

## Short communication

# A rare heteromorphism of chromosome 20 and reproductive loss

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### Abstract

A rare centromeric heterochromatic variant of chromosome 20 was encountered during investigations in a couple with repeated miscarriages. The enlarged segment was G and C band positive and stained positively by Giemsa II. In situ hybridisation of the biotinylated alphoid probe D20Z1 specific for the centromere of chromosome 20 to metaphase cells confirmed the presence of amplified sequences adjacent to the centromere. The variant was found to be familial and was evaluated as having no clinical significance.

We have used, in addition to well established banding techniques, in situ hybridisation with the biotinylated probe D20Z1 to evaluate an uncommon heteromorphism observed in the centromere region of chromosome 20. Differences in fluorescent intensity for this region have been described,<sup>1,2</sup> but only rarely when heterochromatin has extended into either the long or short arm or both.<sup>3</sup>

### Materials and methods

#### CYTOGENETICS

Chromosomes were obtained from PHA stimulated lymphocyte cultures and investigated by routine C,

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GTG, Giemsa II, and high resolution G banding techniques.

#### PROBE

The  $\alpha$  satellite repetitive probe D20Z1 is specific for the centromere region of chromosome 20<sup>4</sup> and was obtained from Oncor Inc Gaithersburg MD.

#### HYBRIDISATION

Hybridisation was for 17 hours at 37°C in a humid chamber with a probe concentration between 1 ng/ $\mu$ l and 2 ng/ $\mu$ l. Washing of the slides and the detection and amplification of the hybridised biotinylated probe were a modification of the technique of Burns *et al.*<sup>5</sup> described in detail in Callen *et al.*<sup>6</sup>

### Case report

A 32 year old male and 18 year old female were referred for chromosomal studies as part of investigations for three first trimester miscarriages. G and

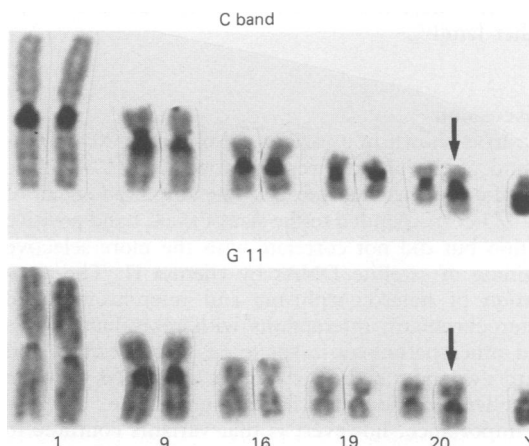


Figure 1 C banding and Giemsa II staining showing the variant chromosome 20.

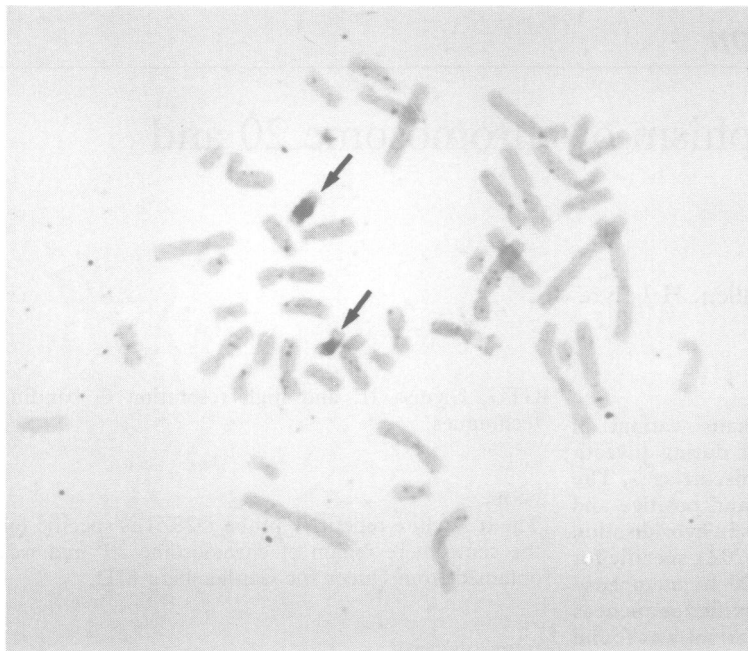


Figure 2 Metaphase spread after in situ hybridisation with the probe D20Z1 showing signal specific to chromosome 20.

HRG banding techniques showed normal chromosomes except for variation in the centromere region of one chromosome 20 in the male. C banding showed positive staining extending into both the short and long arms (fig 1) while Giemsa II staining was seen only in the long arm (fig 1). In situ hybridisation of the probe D20Z1 to metaphase chromosomes confirmed the presence of tandemly repeated alphoid DNA (fig 2). Extended chromosome studies showed the variant to be present in the male patient's mother. There was no history of reproductive loss in either family.

### Discussion

We have shown in a variant chromosome 20 amplification of the alphoid repeat probe D20Z1 which is specific for chromosome 20. The amplified signal of D20Z1 corresponded to the size of the C band positive region but did not correlate with the more selective staining of satellite DNAs by Giemsa II. The association of heteromorphisms and interchromosomal heterochromatin interactions with reproductive loss and other pathology is yet to be substantiated, and until evidence to the contrary is presented they are considered to be of no clinical significance.<sup>7</sup> What is of importance, however, is that variants continue to

be reported and structurally resolved for purposes of genetic counselling, prenatal diagnosis, and frequency in the population.<sup>3</sup> We thus consider this heteromorphism in chromosome 20 to be a normal familial variant with no pathological significance.

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