Monosomy G: Case Report and Review of the Literature

RONALD D. GREENWOOD and ANNEMARIE SOMMER*

From the Department of Pediatrics, Northwestern University Medical School and the Division of Genetics, The Children's Memorial Hospital, Chicago, Illinois, USA

Until recently, pure autosomal monosomy had been thought to be incompatible with extrauterine life and had only been described in spontaneous abortions. The first patient with a complete monosomy was the case reported by Al-Aish *et al* (1967) who had a G monosomy in blood, bone marrow, and skin.

Mosaicism involving the G group chromosome has been reported in the literature several times, most cases showing monosomy of a small acrocentric chromosome in one cell line only. The first such patient was described by Lejeune *et al* in 1964.

We wish to report a patient showing a normal chromosome complement (46,XX) in cultured skin fibroblasts and a mosaic G (45,XX,G- / 46,XX) in blood, a combination which has not yet been reported.

Case Report

This girl was first admitted to The Children's Memorial Hospital at the age of 2 years 10 months for the evaluation of cough, fever, and 'blood on the diaper'.

The patient was the product of a full-term pregnancy and weighed 2464 g (5 lb 8 oz) at birth. The mother's pregnancy had been complicated by vaginal bleeding during the first 4 months of pregnancy and the mother had received 2 injections (actual medication unknown) for threatened abortion. Also, the mother apparently had an upper respiratory infection without rash during the first trimester.

After delivery, the infant was kept in a hospital for 10 days for apparent mild jaundice and failure to thrive. Following discharge, she continued to do poorly, but did not receive any medical attention until 10 months of age when she had 4 febrile convulsions. At that time it was noted that the child was severely retarded. The patient reportedly smiled at 9 months of age and occasionally uttered noises without association, but no other developmental milestones had been reached.

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* Present address and address for reprints: The Department of Pediatrics, Ohio State University Medical School and The Children's Hospital, Columbus, Ohio, USA.

The family history revealed no evidence of heritable disease or frequent abortion. The mother was 30 years of age and the father 31 years old at the time of the birth of the patient. There are 2 female sibs, 4 years and 16 months old, and both are apparently normal and in good health.

On physical examination at admission at age 2 years 10 months, the patient was found to be obviously retarded and had no apparent contact with her environment. She weighed 10.4 kg (22 lb 14 oz) which is below the 3rd centile of her age and was 88.9 cm (35 in.) tall (3rd-10th centile for age). Heart rate was 128/min, respirations 30/min, temperature 101.8° F (38.8° C), and blood pressure 90/60.

She had numerous abnormalities (Fig. 1). She had a scaphocephalic head with peculiar narrow facies. There was a downward slanting of the palpebral fissures with a bilateral ptosis of the lids and a right corneal opacity was observed. The patient had a broad nasal bridge, a 'fish mouth', and a high arched palate. The ears were large and cup shaped and preauricular tags were present bilaterally. She had a short neck with a low hairline. The fontanelles were closed. The chest examination revealed the lungs to be clear, but a grade 3/6 systolic ejection murmur was heard at the mid left sternal border. The murmur radiated to the upper and lower sternal borders and was felt to represent a ventricular septal defect with pulmonic stenosis. The child had no abnormal abdominal findings but the pelvis was quite narrow. There were flexion contractures of both hips. The deep tendon reflexes were very brisk in all extremities. Several small bruises were noted on the skin, but no petechiae were seen.

Laboratory Investigations. A complete laboratory investigation revealed the following significant abnormalities: Hgb 10 g%, Hct 30, white blood count 8650, 76,000 platelets, and 2% reticulocyte count. The platelets decreased to 30,000 on the 6th day in hospital but returned to her normal levels when she was discharged. While prothrombin time, clotting time, and celitite partial thromboplastin time were normal, the bleeding time was prolonged to 9 min 4 sec (normal 3-5 min). The urinalysis revealed numerous red blood cells and 4+ protein and a culture grew out *E. coli* (greater than 100,000

FIG. 1. Patient at 3 years of age.

colonies/cm³). The urinalysis returned to normal after treatment. A bone marrow aspirate contained 14% eosinophils but no other abnormalities. Viral studies were negative for virus, but acute and convalescent haemagglutination inhibition titres were positive for rubeola.

The following studies were within normal limits: C-reactive protein, anti-streptolysin—0 titre, SGOT, SGPT, alkaline phosphatase, glucose, BUN, creatinine, beta-1-complement, true thyroxine, calcium, phosphorus, sodium, potassium, haemoglobin electrophoresis, protein electrophoresis, and immunoelectrophoresis. Cultures of the blood, throat, rectum, and bone marrow revealed no pathogenic organism. The purified protein derivative (tuberculin) was negative.

An EKG showed left atrial and ventricular hypertrophy with a normal axis. The EEG was normal.

Radiological Studies. Skull x-rays revealed slight asymmetry but were otherwise normal. Mild cardiac enlargement, a left aortic arch, and 13 ribs on the right side were noted on the chest films. An IVP and voiding cystourethrogram as well as an oesophagogram were normal. There was minimal osteoporosis and coxa valga.

Cytogenetic Investigations. Chromosome analy-

sis was performed on blood, bone marrow, and skin fibroblasts. The specimens for blood and bone marrow were cultured by the methods of Moorhead *et al* (1970) and for skin using the method of Nadler *et al* (1967). Eighty-four percent of the lymphocytes cultured from the peripheral blood were found to be monosomic for a G chromosome, and the remaining 14% had a normal chromosome complement of 46,XX. The fibroblasts from a skin biopsy were examined after the 3rd passage in tissue culture. Chromosome analysis revealed a karyotype of 46,XX in 98% of the cells and 2% of the cells were monosomic for a G chromosome. We consider this analysis to be representative of the mosaic we described in the patient. The results of the cytogenetic studies are shown in Table I and representative partial karyotypes are illustrated in Figure 2.

TABLE I
CHROMOSOME ANALYSIS

Cell Culture	Counted	Analysed	Type
Blood	100	100	84 45,XX,G- 16 46,XX
Skin	100	100	98 46,XX 2 45,XX,G-
Marrow	1	1	1 45,XX,G-

Dermatoglyphs. There was poor development of the ridges of the fingertips, but certain digital patterns could be identified (Table II).

TABLE II

	Digits				
	1	2	3	4	5
Right hand	A	A	A	U	A
Left hand	A	A	A	U	A

Palm prints of the left hand revealed a distal triradius in the *r'* range. No triradii were present in the *a*, *b*, *c*, *d* areas except for a *c'* triradius. The thenar/first interdigital pattern was open/open, and the hypothenar pattern was arch ulnar/arch carpal. There was also a transverse palmar crease. The right palm was identical to the left except for a bridged rather than a continuous palmar crease.

Course. While in the hospital, the patient developed typical rubeola. She was also treated for her urinary tract infection and we were able to discharge her much improved after 21 days of hospitalization. Subsequently, the patient has done well except for two episodes of otitis media and a fracture of the distal radius. Growth and development have essentially remained unchanged. She has not reached any further developmental milestone and still remains in the 3rd centile for height and weight at the age of 3½ years. She has had some intermittent bruising and a platelet count at the time of this report is 80,000.

FIG. 2. Partial karyotypes from blood (45,XX,G-) and skin (46,XX).

Discussion

Complete monosomy G in a patient has been reported only once in the literature (Al-Aish *et al*, 1967). An abortus with a pure G monosomy (Larson, Aare, and Titus, 1970) and one with mosaic monosomy G (Dhadial, 1967) have also been described. There are, however, at least 15 reported cases of mosaic monosomies for a G group chromosome in the literature. All of these reports show either mosaicism of normal or G deletion and G- cells within one cell line, or if a monosomy was reported, not all cell lines were investigated. These cases are summarized in Table III.

In 1964, Lejeune *et al* described the syndrome of antimongolism or 'le contre-type du mongolisme'. Patients with this syndrome show the following major abnormalities: hypertonia, mental and motor retardation, downward slanting palpebral fissures, large external ears and auditory canals, broadened bridge of nose, and other anomalies. It becomes evident from the literature that patients fitting this description can be found in the group reported as monosomy or mosaic monosomies (patients 1, 2, 4, 5, 6, 9, 11 in Table III) and patients with long arm G deletions or ring G chromosomes (Engel *et al*, 1966; Penrose, 1966; Reisman *et al*, 1966; Hindle in Challacombe and Taylor, 1969 and Weleber, Hecht, and Giblett, 1968; Warren and Rimoin, 1970). Only in the reports of deletions of the short arm of chromosome G do we not find any examples of the 'antimongolism' syndrome since these short arm deletions have been found in normal persons as well as in patients with numerous abnormalities. Warren and Rimoin (1970) suggested that two G deletion syndromes exist: (1) the 'typical' antimongolism; (2) a syndrome consisting of the following stigmata: hypertonia, epicanthal folds, retardation, syndactyly of toes. However, other patients reported fit into neither category.

Our patient does resemble the patients with the antimongolism syndrome. She presented with the 'typical' stigmata and bruising with an increased bleeding time and decreased platelets but no evidence of a clotting deficiency. Platelets have been noted to be decreased in 3 monosomies (Table III, patients 1, 9, 12). One patient (Table III, patient 11) has normal platelets but prolonged bleeding and clotting times, and one patient with a G deletion (Reisman *et al*, 1966) was noted to have thrombocytopenia. In other cases of monosomies and long arm or ring deletions, platelets and blood coagulation studies have been either normal or were not reported.

While familial mosaicism has been reported (Zdansky *et al*, 1969), more commonly, mosaicism is thought to originate after fertilization resulting in an individual who has at least two cell lines with different karyotypes derived from a single zygote. While it appears that degree and type of mosaicism are important in the clinical delineation of severity of disease, no strong relationship seems to exist. For example, the patient described by Al-Aish *et al* (1967), a 4½-year-old girl with complete monosomy has mental retardation and seizures but no other severe deformities, while the patient described by Cohen (1966)—patient 3 in Table III—expired during the first day of life and had multiple severe anomalies. His chromosome analysis showed the

TABLE III
MONOSOMY G REPORTED IN THE LITERATURE

Patient	Author(s)	Age and Sex	Type	Chromosomes		
				Skin	Marrow	Blood
1	Lejeune <i>et al</i> (1964) and Broyer <i>et al</i> (1966)	7½ mth, M	Mosaic	—	—	45,XY,G- /46,XY,Gr?
2	Thorburn and Johnson (1966)	1 yr, F	?	—	—	45,XX,G-
3	Cohen (1966)	1 dy, M	Mosaic	—	—	45,XY,G- /46,XY
4	Al-Aish <i>et al</i> (1967)	4½ yr, F	Complete	45,XX,G-	45,XX,G-	45,XX,G-
5	Hall <i>et al</i> (1967)	1 mth, M	?	45,XY,G-	—	45,XY,G-
6	Schulz and Krmpotic (1968)	8 yr, F	Mosaic	45,XX,G- /46,XX	—	45,XX,G- /46,XX
7	Schulz and Krmpotic (1968)	7 yr, M	Mosaic	45,XY,G- /46,XY	—	45,XY,G- /46,XY
8	Long and Pierre (1968)	68 yr, M	Mosaic	—	45,XY,G- /46,XY	—
9	Challacombe and Taylor (1969)	4 mth, M	Mosaic	45,XY,G- /46,XY, Gq- or Gr	—	45,XY,G- /46,XY,Gq- or Gr
10	Blank and Lorber (1969)	22 mth, F	Mosaic	—	—	45,XX,G- /46,XX,Gr
11	Endo <i>et al</i> (1969)	4 yr, M	Mosaic	—	—	45,XY,G- /46,XY,Gq-
12	Bauchinger <i>et al</i> (1968)	20 yr, M	Mosaic	—	—	45,XY,G- /46,XY,Gcen,(p-q-)
13	Zdansky <i>et al</i> (1969)	16½ yr, M	Mosaic	—	—	46,XY,Gr/45,XY,G-
14	Zdansky <i>et al</i> (1969)	49 yr, F	?Mosaic	—	—	46,XX/46,XX,Gr/45,XX,G-
15	Zdansky <i>et al</i> (1969)	26 yr, M	?Mosaic	—	—	46,XY/46,XY,Gr/45,XY,G-
16	Zdansky <i>et al</i> (1969)	54 yr, M	?Mosaic	—	—	46,XY/46,XY,Gr/45,XY,G-

majority of cells to have a 46,XY complement, and only a small percentage of his cells were monosomic for a G group chromosome. Yet there is still another group of patients with mosaicism (patients 8, 14, 15, 16 in Table III) who showed only a small percentage of monosomic cells and these patients have no congenital malformations and no significant disease.

Our patient is mosaic in blood (16% 46,XX and 84% 45,XX,G-) and 46,XX in skin and presented with severe disease.

It becomes evident from this short discussion, that as yet, the patients reported with various G deletion syndromes, are a very heterogeneous group and much work for more accurate delineation remains to be done in the future.

Summary

Deletion syndromes involving a chromosome of the G group have been discussed. Twelve of these patients are thought to represent examples of the antimongolism syndrome described by Lejeune *et al* in 1964. Reported in this paper is a 3-year-old female with severe mental and motor retardation, hypertonicity, flexion contractures, congenital heart disease, thrombocytopenia, and peculiar facies, the features of the antimongolism syndrome. Her karyotype is 45,XX,G- /46,XX in blood and 46,XX in skin, a variety of mosaic monosomy G previously unreported.

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