FIG 2 Chromosome 2 pairs from the proband, depicting the duplication of 2q11-2→2q14-2.

terminal.¹ The proband's karyotype was therefore designated as 46,XX,dir dup(2)(q11-2q14-2). Both parents had normal peripheral blood karyotypes, so the duplication was considered to be de novo.

Discussion

A duplication of the proximal long arm of chromosome 2 has not been previously reported. The chromosome abnormality appears to have caused the mild dysmorphic features and the mental retardation. The only unusual feature we observed was congenital glaucoma. However, delineation of a 'proximal 2q duplication syndrome' may be possible when other cases are described.

The parental age in this case is consistent with the observation that direct duplications are not

associated with advanced parental age¹ and may arise from unequal crossing over during gametogenesis. We are unaware of any instance of recurrence or inheritance of an autosomal direct duplication. Two inherited duplications of the X chromosome have been reported, but with minor or no physical effects in the carrier females.²⁻³ The risk of recurrence is probably low but unknown and therefore antenatal diagnosis is an option in future pregnancies.

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First trimester fetal karyotyping in twin pregnancy

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SUMMARY Fetal chromosome analysis in a twin pregnancy during the first trimester is described. Problems of the reliability of tissue sampling are also discussed. The authors emphasise the advantage of direct cytogenetic analysis from the tissue specimens used for enzyme determination or DNA studies.

The discovery of twins at the time of fetal diagnosis complicates the counselling problem; for example, it alters the risk of finding an affected fetus or the

twins may be discordant for the abnormality.¹ Moreover, the inability to test both twins may occur and diagnostic procedures which are reliable in a singleton pregnancy may not be so in a twin pregnancy. We present our first experience of fetal chromosome analysis of twins during the first trimester and emphasise the importance of obtaining reliable samples from each twin.

Case report

The proband, a 42-year-old G9 P6 woman, was referred to us because of advanced maternal age. At 9 weeks' gestation ultrasound examination

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revealed two normally developed fetuses in two different sacs and a single anterior placenta (figure a).

A careful study of the uterine cavity allowed us to locate the insertion of both umbilical cords (figure b, c). By transcervical aspiration,² using a Portex catheter, three samplings were attempted: one near the umbilical cord insertion of the first fetus, and two others near the umbilical cord insertion of the other fetus. The amounts of chorionic villi specimens

obtained were 20, 15, and 50 mg from the first, second, and third samplings, respectively.

CYTOGENETIC ANALYSIS

Chromosome preparations were carried out using the direct method.³ The aspirated samples were inspected under the inverted microscope ($\times 50$) and villi showing typical morphology were taken and washed in Hank's saline balanced solution in a 60 mm Petri dish. The villi were then transferred into a 30 mm Petri dish containing 3 ml of medium without serum. Colcemid was added to the medium to reach a final concentration of $0.04 \mu\text{g/ml}$ and the villi were left for one hour at room temperature. The medium was then removed with a Pasteur pipette and replaced with 3 ml of 1% sodium citrate solution for hypotonic treatment (10 minutes). The hypotonic solution was removed and 3 ml of methanol-acetic acid (3:1) fixative were added for 10 minutes. The fixative was aspirated with a micropipette and replaced with 1 ml of aqueous 60% acetic acid solution to cause cell dissociation. Two to three drops of dense cell suspension were placed on slides. The suspension was distributed on the surface of the warmed slides (40 to 50°C) by means of a bent Pasteur pipette. Chromosome preparations were stained using the QFQ banding technique.

A 46,XY fetal karyotype was observed in 31 metaphases obtained from the first sample, while a 46,XX karyotype was present in 10 mitoses from the second specimen. In the third sample a mixed cell population was found in which 50 mitoses were 46,XX and 15 were 46,XY. A diagnosis of dizygotic twins of different sex with a normal karyotype was made.

To date the pregnancy is progressing normally.

Discussion

The study of this case prompts some comments regarding the obstetrical procedure. In order to ensure the best chance of obtaining trophoblastic tissue from both twins, it was necessary to identify the umbilical cord insertion on the surface of the placenta and to guide the tip of the aspiration catheter very near to the insertion point. Nevertheless, a mixed specimen was observed at the third attempt. In order to overcome this, we think that repeated suction movements during the withdrawal of the catheter should be avoided. If these precautions are not taken, particularly in cases of fused placentas, there is a high probability of diagnosing only one twin, a situation which must be discussed with the patient before proceeding.

At cytogenetic diagnosis no difficulties were

FIGURE (a-c) Ultrasound visualisation of the twin pregnancy with anterior fused placentas at 9.6 weeks. In (b) and (c) the arrows indicate the umbilical cord insertion for the first and second twin, respectively.

encountered in the case reported here because the twins were of different sexes. However, when the twins are of the same sex chromosome polymorphism studies should be carried out, even though low banding resolution seems to be a characteristic of chorionic villi chromosomes. Whenever villi specimens are taken for metabolic or DNA studies⁴⁻⁶ fetal karyotyping should help to establish reliable results from each twin.

In conclusion, the discovery of twins at the time of chorionic villi sampling creates concern regarding the ability to diagnose each twin, but this should not be a contraindication to the use of the aspiration technique. By taking samples at the insertion site of the umbilical cord, good reliability in sampling the two different chorionic tissues is attained. Chromosome polymorphism study of the karyotype of the parents and fetus is indicated when the same sex chromosome constitution is present in all the aspirated specimens analysed.

Fetal karyotyping proves to be a very advantageous preliminary approach when chorionic villi are used for metabolic and DNA studies. Sufficient chorionic tissue should always be taken to perform chromosome analysis regardless of the indication for the fetal diagnosis. A very small amount of villi is required for fetal karyotyping using the direct method. If it proves impossible to

obtain samples from both twins, or if one of the twins is shown to be chromosomally abnormal, any decisions on the outcome of the pregnancy should be deferred until amniocentesis or fetoscopy have been performed.

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Cat eye syndrome owing to tetrasomy 22pter→q11

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SUMMARY A case of tetrasomy 22pter→q11 with ocular hypertelorism, downward slanting palpebral fissures, total anomalous pulmonary venous return, and anal atresia is described. The phenotypic variability of the cat eye syndrome is emphasised along with the need for categorisation of these patients according to well characterised cytogenetic findings.

Since the original description of four patients with a small extra chromosome,¹ the delineation of the cat eye syndrome² has been hindered by both phenotypic and cytogenetic variability. Certain component defects of the cat eye syndrome, such as

the ocular colobomata, preauricular tags, anal atresia, cardiac anomalies, and renal anomalies, occur in a variety of disorders including the VATER and CHARGE associations. Schinzel *et al*³ provide convincing evidence that the extra small chromosome associated with the cat eye phenotype represents trisomy or tetrasomy of 22pter→q11 rather than the phenotypically different trisomy 22,⁴ translocation 11;22,⁵ or tetrasomy 15pter→q11-13.⁶ Syndromes caused by these distinct cytogenetic entities can now be defined and separated from non-chromosomal causes of the cat eye phenotype.⁷

Case report

The patient was the 3 kg (40th centile), 52 cm (60th centile) male product of an uncomplicated 37-week gestation. The mother, aged 27, and the father, aged