

sufficiently large portion of the short arm has been deleted before ring chromosome formation. In the present case, however, it is suggested that the clinical malformations are more realistically ascribed to the effects of the diploid/monosomy 4/polysomy 4 mosaicism than to the deletion of the telomeric regions of the chromosome.

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## Prenatal recognition of 4p- syndrome

**SUMMARY** A fetus with the rare 4p- syndrome was detected by chromosome analysis of amniotic cell culture, and the pregnancy terminated. The fetus showed a number of the physical stigmata of the syndrome.

Deletion of a portion of the short arm of chromosome number four is associated with a constellation of defects, first recognised as a distinct syndrome by Wolf and his colleagues in 1965. The most common features are severe growth retardation, profound mental deficiency, hypotonia, multiple craniofacial anomalies, cardiac defects, genital anomalies, mid-line scalp defects, and dermatoglyphic abnormalities. Despite these defects, the condition is compatible

with life, and though complications arising from the abnormalities may cause death in the first few years of life, survival into the second and third decades is not uncommon.

We report a fetus with 4p- syndrome, selectively aborted after prenatal diagnosis, and found to have many characteristics of the syndrome reported in survivors.

#### Case report

Mrs. S.P., aged 39 years, gravida 4, para 3, underwent diagnostic amniocentesis at 17 weeks in her fourth pregnancy because of her age. The fluid was dark brown in colour and the alpha-fetoprotein level of the supernatant was 21 µg/ml (normal range for 17 weeks 6 to 43 µg/ml). Culture of the amniotic cells was technically very difficult, as they grew extremely slowly. Chromosome preparations were eventually able to be made after 30 days in culture (the average time being 16 to 18 days). The quality was good and 62 fetal cells were analysed using G-banding. 59 had a chromosome complement of 46,XX,4p-, and 3 had a normal male complement. The pregnancy was terminated at 24 weeks by intra-amniotic infusion of hypertonic saline with 10 mg prostaglandin E<sub>2</sub>.

The female fetus was fresh and weighed 371 g, crown-rump length 17 cm. This is small for 24 weeks (630 g and 20.7 cm, Streeter, 1921). The face (Fig. 1) was strikingly odd. There was ocular hypertelorism and the eyes were open and bulging. There was micrognathia, lowset ears, a high arched palate, cleft



Fig. Fetus showing characteristic facies of 4p- syndrome at 24 weeks' gestation.

posteriorly, unilateral talipes equinovarus, and a single umbilical artery. The uterus was bicornuate and the kidneys were small and polycystic. The palmar creases were normal. On both hands, 4 digits had arches, and 1, the fourth, had an ulnar loop. The distal 't' triradius was displaced a short, but significant, distance distally. The placenta was obtained by evacuation 2 hours after delivery, and was in several pieces. The total weight was 152 g and there was no evidence of twinning. The amnion and placenta appeared perfectly normal.

Four skin, 4 amnion, and 2 gonadal cultures were set up from the fetus. Growth was obtained only from the gonads, which is not unusual for a saline termination. The chromosome constitution was established as 46,XX,4p-, using G-banding.

The 3 previous children and the parents are normal and healthy. Peripheral blood cultures and G-banding of the chromosomes of the parents showed a normal karyotype in both cases.

### Discussion

We believe this to be the first case of 4p- syndrome diagnosed prenatally. In view of the extreme rarity of the syndrome and of the relatively few pregnancies examined chromosomally, it was a quite unexpected finding, which made us wonder if it was a cultural artefact. This particular chromosome deletion has been described only in living individuals, it has not been reported in 3 large surveys of spontaneous abortions (Dhadiyal *et al.*, 1970; Boué *et al.*, 1975; Creasy *et al.*, 1976) so there was the likelihood that this chromosome anomaly was compatible with intrauterine life and would not be aborted, as so many chromosome anomalies are. However, the possibility that affected embryos might be aborted at a very early stage of pregnancy cannot be excluded.

The dark brown colour of the amniotic fluid was considered to be of no consequence since the alpha-fetoprotein level of that fluid was normal. Our experience with approximately 2000 samples of amniotic fluids over the course of 3½ years is that one should be concerned for the well-being of the fetus only if the dark brown colour is associated with a distinctly high AFP level (Seller, unpublished observations). The colour is presumably the result of old haemoglobin, indicating that there has been an intra-amniotic bleed some time before the amniocentesis.

It is interesting to note that the growth retardation and the odd facies typical of the 4p- syndrome were evident in the fetus at 24 weeks. By contrast, in our experience, fetuses with Down's syndrome terminated around this time rarely show the facial characteristics of Down's syndrome. It is unlikely that the small size and low weight of the fetus could be attributed to an error in the gestational age, as the pre-delivery ultrasound measurements were compatible with the menstrual age, and at necropsy the degree of development of the fetus was consistent with 24 weeks.

We thank the Department of Photography and Medical Illustration, Guy's Hospital for the photograph, the Spastics Society and the Department of Health and Social Security for financial support, and Dr Tabuteau, general practitioner, for referring the case to us.

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