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PGD to select unaffected embryo for hemophilia A carrier woman

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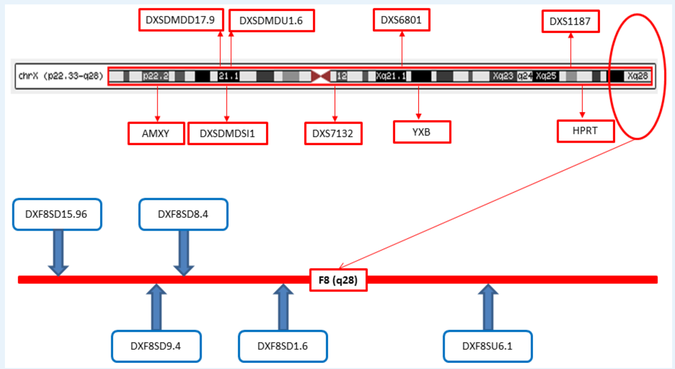
Introduction

Preimplantation genetic diagnosis (PGD) combined with in vitro fertilization (IVF) method is a powerful diagnostic tool which is recommended to carrier couples who want to assure their child's health regarding monogenic disorders before pregnancy. In this method, diagnoses performed on blastomeres biopsied from 8-cell stage embryos which are created by IVF method. Here we present application of molecular PGD to select unaffected embryo for hemophilia A carrier woman. This study was approved by Kawsar Human Genetics Research Center ethic committee.



Locations of STR markers on X chromosome

Method

A couple who was candidate for PGD referred to our laboratory. The woman was obligate carrier of hemophilia A. Peripheral blood samples were collected and genomic DNA was extracted using salting out method. Mutation detection in Factor 8 gene carried out using sanger sequencing. Fragment analysis and haplotype mapping performed to trace defective alleles in the family using multiplex Short Tandem Repeats (STRs). Fertilization procedure carried out at IVF clinic. After three days one or two blastomeres were removed from each embryo. Causative mutation (p.F2002Lfs*28) and informative STR markers associated with X chromosome (5 loci for F8 and 9 additional loci for sex selection) were checked for each blastomere using nested PCR. Linkage analysis performed and 2 unaffected embryos (one male and one female) implanted to mother's uterus.

Result

Implantation leads to *triplet* pregnancy. Results obtained from prenatal diagnosis (PND) at 16th week of gestational age confirmed PGD results and clarified that the male embryos are monozygotic siblings come from one egg.

Conclusion

Preimplantation genetic diagnosis has become a useful option for couples with a risk of transmitting a genetic disease to prevent birth of children affected with monogenic disorders. In this way, one could prevent medical abortion by selecting and transferring unaffected embryos. In molecular PGD, results obtained from linkage analysis and haplotype mapping in parallel with direct mutation detection make the method more accurate and reliable.

Keywords

IVF, PGD, STR, Hemophilia.