Prenatal detection of monosomy 18p and trisomy 18q mosaicism with unexpected fetal phenotype

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SUMMARY A mosaic karyotype 46,XX,del(18)(p11)/46,XX,-18,+?i(18q) was found in cultured amniotic cells. Fetal blood sampling confirmed the presence of both cell lines. The pregnancy was terminated and the two cell lines were demonstrated in varying proportions in the fetal tissues. The few abnormal features seen in the fetus may represent a mild expression of the 18p—phenotype inhibiting the effects of the trisomy 18q.

Case report

A 36 year old woman was referred for prenatal screening because of maternal age. Her husband was aged 40 years. They had two normal daughters and there was no record of fetal losses or other significant family history. The amniotic fluid sample was taken at 16 weeks of gestation. AFP concentration was below the lower limit of the normal range (5 to 35 g/ml). A mosaic karyotype was found. The patient was then referred for fetal blood sampling. Chromosome analysis from the fetal blood carried out in two other laboratories confirmed the presence of the mosaicism. The pregnancy was terminated at 20 weeks' gestation. Further culture of amniotic fluid cells and of fetal blood (taken by heart puncture) were set up at the time of termination.

The fetal measurements corresponded to the stated gestational age. No gross malformations were seen, but the fetus had a receding forehead, micro- and retrognathia, small, round, low set ears, slight contractures of both knees and the right elbow, and rocker bottom feet (fig 1).

CYTOGENETIC STUDIES

The amniotic fluid sample, grossly blood stained, gave poor growth with only a few cells suitable for analysis when harvested after 14 days. In two of the three replicate cultures a mosaic karyotype was found and interpreted as 46,XX,del(18)(p11)/46,XX,-18,+?i(18q). The two cell lines were in the proportion of one to four respectively. A third culture showed only the 18p— cell line in the few cells

available. There is doubt about the exact nature of the ?i(18q) chromosomes. Our results showed symmetry of G banding and staining intensity in both arms (fig 2). Only a single centromeric region was seen with C banding. However, one of the collaborating laboratories reported slight asymmetry and proposed a translocation of the greater part of the long arm of one chromosome 18 onto the proximal short arm of another.

Fetal lymphocyte cultures gave poor, atypical growth with reduced response to mitogenic stimula-

FIG 1 Fetus after termination at 20 weeks' gestation.

FIG 2 G banding of chromosome 18: (a) normal 18, (b) isochromosome 18q, (c) 18p—.

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TABLE Complete cytogenetic findings of the present case.

Cell type	Culture	46,XX,18p- (%)	46,XX,-18,+?i(18q) (%)
Amniotic fluid cells at this laboratory	A	2 (28.5)	5 (71.5)
	B	8 (100)	0 (0)
	C	3 (37.5)	5 (62.5)
Amniotic fluid cells at fetoscopy	Guy's	10 (52.6)	9 (47.4)
	Edinburgh	16 (80)	4 (20)
Fetal blood at fetoscopy	Guy's	0 (0)	11 (100)
	Edinburgh	9 (45)	11 (55)
Fetal blood after TOP at this laboratory		5 (25)	15 (75)
Fetal tissue from Chorionic membrane		Culture failed	
Liver		Culture failed	
Kidney		36 (72)	14 (28)
Muscle		24 (96)	1 (4)
Ovary		48 (96)	2 (4)
Maternal blood		Normal female	
Paternal blood		Normal male	

tion. The chromosomes of both parents were normal. The results of all cytogenetic studies are shown in the table.

Fetal tissue biopsies were taken from chorionic membrane, liver, kidney, muscle, and ovary for culture. Multiple tissue biopsies were also taken for electron microscopic studies which will be reported separately. Chorionic membrane and liver failed to grow. The other cultures confirmed the presence of the two cell lines.

Discussion

Whatever the true structure of the 'isochromosome' in our case, the greater part of the 18 long arm was present in triplicate in a variable number of cells, with partial monosomy of the short arm in all cells. It was surprising to find only mild abnormalities in the fetus with only minimal signs of trisomy 18. The great variation in the proportion of the two cell lines between and within tissues is thought to reflect differential clonal growth rather than true in vivo distribution. The phenotype is thus likely to have been largely that of the 18p- syndrome which, in some cases, can present with mental retardation and few physical abnormalities.

Generally, cases with iso 18q or with other types of 18q trisomy have shown features of full trisomy 18q syndrome.¹⁻³ Bass *et al*⁴ reported iso 18q in a case with features of both trisomy 18 and monosomy 18p. An example of an isopseudodicentric 18 has been described with full trisomy 18 phenotype.⁵ Only two instances similar to our case have been found⁶ (C Gosden, 1984, personal communication). The absence of full expression of cells with trisomy 18q is difficult to explain. It is possible that the effect is diluted by the mosaicism. A more likely explanation would be that of inactivation due to positional

effect, particularly if a restricted chromosomal segment, such as 18q21, is responsible for the stigmata of trisomy 18.⁷ The present case exemplifies the need for caution in predicting fetal phenotype after prenatal detection of structural abnormality and partial aneuploidy of chromosome 18.

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