Case Reports


Klinefelter's Syndrome and G Trisomy

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The occurrence of Klinefelter's syndrome and mongolism in the same individual reported by Ford et al in 1959, was the first instance of double aneuploidy known in man. Since then several other cases of individuals with these two types of chromosome aberrations were described. A condition that cannot be easily distinguished on cytological grounds alone from double aneuploidy is the XXY type of chromosome aberration (Uchida, Miller, and Soltan, 1964). On the other hand, we have found no report of the joint occurrence of Klinefelter's syndrome and chromosome 22 trisomy. The present paper describes a malformed boy who presented simultaneously with XXY sex chromosomes and an additional chromosome in the G group. Since his features are not sufficiently distinctive for a diagnosis of mongolism, and for other reasons to be described below, it is possible that we may be dealing with this apparently rare combination (48,XXY,22+).

Case Report

A 2-year-old white boy was referred to us for cytogenetic studies because of multiple congenital anomalies and underdeveloped genitalia. He was the fourth child of apparently normal, nonconsanguineous parents, both of whom were aged 28 years at the time of his birth. He had two sisters aged 8 and 7, and a brother aged 5. There was no history of known exposure to infectious disease, radiation, or drugs during pregnancy. Details of delivery, which occurred at home, were not available. The mother, however, reported some difficulties and the child showed signs of cyanosis at birth. He was admitted to the Hospital of Santa Casa de Misericórdia in Porto Alegre with bronchopneumonia. At physical examination his weight was 7900 g, height 73 cm, arm span 70 cm, upper segment 44.5 cm, lower segment 28.5 cm, maximum head circumference 45 cm, thorax circumference 46 cm. The skin was loose and presented several hypochromic spots. The muscles were hypotrophic and slightly hypotonic. No clear demarcation of the hair at the forehead could be seen because of high pilosity. The head was brachycephalic, showing a typical caput quad-ratum (Fig. 1). The face was asymmetrical, the mouth showing a deviation to the right. A narrow palatal arch, cone-shaped incisors, and a slight micrognathia were also observed. The nasal bone was hypoplastic. The ears were implanted low and malformed. The eyes showed bilateral epicanthus and were small. The neck was short, with pterygium colli. In the thorax, the nipples showed low implantation and were widely spaced. The liver was palpable 3 cm below the midcostal margin and the spleen 1 cm below it.

The penis was small, the testicles were undescended and of soft consistency; surgical treatment was performed to place them in the scrotum.

The second toe was slightly hypoplastic and showed abnormal implantation in both feet. The right fourth

FIG. 1. The patient's appearance.
Klinefelter's Syndrome and G Trisomy

Fig. 2. Low power view of the patient's gonad. The picture is typical of a normal, immature testis (haematoxylin and eosin, × 145).

Fig. 3. The patient's karyotype showing an XXY,G + constitution.

toe also showed problems of implantation. The metatarsophalangeal joint showed decreased mobility. He also presented hyperconvex narrow fingernails on thumbs and halluces.

Radiography of the lungs showed atelectasis in the anterior segment of the right upper lobe. The heart was slightly enlarged. Cardiac examination (performed by Dr A. Achutti) and an electrocardiogram led us to conclude that there was a surcharge of the right auricle and ventricle compatible with the clinical diagnosis of isolated lung stenosis of moderate haemodynamic consequence.

At age 23 months his bone age was assessed as that of a boy of 18 months. A psychological evaluation performed at 2 years by Dr Elma H. Kristensen, showed his evolutive stage to be equivalent to that of a child with an
IQ around 30. A testicular biopsy was obtained and the histological examination (Fig. 2) performed by Drs L. A. Fagundes and D. C. Johann showed cords of undifferentiated cells sometimes with open spaces and pseudolumina. The stroma was not very dense and the presence of Leydig cells was not evident. The findings were typical of a normal, immature testis.

The child’s finger dermatoglyphics were as follows: right hand (from finger one to five): whorl (W), arch (A), A, W, A; left hand: W, A, ulnar loop (L), W, W; total ridge count was 56. His mother’s patterns were: right hand: L, A, A, L, L; left hand: L, A, L, L, L; total ridge count 57. His father’s right hand: W, W, L, W, L; left hand: W, W, L, L, W, W; total ridge count 183. The palmar configurations showed an adt angle of 38° in his right hand and 42° in the left, while the corresponding values in both his mother and father were 40° in the right and 38° in the left hand. Despite the similarity of these values in the child and his parents, a noticeable difference was that in the child the triradius, r, showed a marked displacement into the thenar region. There were also somewhat atypical simian creases in both hands, absence of patterns in the thenar and hypothenar areas, open fields in the second and third, and a loop in the fourth interdigital.

In the toes the patterns were as follows: right: W, W, W, L, A; left: L, L, W, L, A; the halucal area showed a distal loop, no patterns appearing in the interdigitals.

After treatment the child’s health showed some improvement and he was discharged from the hospital after about 6 weeks. He was readmitted 3 weeks later in very bad condition and died after 2 hours, apparently from bronchopneumonia. Unfortunately it was not possible to perform a necropsy.

Cytogenetic Studies. The buccal smear showed 16% of sex chromatin at the right side and 26% at the left, while his normal mother presented 28% and 30% respectively. Twenty-three of 1000 polymorphonuclear leucocytes presented a drumstick. Chromosome studies of a peripheral blood sample showed that 48 of the 50 cells counted had 48 chromosomes. Eleven cells were karyotyped all showing a pattern compatible with an XXY, G+ constitution (Fig. 3).

Discussion

Three hypotheses can be put forward to interpret these findings. (1) The child’s chromosome constitution is XXYY; (2) he is an atypical case of XXY,
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SYNDROME AND MONGOLISM REPORTED IN THE LITERATURE

<table>
<thead>
<tr>
<th>Tongue</th>
<th>Ears</th>
<th>Cardiovascular Problems</th>
<th>Dermatoglyphs</th>
<th>Short Hands and Fingers</th>
<th>Hair Distribution</th>
<th>Genitalia</th>
<th>Testicular Biopsy</th>
<th>IQ</th>
<th>Chromosome Studies</th>
<th>No. of Cells Counted</th>
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<td>Under-developed</td>
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<td>Low</td>
<td>Bone marrow; skin</td>
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<td>NI</td>
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<td>NI</td>
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chromosome 21 trisomy, or (3) he is XXY, 22+. We have examined all cells carefully to see if they could be interpreted as showing two Y’s, but this was not the case for generally one chromosome only could be assigned as Y. On the other hand, all previous cases of XXY individuals showed only minor anomalies. It seems likely therefore that this hypothesis can be rejected.

It is more difficult to decide whether we are dealing with an atypical 21 or with a 22 trisomy. Table I gives details of the 13 patients previously reported in the literature as showing Klinefelter’s syndrome and mongolism; and the data is compared with the present case. As shown in Table I, several phenotypical signs of mongolism are present in the 13 patients. Thus, brachycephaly was reported in 6 of the 7 cases from whom information on the cephalic index was available. Speckling of the iris, cataract, and nystagmus in 3 of 6 patients. Fissured tongue in 5 of the 6 for whom data are available. The other characteristics were distributed as follows: low set and malformed ears (4/5), cardiovascular problems (4/7), typical dermatoglyphic pattern (7/8), and short hands and fingers (6/7). Other characteristics may have been due to the autosomal or sex chromosome disturbance, namely the scanty and feminine hair distribution found in the three adult cases and the underdeveloped genitalia (present in 10 of the 13 patients). Testicular biopsies were obtained from six subjects. Atrophic changes were seen in two adult patients (Harnden, Miller, and Penrose, 1960; Milcou and Maicanesco, 1963) and even in one patient aged 6 years of age (de Grouchy et al, 1965). Studies on younger patients were inconclusive. Lanman et al (1960) suggested an increased frequency of germinal epithelium absence in a 10-month-old individual but a normal histology was found by Sénéze et al (1964) in a patient aged one year. Mental deficiency is reported in the 8 cases where information on intelligence was available.

Our patient presents 3 of the 7 characteristics listed in Table I which can be regarded as signs of mongolism (brachycephaly, low set and malformed
ears, and cardiovascular problems. On the other hand, his dermatoglyphics are atypical, and he does not show eye abnormalities, fissured tongue, or short hands and fingers. The underdeveloped genitalia and low IQ may result from the sex chromosome disturbance. It is noteworthy that a normal histological picture was found in his testes.

As it is impossible to delineate the main clinical findings of chromosome 22 trisomy clearly and, even by autoradiography, difficult to distinguish chromosomes 21 and 22 we prefer to leave undecided the question of the autosomal disturbance in the case presented here. Detailed descriptions of further XXY, G+ individuals are necessary for the differentiation of the two syndromes.

**Summary**

Clinical and cytogenetic data about a 2-year-old malformed boy with an XXY, G+ chromosome constitution are given. He does not show the classical signs of mongolism and the suggestion is made that, besides the sex chromosome disturbance, he may have 22 trisomy. Reports from 13 other patients showing Klinefelter’s syndrome and mongolism are reviewed for comparison.

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