PARTIAL DELETION OF THE SHORT ARMS OF A CHROMOSOME OF THE 4-5 GROUP (DENVER)

BY

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Whereas in man life is possible in the presence of an extra autosome (though not without considerable defects), absence of an autosome appears to be incompatible with life. Even absence of parts of an autosome appear, as a rule, to be lethal and may lead to spontaneous abortions (Jacobsen, Dupont, and Mikkelsen, 1963).

Grouchy, Lamy, Thieffry, Arthuis, and Salmon (1963) described a child with various malformations in addition to defective intelligence, who had absence of the short arms of a chromosome No. 17 or 18. Shortly after this, Lejeune, Lafourcade, Berger, Vialatte, Boeswillwald, Seringe, and Turpin (1963) described 3 patients all of whom presented the same cytological picture, in that part of the short arms of a chromosome in the 4-5 group were absent. All 3 patients were mentally retarded, their somatic development was retarded, they had microcephaly, hypertelorism, epicanthus, low-set ears, and cat-like mewing.

We have had the opportunity of examining a child with similar clinical symptoms who also presented deletion of the short arms of a chromosome in the 4-5 group.

Case Report

L.M.C., a male, was born on June 5, 1960. There was no known disposition to mental retardation, dwarfing, or deformities in the family. The parents were healthy, normal, and were not blood relatives. The patient is the fifth of six children. The first three children were triplets (two boys and a girl) who were born two and a half months prematurely and died shortly after birth. They did not present any visible malformations but no necropsy

FIG. 1.—The appearance of patient at the age of 2 months. Note hypertelorism, epicanthus, retrognathia, low-set ears, and a dimple anterior to the right ear.
was performed. The fourth and the sixth children are normal boys, born in 1957 and 1961.

Both parents were 33 years at the patient's birth. The pregnancy was uneventful. The delivery was normal and at term. Birth weight 3,200 g., length 51 cm. There was marked inspiratory stridor with a tendency to cyanosis from birth. Feeding difficulties occurred and the infant failed to thrive. He was admitted to hospital from the age of 1 month until the age of 2 years. At the age of 2 months, the circumference of the head was 35 cm. (normal 39 cm.) (Fig. 1).

At the age of 2 years, the boy weighed only 7.7 kg. and inspiratory stridor and feeding difficulties persisted. A marked tendency to respiratory infections was present. At the age of 4 years, he could walk only with support and could not speak. Slightly stridulous respiration on exertion persists. No epileptic seizures have occurred.

Physical examination at the age of 4 years showed his height to be 94 cm., his weight 11 kg.; head circumference 45 cm. Nuchal region was rather prominent. Epicanthus and hypertelorism were present but no other ocular changes. The ears were low set but otherwise normal. A dimple without cartilage was observed anterior to the right ear. The palate was high and formed an inverted V and the chin was small and retracted (Figs. 2a, b, c). There was no webbing of the neck. A moderate systolic murmur was heard inferiorly along the left sternal margin; no cyanosis or retraction occurred during inspiration.

The external genitalia were normal. Transverse palmar creases were present in both palms (Fig. 3a, b). The extremities were otherwise normal with normal tone and tendon reflexes.

The child was able to walk with slight support in a rather bent position. The voice had a peculiar bleating character. He could say 'Ja' (yes) but no other intelligible words. His play and behaviour correspond to the normal for a child of approximately 1 year.

Investigations. Repeated thoracic radiographs have shown the heart to be normal in form and size. Screening revealed that the excursions of the diaphragm were limited but otherwise normal. Neither dislocation nor compression of the trachea were present. The position of the oesophagus was shown to be normal on contrast filling. Radiograph of the cranium revealed no abnormality.

Direct and indirect laryngoscopy (under anaesthesia) revealed no congenital malformations. 'The case is one of pronounced congenital inspiratory stridor.'

No abnormality was revealed on electroencephalography. The urine contained no sugar, albumin, or phenyl-pyruvic acid, and microscopic examination was normal. Serum calcium and phosphorus, and acid and alkaline phosphatases all showed normal values. Blood group studies are set out in the Table.

Cytology. The patient and his parents were examined. Sex chromatin was determined on Feulgen-stained

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<th>BLOOD GROUP STUDIES</th>
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<tr>
<td>The father</td>
<td>O Ns P + R1 R1 Le (a − b +) Fy (a +) K −</td>
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<tr>
<td>The mother</td>
<td>A1 Ns P + Rgr Le (a + b −) Fy (a +) K −</td>
</tr>
<tr>
<td>The patient</td>
<td>A1 Ns P + R1r Le (a + b −) Fy (a +) K −</td>
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buccal smears and was, in all cases, in agreement with the phenotypical sex. The patient's karyotype was studied in cells from peripheral blood, cultured according to the micromethod described by Froland (1962) and in fibroblasts from skin culture according to Froland (1961). In both blood and skin culture, the modal number was 46. In all 60 cells examined, one chromosome of the 4-5 group showed deletion of the short arms. The other chromosomes were as in a normal male (Fig. 4).

The parent's karyotypes were studied in blood cells cultured according to Moorhead, Nowell, Mellman, Battips, and Hungerford (1960). Both had normal karyotypes.

Fig. 3.—Right and left hand of the patient. Transverse palmar creases are evident in both palms.

Fig. 4.—The karyotype of the patient. 46 chromosomes. Note the deletion of the short arms of one chromosome in the 4-5 groups. Blood culture. (Giemsa stain.)


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The boy presented somatic dwarfing, microcephaly, micro-retrognathia, congenital stridor, hypertelorism, epicanthus, low-set ears, transverse palmar creases in both hands, and severe mental retardation.

Similar findings were described previously in three somewhat younger patients by Lejeune and his co-workers.

**References**


**Addendum**

Since this paper was prepared at least four more cases have been described: Lejeune, Lafourcade, Grouchy, Berger, Gautier, Salmon, and Turpin (1964), Boöök, Atkins, and Santesson (1963) and Grouchy, Arthuis, Salmon, Lamy, and Thieffrey (1964).

In addition one of us (M.M.) has examined a newborn girl with hypertelorism, round face, transverse palmar crease, and low-set ears. Again chromosome studies revealed a partial deletion of the short arms of a chromosome in the 4-5 group. The child was referred to cytological investigation on account of its cat-like cry by Dr. N. Hobolth, Pediatric Department, Copenhagen County Hospital, Gentoft.

A full report will be published elsewhere.
Partial Deletion of the Short Arms of a Chromosome of the 4-5 Group (Denver)

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