Short reports

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Prenatal diagnosis of haemophilia B in the first trimester

DNA techniques have been used to detect carriers of haemophilia B^{1,2} and to exclude haemophilia B in a fetus.³ Here we report a case of prenatal diagnosis of haemophilia B through which a coagulant factor IX deficiency in the fetus was predicted by restriction mapping with a human factor IX probe in the first trimester of gestation.

A 27 year old Chinese woman (figure, II.2), whose brother (II.4) was a haemophilia B patient with severe factor IX deficiency of less than 2% activity, consulted us in the eighth week of pregnancy and asked for prenatal diagnosis. Coagulant factor assay showed that she and her mother (I.2) were both carriers of the defective factor IX gene, with IX:C of 38.9% and 32.5%, respectively. Genomic DNA, extracted from leucocytes of the members of this family, was digested with a variety of restriction endonucleases and then hybridised with probe VIII, the genomic factor IX of 2.5 kb (kindly given by Professor G G Brownlee). A 6.5 kb *XmnI* fragment and an 11.5 kb *EcoRI* fragment, which were both specific for the defective factor IX gene in this family, were observed in the affected male. All the normal subjects in the family had the 11.5 kb *XmnI* factor IX fragment and the 5.0 kb *EcoRI* factor IX fragment, which is normal in the Chinese, but did not have the specific DNA fragments for the defective factor IX gene. The pregnant woman (II.2) and her mother (I.2) were heterozygous for the allele of the *XmnI* site (*XmnI* 11.5/6.5) as well as the allele of the *EcoRI* site (*EcoRI* 5.0/11.5). Using these specific DNA fragments as genetic markers, we could undertake prenatal diagnosis in the at risk pregnancy.

Chorionic villi samples were collected in the ninth week of gestation and DNA was prepared from the villi. By hybridisation of villus DNA with a Y specific DNA probe (kindly given by Dr Y W Kan), the sex of the fetus was determined to be male. *XmnI* restriction mapping of the fetal DNA showed that the fetus had the specific DNA fragment received from his carrier mother (figure). The fetus was therefore diagnosed prenatally as having haemophilia B and the pregnancy was terminated at 12 weeks' gestation. The prenatal diagnosis was confirmed by analysis of coagulant factors of the blood from the abortus's heart.

XmnI and *EcoRI* mapping of DNA from the abortus showed the same DNA fragments specific for the defective factor IX gene observed in the DNA from the haemophilia

FIGURE Family pedigree.

B patient and from the chorionic villi. In addition, *BglII*, *PvuII*, *MspI*, and *TaqI* restriction mapping of DNA from the abortus was also performed and abnormal fragments specific for the defective factor IX gene were found. All these results indicated that this case of haemophilia B was derived from an intragenic deletion of the factor IX gene. Details of the structure of the factor IX gene will be published elsewhere in detail.

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