

Short reports

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First trimester diagnosis from chorionic villi of a der(15),t(9;15)(q33;q14)mat identified by DA/DAPI staining

The proband (III.2, fig 1) requested prenatal diagnosis during her first pregnancy because of three relatives with Down's syndrome (I.1, III.12, and IV.3). Her sister (III.6), who has a normal karyotype, had an amniocentesis during her first pregnancy, which resulted in a normal male.

Chorionic villi aspiration¹ was performed during the ninth week of pregnancy. Direct cytogenetic analysis from chorionic villus cells showed a male karyotype with a supernumerary chromosome resembling chromosome 21 in size and centromere position, but without the typical GTG banding (fig 2c).

Analysis of the parental chromosomes (III.1 and III.2) showed a t(9;15)(q33;q14) in the mother (fig 2a, b) and a normal karyotype in the father. Examination of the fetal chromosomes with DA/DAPI staining² identified the fetal karyotype as 47,XY,+der(15),t(9;15)(q33;q14)mat (fig 2d), resulting from a 3:1 meiotic segregation. The parents decided to terminate the pregnancy. Chromosome analysis from tissue of the abortus confirmed the fetal karyotype.

The feasibility of using DA/DAPI staining for the identification of rearrangements of chromosome 15 in the

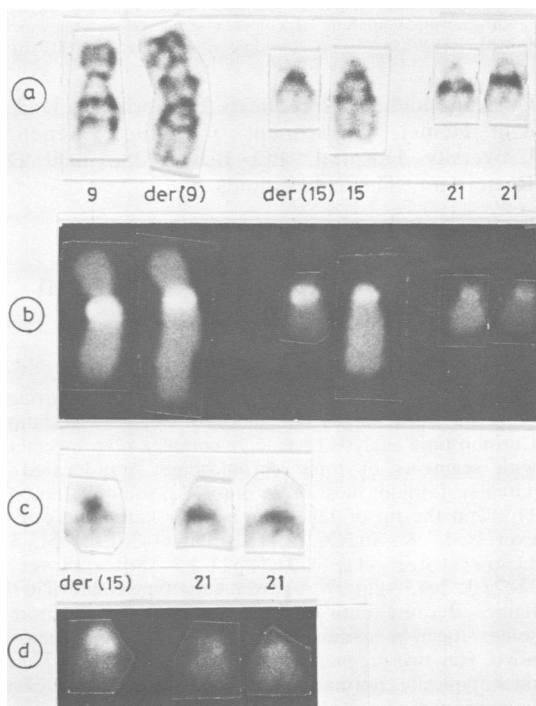


FIG 2 Partial karyotypes of (a,b) the mother with t(9;15)(q33;q14) and (c,d) the fetus with 47,XY,+der(15)mat. (a) and (c) GTG banding, (b) and (d) DA/DAPI staining.

analysis of first trimester fetal chromosomes has been demonstrated by our studies. The positive fluorescence of 15p allows correct discrimination between chromosome 15 derivatives and other acrocentric chromosomes. The present report emphasises once more³ that high quality chromosomes can be obtained from chorionic villi using the direct method and underlines the benefits of this procedure to couples at risk.

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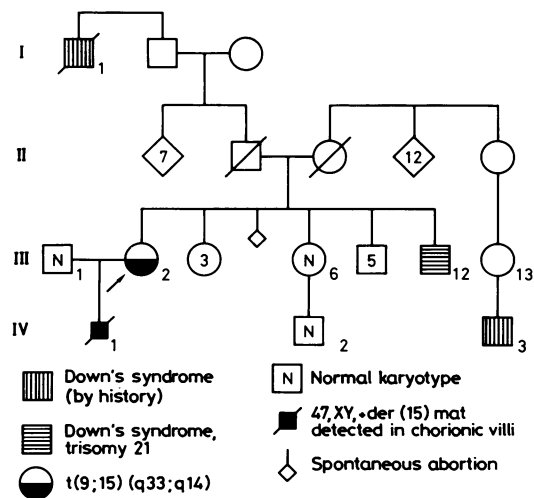


FIG 1 Pedigree of the family.

chorionic villi samples in the first trimester of pregnancy. *Hum Genet* 1983;63:349-57.

² Schweizer D, Ambros P, Andrlé M. Modification of DAPI banding on human chromosomes by prestaining with a DNA-binding oligopeptide, distamycin A. *Exp Cell Res* 1978;111:327-32.

³ Sachs E, Van Hemel J, Galjaard H, *et al*. First trimester chromosomal analysis of complex structural rearrangements with RHA-banding on chorionic villi. *Lancet* 1983;ii:1426.

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A three way translocation in mother and daughter

A woman presented with a history of six miscarriages occurring between the 6th and 14th weeks of gestation. Chromosome analysis revealed a complex rearrangement, with segments of three chromosomes translocated in 'circular' fashion: most of 2q onto 18q; some of 18q onto 11p; and the tip of 11p onto 2q. Her karyotype can be expressed as 46,XX,t(2;11;18)(2pter→2q13::11p15.3→11pter;11qter→11p15.3::18q21.1→18qter;18pter→18q21.1::2q13→2qter). A partial karyotype is shown in the figure. Because both her parents had normal chromosomes, it can be assumed that the rearrangement arose de novo. Her two pregnancies which went to term produced phenotypically normal daughters, one with the same balanced three way translocation, the other with a normal karyotype.

Complex chromosomal rearrangements are rare.^{1,2} In most cases where the translocation is familial, it is the mother who is the transmitting parent,¹ in one family through three generations.³ Oogenesis may be a more robust mechanism of gamete formation than spermatogenesis in the presence of this particular disruptive influence. A maturation arrest at the secondary spermatocyte stage has been demonstrated in one sterile male heterozygote.²

If, at pachytene, pairing of homologous chromosomal segments is successfully achieved, this will lead to the formation of a hexavalent configuration. At the first meiotic division, then, 3:3, 4:2, 5:1, and 6:0 disjunctions are theoretically possible. The great majority of theoretically possible segregant gametes could be expected to give rise to conceptuses with such an unbalanced genetic complement that loss would occur in early pregnancy, often in very early pregnancy ('occult abortion'). Given the enormous theoretical range of gamete abnormality, and bearing in mind the modifying factor of selection against unbalanced forms, the fact that our proband had two conceptuses arising from alternate 3:3 segregation out of

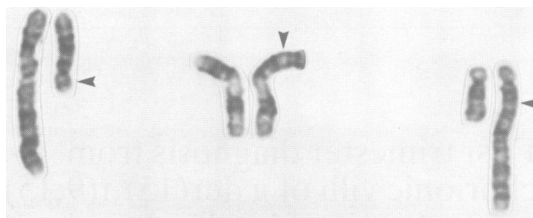


FIGURE Partial karyotype. The normal homologue is the left of each pair, and the derivative chromosome the right. Arrows indicate breakpoints.

eight recognised pregnancies might indicate this category of chromosomal distribution to be favoured. In our advice to her 19 year old heterozygous daughter, we have indicated the high probability of her having miscarriages in the future, but have also counselled cautious optimism that the same good fortune that attended two of her mother's meioses may also dwell in her (although advising that a heterozygous son might possibly be sterile). Prenatal diagnosis would be indicated to detect an unbalanced but viable chromosomal complement.

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Familial inv(1)(p36.3q12) associated with sterility

Chromosomal abnormalities are among the more important causes of reproductive failure. Three instances of familial pericentric inversion of chromosome 1 associated with sterility have been reported.¹⁻³ In this paper we