Multiple Congenital Defects Associated with an Abnormal Unclassifiable Karyotype

We report the case of an infant with multiple congenital anomalies, and a karyotype that we were unable to classify.

Case Report

The propositus was born to a 29-year-old, gravida 5, para 4, mother after 42 weeks of uncomplicated gestation by Caesarean section because of malposition and fetal distress. One-quarter of the placenta had been abruped. The infant's Apgar score at 1 min and again at 5 min was 2. The birth weight was 4120 g, length 53 cm, head circumference 39-5 cm, 5-5 cm greater than the chest circumference. He appeared lethargic, limp, and had a feeble cry. He had a wide forehead, orbital hypertelorism, and a capillary haemangioma near the right eyebrow. The palpebral fissures pointed outwards and upwards. (Fig. 1). Grey-white opacities mottled both corneas. He had coloboma of the left iris and choroid. The left pupil was dilated; neither pupil reacted to light. The optic fundi were normal. The ears were low-set and poorly developed, the base of the nose depressed, the chin receding. The heart was enlarged. A grade I/IV systolic murmur was heard at the left sternal border. The liver and spleen and both kidneys were palpable. External genitalia were normal male. The limbs were normal.

Laboratory Investigations. The peripheral blood count, blood urea nitrogen, blood sugar, serum calcium, phosphorus, sodium, potassium, and chloride were normal. An electrocardiogram was read as normal. Urinary amino-acid chromatogram was also normal.

Radiological Investigations. The vault of the skull was enlarged, the sutures widened indicating increased intracranial pressure. X-rays of the chest showed marked cardiomegaly and pulmonary vascular congestion. Bilateral gross hydronephrosis and hydroureter were shown on IVP. A cystogram showed wide dilatation of the bladder neck and prostatic urethra.
The urethra was almost completely obstructed by posterior valves at the level of the urogenital diaphragm.

Hospitalization. The posterior urethral valves were resected and the degree of hydronephrosis became less. A urinary tract infection developed and was treated with appropriate antibiotics. Three weeks after admission he had difficulty swallowing and aspirated food frequently. His condition gradually deteriorated. He had frequent dusky spells, his head size increased and the anterior fontanelle bulged. Subdural taps were negative. He died of aspiration at the age of 2 months. No necropsy was performed.

Cytogenetic Investigations. Cultures of the patient’s peripheral blood leucocytes and skin fibroblasts and cultures of the parents’ peripheral blood leucocytes were made.

Most of the patient’s metaphase cells (Table I) contained 46 chromosomes; only 3 chromosomes in 21-22 pairs and an additional metacentric slightly larger than chromosome number 16. The extra chromosome did not show satellites or satellite association. In many cells a normal-looking Y chromosome could be identified (Fig. 2). Fibroblasts were sex chromatin negative.

Autoradiographic studies with tritiated thymidine were made on cultured lymphocytes. The extra chromosome and the Y chromosome were heavily labelled as compared to the E group chromosomes. Two of the 21-22 chromosomes were early replicators and one was late replicator.

The fluorescence banding pattern of the chromosomes was not adequate when Giemsa stained slides of peripheral blood cultures were de-stained in distilled water and restained with 0.5% quinacrine dihydrochloride. These studies could not be repeated as we do not have unstained slides and the patient is dead.

The karyotypes of both parents were normal.

Dermatoglyphs. Palmar prints showed bilateral simian creases, a ridge count of 73 (which is one standard deviation below the mean for normal males) and slightly raised axial triradii (t'). Arch fibular patterns (seen in only 3% of normal persons) were present on plantar hallucal areas of both feet.

Discussion

The multiple congenital anomalies were not characteristic of any known chromosomal syndrome. The normal karyotypes of parents, the presence of normal Y chromosome, and the absence of sex chromatin mass in fibroblasts exclude several possibilities. A G/G translocation-Down's syndrome

<table>
<thead>
<tr>
<th>Tissue Examined</th>
<th>Chromosome Counts</th>
<th>Total Cells</th>
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<tbody>
<tr>
<td></td>
<td>&lt;45</td>
<td>45</td>
</tr>
<tr>
<td>Blood</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Skin</td>
<td>1</td>
<td>1</td>
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![Fig. 2. Partial karyotypes of the propositus. The arrow indicates the extra chromosome.](Image)
and isochromosome for the long arm of 21 were excluded by the clinical findings, dermal patterns (Walker index), and the size of the abnormal chromosome. Trisomy 22 with a G/G translocation was ruled out by the size of the abnormal chromosome. Trisomy 16 with monosomy G was excluded because the abnormal chromosome was always metacentric and slightly bigger than the number 16. Trisomy 17 with 17/G translocation or monosomy G with isochromosome for short arm of one of the group C or group B chromosomes remain possibilities.

At present, classification of this karyotype is inadvisable, especially in view of inconclusive autoradiographic studies and inadequate banding pattern of the chromosomes. Perhaps similar cases will be reported.

**Summary**

We report the case of an unusual-looking infant with multiple congenital anomalies such as coloboma of the iris, corneal opacities, congenital heart defect, hepatosplenomegaly etc, who had an abnormal karyotype which appears to be unique and remains unclassified.

The authors wish to thank Dr Herbert A. Lubs, Jr of the University of Colorado Medical Center, Colorado, for his suggestions; and Donna Nerima and Carol Crabtree for their technical assistance.

**Corrigenda**


The last sentence in the section on the X-linked and haemolytic predisposition (p. 465, column 2) should read:

For instance, a difference ranging between 0·198 and 0·290 for G6PD deficiency corresponds to a difference ranging between as little as 0·107 and 0·120 for favism in Seneghe and Lodé respectively.


The 10 cells counted and analysed from both the father and the mother of case 4 contained 46 chromosomes and not 47 as shown in Table I (p. 1).