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سومین کنگره بین المللی تولید مثل

PGD to select HLA matched embryo for stem cell therapy for beta thalassemia

Medical Genetics Laboratory of Dr.Zeinali

Solmaz Sabeghi[1], Kiyana Fatemi[1], Panti Fouladi[1], Zohreh Sharifi[1], Ameneh Bandehi Sarhadi[1], Leili Rejali[1], Masumeh Amini[1], Hamideh Bagherian[1], Mohammad Sadegh Fallah[1,2], Sirous Zeinali[1,3], Saeid Amanpour[4]

1. Dr. Zeinali's Medical Genetics Lab, Kawsar Human Genetics Research Center (KHGRC), Tehran, Iran
2. Cellular and Molecular Endocrine Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences
3. Department of Molecular Medicine, Biotech Research Center, Pasteur Institute of Iran, Tehran, Iran
4. Reproductive Research Center, Vali-e-Asr Hospital, Imam Khomeini Hospital Complex, Tehran University of Medical Sciences, Tehran, Iran

Background

Preimplantation genetic diagnosis (PGD) combined in vitro fertilization (IVF) with genetic testing, allow families to assure their child's health regarding genetic disorders before pregnancy. Using PGD could avoid medical abortion which can be consequence of prenatal diagnosis (PND) during pregnancy. Molecular PGD is based on using short tandem repeats (STRs) and direct sequencing method. Linkage analysis and haplotype mapping of different polymorphic STR markers flanking the gene which is associated with the disease has been extensively used in PGD for single gene disorders to confirm direct mutation detection.

Method

A family with a 6 year's old child affected with beta thalassemia major was referred for PGD to have a non-thalassemic HLA-matched child whose stem cells can be used for transplantation for their affected child. This study was approved by Kawsar human genetics research center ethic committee. Peripheral blood samples were collected and genomic DNA was extracted using salting out method. Mutation detection in HBB gene was carried out using direct sequencing method. Fragment analysis and haplotype mapping were performed to track the defective alleles in the family. Fertilization was carried out at the IVF clinic. On day 3 post fertilization, one blastomere was removed from each of the 8 embryos and used for PGD. Selected mutation was investigated using direct sequencing and informative STR markers (16 loci for HLA and 4 for HBB) were checked in the family using multiplex nested PCR method. Fragment analysis of the PCR products were run on capillary electrophoresis and analyzed using GeneMapper® software. Unaffected HLA-matched embryos were selected and were implanted. Prenatal diagnosis (PND) was performed at 16th week of gestational age to verify PGD results.

Result

HBB:c.51delC mutation was diagnosed in patient and from 8 analyzed blastomeric, 2 (25%) were unaffected HLA-matched. The others were either affected or not-matched. Both embryos were implanted and PND confirmed PGD result. A singleton baby was born in 2015.02.14 and she was healthy according to the pediatric dermatologist examination.

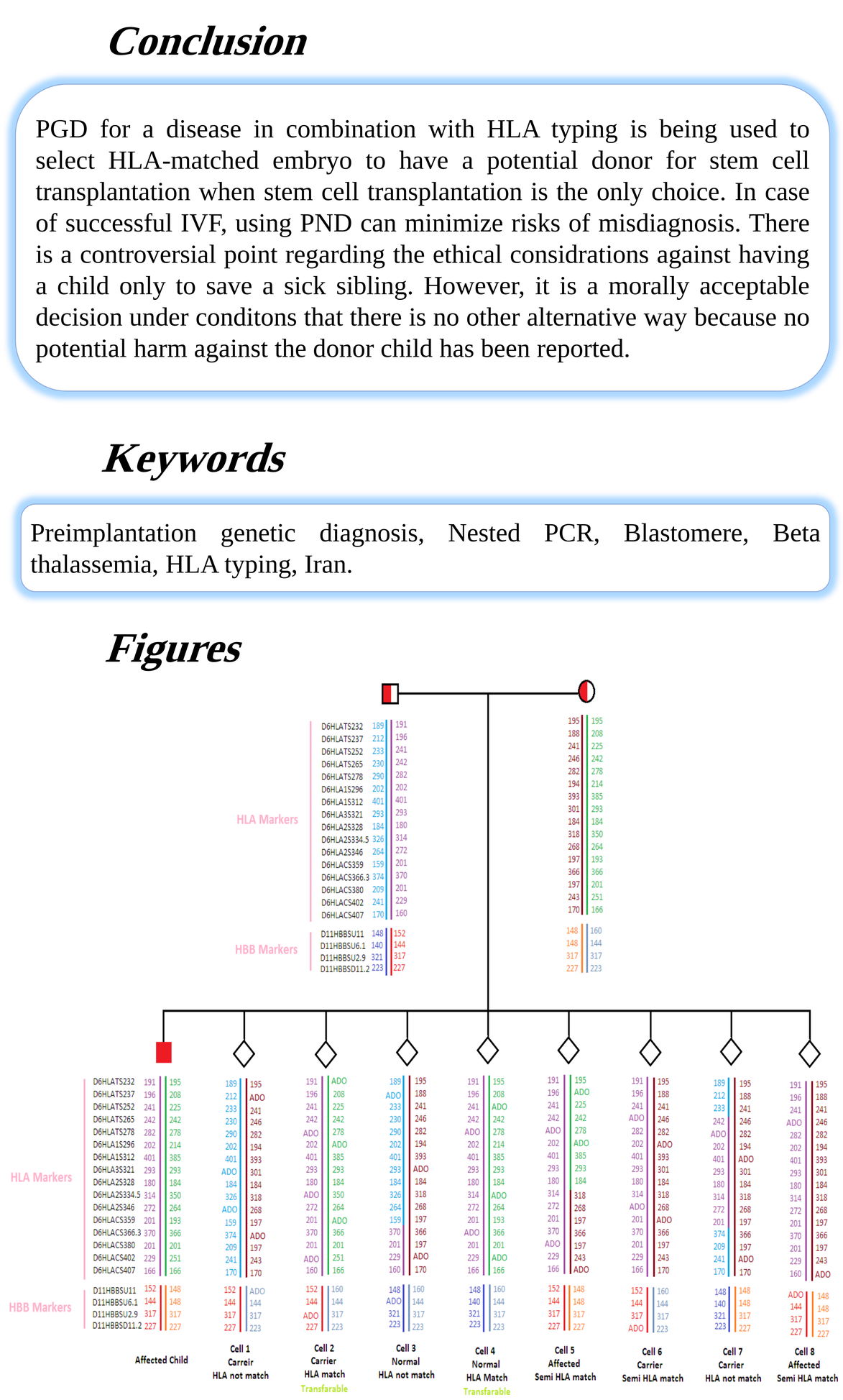
Conclusion

PGD for a disease in combination with HLA typing is being used to select HLA-matched embryo to have a potential donor for stem cell transplantation when stem cell transplantation is the only choice. In case of successful IVF, using PND can minimize risks of misdiagnosis. There is a controversial point regarding the ethical considrations against having a child only to save a sick sibling. However, it is a morally acceptable decision under conditons that there is no other alternative way because no potential harm against the donor child has been reported.

Keywords

Preimplantation genetic diagnosis, Nested PCR, Blastomere, Beta thalassemia, HLA typing, Iran.

Figures



Haplotype illustrating transferable embryos