk. She could say only three words.

Physical features include moderate generalized hypotonia and reduced muscle mass with kyphoscoliosis (Fig. 1). The ears are large and low set, and there is an antimongoloid slant of the palpebral fissures, a somewhat broad nose, and a small chin (Fig. 2). The head circumference is 43.5 cm. She has downy hair on her arms, thighs, and back and her nipples are hypoplastic. The heart is enlarged and a grade 3/6 pansystolic murmur is heard maximally at the lower left sternal border followed by an early diastolic murmur. Presystolic and early systolic apical murmurs are also present. There is partial syndactyly of the second and third toes bilaterally, and contractures of the proximal interphalangeal joints of the left fourth and fifth fingers. Both the mother and the maternal grandmother have a similar degree of antimongoloid slant of the eyes and minimal syndactyly of second and third toes.

Blood count and urinalysis were normal. Chest radiology revealed generalized cardiac enlargement and the electrocardiogram revealed a normal electrical axis, peaked P waves in lead II and an rsr pattern in lead V1. Skeletal radiology at 18 months showed mild scoliosis, coxa valga, and a bone age of 12 months.

Dermatoglyphic studies of the patient revealed r and r' palmar axial triradii bilaterally. Digital patterns showed ulnar loops on the fourth and fifth fingers bilaterally and on the left thumb, a radial loop on the left index finger and simple arches on the other digits. Palmar creases were normal but there was an extra crease on the proximal phalanx of each thumb.

Tests of eight blood group systems in the mother and the proposita (ABO, Rhesus, MNSs, Lutheran, Kell, Duffy, Kidd, Wright) and of the antigens haptoglobin, Invα, Gmα, and Gmβ were non-informative. The father was not available for study.

**Cytogenetic studies**

Chromosome analysis was done on 115 cells from two blood cultures and 111 cells from a skin fibroblast culture. Two hundred and four cells had a chromosome count of 45 and 17 had a count of 44; no cell had 46 chromosomes or two No. 21 chromosomes. Metaphase cells from both the lymphocyte and fibroblast culture were examined using both quinacrine fluorescence and Giemsa-banding techniques. In addition, cells were examined by acridine orange fluorescence after heat treatment (Bobrow, Collacott, and Madan, 1972). This procedure produces chromosome banding patterns...
which are the reverse of those obtained with quinacrine fluorescence. The studies established a 45,XX,-21 karyotype (Fig. 3). There was no evidence of translocation by any of these methods, nor any evidence for mosaicism. Lymphocyte karyotype of the mother was normal. The father could not be located for study.

Discussion

In all reported cases, differentiation of complete from partial monosomy for chromosome 21 has been difficult. With banding techniques, some cases of apparent G monosomy have proved to have translocations resulting in only partial monosomy of chromosome 21 or 22 (Cohen and Putnam, 1972). Even with quinacrine and Giemsa banding, the translocated distal segment of the long arm may not be found since it stains less intensely. However, a translocated portion may become apparent with reverse Giemsa banding since the ends then will stain positively, as shown by Dutrillaux et al (1973) in a case of an unbalanced 4q/21q translocation. In that case, the translocation could be identified by the change in length of the dark band at the tip of chromosome 4. On the other hand, a 21q translocation to another positively staining chromosome region might not be obvious if the length of the band were not significantly changed. Thus the possibility of a small translocation of this type cannot be ruled out in the present case.

Clinically, cases with an apparent deletion of a G-group chromosome have been classified into G deletion syndrome I (loss of material from chromosome 21) and G deletion syndrome II (loss of material from chromosome 22) (Richmond et al, 1973). Mental and physical retardation, microcephaly, musculoskeletal abnormalities, and low set ears are common to both deletion syndromes. Epicanthal folds, ptosis, a flat nasal bridge, and cutaneous syndactyly are features of syndrome II, while an antimongoloid slant, large ears, protruding nose, micrognathia, simian creases, and cardiac and renal anomalies are characteristic of syndrome I. Both

Fig. 3. Karyotype of the patient (Giemsa banding), showing the absent No. 21 chromosome.
this case and that of Gripenberg et al (1972) resemble syndrome I more than syndrome II. An infant recently reported to have monosomy 22 had congenital heart disease but lacked the epicantus and syndactyly of syndrome II (DeCicco et al, 1973). Hence these distinctions need further refinement and correlation with karyotypes if they are to prove useful for clinical diagnosis.

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Karyotype 45,XX,21/46,XX,21q-- in an infant with symptoms of G-deletion syndrome I

Summary. An infant with antimongoloid eye slants, achalasia, broad nose, one low-set large and one rudimentary ear lobe, and rudimentary nails with a retarded psychomotor development showed an 45,XX,21/46,XX,21q-- karyotype. By fluorescence and Giemsa staining it was shown that the missing or deleted chromosome 21 was of paternal origin.

Since Lejeune et al (1964) first reported a case with a mosaic of cells with 45 chromosomes and a missing G chromosome and cells with 46 chromosomes with a deleted G, a number of such mosaic

Fig. 1. The proposita at 6 weeks of age. Note large low-set hypoplastic ear and receding chin.

Fig. 2. The proposita at 6 weeks of age. Note antimongoloid slants, blepharochalasia, and broad nose bridge.

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