Deletion of the short arm of chromosome No. 10*

Summary. A newborn male infant, whose karyotype was 46,XY,del(10) (p13) is presented. The clinical features included cleft lip and palate, preauricular pits, low set malpositioned auricles, antimongoloid slant of the eyes, microcephaly, micrognathia, congenital heart disease, hypertrophic pyloric stenosis, cryptorchidism, and abnormal dermatoglyphics. The child died at the age of 3 months in overwhelming urinary infection with septicemic complications. It is suggested that the features described here may represent a new, clinically recognizable chromosomal syndrome.

Characteristic phenotypes have been consistently observed in association with specific numerical or structural chromosomal alterations. The latter have been reported in the B group; for instance, the cri-du-chat syndrome resulting from partial deletion of the short arm of chromosome No. 5 (Lejeune et al, 1963; German et al, 1964) and Wolf's syndrome in partial deletion of the short arm of chromosome No. 4 (Wolf et al, 1965; Leão et al, 1967). Similarly, deletions of the long arms of chromosomes 18 (de Grouchy et al, 1964) and 21 (Lejeune et al, 1964) have been associated with specific clinical features.

Structural abnormalities of the C-group chromosomes, however, have hitherto been only rarely linked to specific identifiable patterns of malformations. This has been variously interpreted to indicate inviability of conceptuses in whom these anomalies occur (Hamerton, 1971). Alternatively, the difficulties encountered in identification of individual C-group chromosomes before the advent of banding techniques, may have hindered the establishment of associations between clinically recognizable syndromes and the specific chromosomal structural alterations.

Nevertheless, de Grouchy et al (1968) reported on a case of suspected Cp—chromosomal aberration with prematurity and multiple congenital abnormalities including large, low set ears with preauricular tubercles, retrognathia, hypospadias, inguinal testes and herniae, abnormal dermatoglyphics, short stature, and developmental retardation. The exact identification of the chromosome involved was not, however, possible. Further, Biscatti (1965) reported a mentally retarded 3-year-old girl with low set ears, simian creases, clinodactyly, and hypertelorism. One of her C-group chromosomes was missing and replaced by a small metacentric chromosome similar in size to members of the E group. A deletion of the long arm of a C-group chromosome was therefore suggested. A more complex rearrangement cannot, however, be ruled out. As neither of her parents was cytogenetically studied, the origin of the chromosomal anomaly was not ascertained.

With the precision now available for identifying unambiguously individual chromosomes or parts thereof, more of these associations are coming to light (Alfi et al, 1973; Shokeir, Ying, and Pabello, 1973).

In this communication we report a male infant with multiple congenital anomalies whose karyotype disclosed partial deletion of the short arm of chromosome No. 10.

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Fig. 1. Pedigree.
Case report

The propositus (IV.2, Fig. 1), a male infant was born on 20 June 1973 to healthy young parents (III.7 and III.8), both aged 22 years. He was the second in the sibship with an older brother (IV.1), aged 3 who is normal and healthy. Exploration of the family history revealed only a haemophiliac paternal patrilineal cousin of the propositus' father. The mother, however, had a previous spontaneous miscarriage at 10 weeks of gestation some 18 months before her pregnancy with the propositus. The pregnancy was marred by pre-eclamptic toxaemia and urinary infections but ended at term in a minimally assisted delivery.

At birth he weighed 2530 g and had an apgar of 3 and 6 at 1 min and 5 min, respectively. A unilateral complete left cleft lip and palate anomaly was evident. Because of feeding difficulties and the prospect of surgical repair of the lip, he was transferred to the Children's Centre in Winnipeg. The infant was seen in consultation and he was noted to have, in addition to the obvious cleft lip and palate (Fig. 2), widely open anterior and posterior fontanelles and metopic suture, antimongoloid slant to the palpebral fissures, bilateral preauricular sinuses, micrognathia, abnormal dermatoglyphics with distal palmar triradii, a simian crease in the left palm and a transitional one in the right, longitudinal groove in the soles of both feet along the course of the second metatarsals, pectus excavatum and widely spaced nipples, small umbilical hernia, and right undescended testis. Weak peripheral pulses, both femoral and brachial were discerned with difficulty. Cardiac examination revealed a widely split second sound, an ejection click and 3/6 ejection systolic murmur best heard in the pulmonary area and left parasternal zone. The infant was in no distress.

The presence of multiple congenital malformations which did not fit a known syndrome, suggested the possibility of a chromosomal abnormality. Surgical intervention was therefore deferred and cytogenetic studies were initiated.

Laboratory investigations. An electrocardiogram showed right ventricular overload and strain. Radiology of the chest revealed cardiomegaly but no detectable pulmonary parenchymal lesions. Cardiac catheterization confirmed the clinical diagnosis of pulmonic stenosis and revealed atrial septal defect with left to right shunt. Post-stenotic dilation of the pulmonary artery and pulmonary hypertension were also noted.

Fig. 2. Front (a) and side view (b) of the propositus.

<table>
<thead>
<tr>
<th>Technique Used</th>
<th>Total No. of Cells</th>
<th>Karyotype</th>
</tr>
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<tbody>
<tr>
<td>G-Banding</td>
<td>Q-Banding</td>
<td>Orcein</td>
</tr>
<tr>
<td>Propositus</td>
<td>23</td>
<td>18</td>
</tr>
<tr>
<td>Mother</td>
<td>12</td>
<td>14</td>
</tr>
<tr>
<td>Father</td>
<td>19</td>
<td>14</td>
</tr>
<tr>
<td>Sib</td>
<td>5</td>
<td>—</td>
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</table>
FIG. 3. Partial karyotypes of the C-group chromosomes (G- and Q-banding) from the propositus and his parents.
Cytogenetic studies

Chromosome analysis of the propositus IV.2 using conventional Orcein staining, Q-banding, and G-banding revealed a 46,XY,del(10)(p13) chromosome constitution. The karyotypes of the mother, the father, and the one living sib showed normal chromosomes, with no evidence of a deletion or of any other detectable rearrangement which might account for the chromosome abnormality observed in the propositus (Table I). Partial karyotypes of the C-group from the propositus, his mother and father are shown in Fig. 3 and the position of the deletion in Fig. 4. The breakpoint has been identified at (10)(p13), the material distal to that point being deleted.

Chromosome measurements were carried out on the C-group from five Q-banded cells from each of the propositus, his mother, and father; the relative length, arm ratio, and centromeric index were calculated. Examination of the data summarized in Fig. 5, which depicts the mean relative length of p plotted against the mean relative length for q, shows that with the exception of the del(10) carried by the propositus, none of the chromosomes fall outside of the expected range of variation for each homologue, thus confirming that no other visually detectable chromosome rearrangement can be found. The chromosome measurements show that 9-8% of the total length, or 27-5% of the short arm of one homologue of chromosome 10 is missing. The most likely explanation for these observations is a simple terminal deletion with a breakpoint at (10)(p13) and loss of the distal segment (10)(pter→p13). Banding of the short arm of chromosome 10 is such that a two-break interstitial deletion cannot be excluded. We feel, however, that it is less likely.

Clinical course

When his feeding stabilized, the propositus was discharged, having been fitted with a palatal prosthesis.

At 6 weeks of age he suffered repeated post prandial vomiting which was projectile in character. Subsequent investigations including barium study disclosed hypertrophic pyloric stenosis, for which pyloromyotomy was successfully performed at 7 weeks.

At 10 weeks of age he developed fever, pallor, and tachypnea with subcostal indrawing. Examination revealed hepatic enlargement (5 cm below the costal margin), muffled first heart sound, and a loud systolic murmur. A chest radiograph disclosed bilateral broncho-pneumonia and an enlarged cardiac silhouette. An electrocardiogram showed evidence of biventricular overload. Diuretics and digitalization appeared temporarily to improve his condition. However, he ultimately died at 13 weeks of age. Shortly before his death urinalysis showed E. coli and Klebsiella growth.

Throughout his hospital stay, the water and electrolyte balance of the propositus was satisfactorily maintained. He also received antibiotic therapy to combat the infections he developed particularly the pyelonephritis with possibly septicemic complications which ensued a few days before his demise.

Necropsy

Weight was 3510 g, crown-rump length was 39 cm, and crown-heel length 56 cm. Head circum-
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The findings with this were negligible.

The heart showed bicuspid aortic valve and stenosis of the pulmonary valve.

Two more systems showed evidence of congenital malformations; the brain which weighed 560 g, revealed aplasia of the olfactory bulbs and olfactory tracts. Both kidneys showed evidence of sepsis—acute pyelonephritis. While the right kidney was of relatively normal size and weight (31 g), the left kidney weighed less than 7 g, had only three calyces and was supplied by tiny, patent vessels. Both kidneys were studded with scattered mature cartilage throughout the parenchyma. Both ureters were dilated. The right testis was found to be high in the inguinal canal.

Apart from confirming the clinically visible malformations, such as cleft lip and palate involving the alveolus, hard and soft palates, preauricular sinuses, pectus excavatum, and umbilical hernia together with the evidence of pylorotomy, the remainder of the necropsy disclosed findings consistent with congestive cardiac failure and urinary sepsis.

Discussion

It appears plausible that the observed anomalies in the propositus are ascribable to the partial deletion in the short arm of chromosome No. 10. In conformity with the rest of chromosomal syndromes there is no underlying common pathogenetic mechanism to account for the diverse and variable phenotypic features.

Since cytogenetic studies performed on the propositus' parents and his older sib revealed no detectable abnormality it appears most likely that the chromosomal deletion in the propositus had arisen de novo. The failure to find any cell with a normal karyotype in the propositus suggests that the lesion had arisen either during gametogenesis in the parents or immediately after fertilization. This inference has, of course, important implications in terms of genetic counselling for the family, as the risk of recurrence of a similar abnormality must be almost negligible.

In view of the limitations of the available techniques, it cannot be entirely ruled out that the deleted chromosome is in fact a derivative or recombinant chromosome resulting from some type of chromosome rearrangement carried by one or other of the parents. There is, however, no evidence for this and the simplest explanation for the observed findings is a terminal deletion in the propositus with significant loss of genetic material. This could account for the substantial clinical abnormalities observed.

Confirmation of the role of the specific chromosomal aberration in the genesis of the clinical syndrome described should await further investigation of similar patterns of malformations. Should the chromosome No. 10 deletion be consistently implicated, clinical recognition of the syndrome will be rendered more feasible and the management of the respective cases doubtless modified.

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