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Prenatal diagnosis of mosaicism for del(18)(q12·2q21·1) and a normal cell line

A 37 year old single Hispanic woman had amniocentesis because of maternal age. She had had five pregnancies, resulting in two normal children with a previous partner, one elective abortion, and one tubal ectopic pregnancy with the present 20 year old partner. The medical and family histories were unremarkable.

Two separate primary amniotic fluid cell cultures at 21 weeks' gestation showed mosaicism for 46,XY/46,XY, del(18)(q12·2q21·1)(fig 1). Six of 25 cells (24%) from one primary culture and eight of 25 cells (32%) from the other primary culture showed the deletion. The chromosomes of the parents were normal.

The pregnancy was electively terminated by prostaglandin at 24 weeks' gestation. The fetus weighed 740 g (at about the 50th centile). Noted were the following craniofacial anomalies: high and narrow forehead, long philtrum, small and thin lips especially the lower (fig 2), long and broad thumbs, contractures at the middle interphalangeal joints, bilateral transverse palmar creases, long and broad big toes, and long toes. Necropsy showed a large foramen

FIG 2 The fetus at 24 weeks.

ovale that was indistinguishable from an atrial septal defect.

The deletion was found in 24% (6/25) of cultured cells from amniotic fluid, in 2% (1/50) of cells from cord blood, and in 47% (35/75) of cells from umbilical cord tissue obtained at the time of pregnancy termination.

Since this pregnancy, the couple has had another pregnancy resulting in a normal son.

Mosaicism for a structural anomaly at prenatal diagnosis is an uncommon event, occurring in only 15 of about 60 000 genetic amniocenteses.¹ Since de Grouchy *et al*² first described a syndrome associated with partial deletion of the long arm of chromosome 18, several other physical anomalies associated with deletion of 18q12·2→q21·1 have been described.³ This deletion was found in a proportion of cells from the present fetus, who showed some craniofacial features similar to those of the child previously reported, including a high and narrow forehead and long philtrum. The deletion responsible for this case is more proximal than the deletion associated with de Grouchy syndrome, which appears to involve 18q21 (probably q21·3).

We thank Mr William Herbert who participated in the patient's care. Partial support was provided by US Public Health, Maternal and Child Health Services, Grant No 286.

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FIG 1 Partial GTG banded karyotype from an amniotic fluid cell. The arrows indicate the breakpoints in the normal chromosome 18 (left) and in the idiogrammatic 18 (right). The dark band q12·3 and some of the light staining band q21·1 are deleted in the anomalous chromosome 18.

Received for publication 9 June 1987.

Revised version accepted for publication 10 August 1987.

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A new centromeric heteromorphism in the short arm of chromosome 20

An apparently new type of 20ph+ centromeric heteromorphism was detected in two unrelated patients. It segregated within the families of both index patients without any harmful phenotypic effect.

The index patient in the first family was a dysmorphic male neonate born after a 32 week pregnancy complicated by polyhydramnios. Birth weight was 1600 g (25th centile); length and head circumference were 46 cm and 32.5 cm respectively (both 90th centile). Extreme hypotonia resulted in severe perinatal problems, and feeding difficulties with poor sucking persist up to the present. At the age of 11 months his mental and motor development were at the level of five months and three months, respectively. Craniofacial dysmorphism included a prominent forehead, high nasal bridge, and posteriorly rotated ears. There was camptodactyly of all fingers and overriding of the second, third, and fourth fingers. Extensive laboratory and neurotechnical examinations, including CT scan and electromyography, were normal. At the birth of this child, the mother and father were 39 and 34 years old, respectively. Two previous pregnancies ended in spontaneous first trimester abortions. After the third pregnancy an apparently normal looking girl died of perinatal asphyxia. No necropsy was performed. Further family history is negative. Both parents are phenotypically normal and unrelated.

Sixty-eight prometaphases from two different peripheral lymphocyte cultures were analysed with G, C, and R banding. One of the chromosomes 20 showed a distinct C positive heterochromatic block in the juxtacentromeric region of its short arm (figure (a)). The karyotype was otherwise normal and, more particularly, the heterochromatic blocks of chromosomes 1, 9, and 16 were within the limits of normal population variability. The karyotype of the child was thus interpreted as being: 46,XY,20ph+. The identical variant of chromosome 20 was present in the karyotype of the father and paternal grandfather, both of whom were phenotypically normal.

Cytogenetic examination in a couple with two spontaneous first trimester abortions revealed a heterochromatic heteromorphism in the short arm of one of the chromosomes 20 in the husband (figure (b)). The size and the position of the C positive material in the short arm of chromosome 20

(46,XY,20ph+) was identical to that found in the first family. Recently, we had the opportunity to karyotype the proband's father who also appeared to be a carrier of the same chromosome variant. As far as we could investigate, both families were unrelated.

Human C heteromorphism is one of the best classified human chromosome polymorphisms^{1,2} and the mechanism of its duplication/deficiency process is well explained.³ Rare chromosomal heteromorphisms inherited as a Mendelian trait have been described several times. The juxtacentromeric accumulation of a C positive heterochromatin block in the short arm of chromosome 20 in the two index patients of this report is apparently another example of a rare polymorphic variant in human constitutive heterochromatin. The first index patient presented a MCA/MR syndrome with severe hypotonia and craniofacial dysmorphism, but the 20ph+ morphology was also found in the normal father and grandfather. In the second index patient, the indication for chromosomal analysis was recurrent early fetal wastage but his parents' reproduction was normal. The heterochromatic blocks of the 20ph+ variant were stable in size in all five persons under investigation, as were the qh regions of chromosomes 1

FIGURE The 20ph+ morphology in the first patient (a) and the second patient (b).

Received for publication 30 October 1987.

Revised version accepted for publication 13 November 1987.