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Women's Health Science Journal
ISSN: 2639-2526

Preimplantation Genetic Diagnosis for Human Leukocyte Antigen Matching: The Generation of the Savior Sibling and the "Gift of Life"

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Editorial

Volume 2 Issue 2

Received Date: June 11, 2018

Published Date: June 18, 2018

DOI: 10.23880/whsj-16000115

Abstract

In vitro fertilization (IVF) in conjunction with preimplantation genetic diagnosis (PGD) for mutation detection and human leukocyte antigen (HLA) matching for hematopoietic stem cell transplantation (HSCT) is a unique technology of modern clinical embryology. The technology should be offered to any family with a condition that requires matched-related HSCT. Today, PGD-HLA matching is a realistic option for families in need of treating an affected sibling, when no HLA-matched donor is available. Offering the option of HSCT from a savior sibling immediately upon the diagnosis of the condition in the child of a family is crucial, since it shortens the time until the birth of the savior sibling through IVF-PGD and increases the probability of cure by HSCT. The success of the treatment can be achieved only through a multidisciplinary team work and the cure can be "gifted" to the sick child through the savior sibling.

Keywords: Preimplantation Genetic Diagnosis; In Vitro Fertilization; Human Leukocyte Antigen Matching; Hematopoietic Stem Cell Transplantation; Savior Sibling

Abbreviations: IVF: In Vitro Fertilization; HLA: Human Leukocyte Antigen; PGD: Preimplantation Genetic Diagnosis; HSCT: Hematopoietic Stem Cell Transplantation; GVHD: Graft Versus Host Disease.

Editorial

Creating an embryo through in vitro fertilization (IVF) and further a human life to provide a match umbilical cord or bone marrow as a stem cell source to cure a living sick child? This was a science fiction film scenario before 2000. It was in 2000 when this idea became a reality and Adam Nash was born unaffected from Fanconi anemia and human leukocyte antigen (HLA) matched to his sibling, after IVF with preimplantation genetic diagnosis (PGD) for the mutation and HLA matching [1].

The 6-year old sister of the sibling born after IVF was suffering from bone marrow failure secondary to Fanconi anemia. IVF in conjunction with PGD was employed to first identify the preimplantation embryos free from Fanconi anemia and second, among the healthy embryos,

HLA typing resulted in identifying the ones that matched the sick child. The matched unaffected embryos were transferred and a healthy HLA-matched boy was born; the savior sibling. Cord blood of the healthy matched newborn boy was used for hematopoietic stem cell transplantation (HSCT), which was successful, and the girl was cured [2].

Eighteen years after the first successful PGD for HLA typing and the cure of a sick sibling by the savior one, PGD for HLA matching is a well established technique. Today, there is a long list of diseases where an affected child has been cured by the savior sibling providing the "gift of life": cord blood or bone marrow hematopoietic stem cells. The list includes [3] the cure of beta-thalassemia, Fanconi anemia, Diamond-Blackfan anemia, sickle-cell anemia, Wiskott-Aldrich syndrome, X-linked adrenoleukodystrophy, Glanzmann's thrombasthenia, Hurler syndrome, acute mueloid leukemia, acute lympoblastic leukemia and Shwachman-Diamond syndrome [4].

There is currently a rise in the PGD-HLA matching IVF cycles worldwide with the intention to cure affected children for even more diseases. The treatment, after the initial bioethics debate around it subsided worldwide, is now offered routinely to families in need [5]. But despite the rise of the use of the technology there are still families in need of a compatible bone marrow donor that are unaware of this IVF option [5]. The benefits of PGD-HLA matching for generating the matched savior sibling and the matched HSCT compared with an unrelated matched HSCT are the decreased risk of graft versus host disease (GVHD), improved prognosis and long term disease-free survival in malignant conditions, elevated overall survival, decreased risk of treatment failure and decreased risk of post-transplantation morbidity.

IVF combined with PGD for mutation detection and HLA matching for HSCT, is a unique and valuable technology that is here to stay. The technology should be offered to any family with a condition that requires matched-related HSCT. The option of creating the savior sibling and offering the "gift of life" to the suffering child should be offered immediately to an affected family. It has been reported that the average time from diagnosis to first consultation with the IVF-PGD centre can well be 1.5 years, something that in some cases may have contributed to the death of children with acute forms of leukemia while awaiting HSCT either before or immediately after the birth of their savior sibling [3]. There have been specific guidelines [5] that need to be followed by the IVF-PGD clinic and team providing IVF for PGD-HLA matching.

Offering the option of HSCT from a savior sibling immediately upon the diagnosis of the condition in the child of a family shortens the time until the birth of the savior sibling through IVF-PGD and increases the probability of cure by HSCT. Since international data demonstrate the feasibility and efficiency of the technique, the success can be achieved only through a multidisciplinary team work involving clinical embryologists, geneticists, gynecologists, pediatric hematologists and oncologists.

Global awareness should be increased that in our era preimplantation HLA matching is a realistic option for families in need of treating an affected sibling, when no HLA-matched donor is available. What could be a better "gift" to a sick child than that of life from the savior sibling!

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