The Expanding Indications for Preimplantation Genetic Diagnosis

By Steven Joffe, MD, MPH

A recent report describes the use of preimplantation genetic diagnosis (PGD) combined with in vitro fertilization (IVF) to conceive a child who could serve as a stem cell donor for a sibling with Fanconi's anemia (FA).[1] This event, which was widely reported in the popular press,[2] represents a novel clinical use of genetic technology. As a result, it bears scrutiny to consider whether any ethical boundaries were breached.

FA is a rare autosomal recessive disorder. Its manifestations include congenital malformations, bone marrow failure, and a high likelihood of acute leukemia in childhood. The only curative therapy for the hematologic manifestations of FA is bone marrow transplantation (BMT). Ideally, a human leukocyte antigen (HLA)-matched sibling will be available as a donor, since transplants from unrelated donors carry markedly increased risk. Unfortunately, on average only 3 of 16 siblings will be both unaffected by FA and an HLA match, and therefore eligible to donate stem cells for BMT. Most children affected by FA do not have an HLA-matched sibling.

In the current case, the investigators used IVF to conceive multiple embryos for a couple whose 6-year-old daughter required a BMT for FA. Three days after conception (at the 5- to 8-cell stage), a single cell was removed from each embryo. Biopsied cells were tested for both FA and HLA type using single-cell polymerase chain reaction. Despite the identification and uterine transfer of unaffected matched embryos, the first three IVF cycles did not result in a pregnancy. However, the fourth cycle resulted in the delivery of a healthy, HLA-matched boy. Cord blood was collected and the sibling with FA underwent successful BMT.

Should this use of genetic technology trouble us? Before we can answer that question, we must consider what is unique about the procedure. Essentially, it consists of three components: 1) IVF; 2) PGD to ensure a child who is unaffected by FA; and 3) PGD to select a child with the appropriate HLA type.

IVF to treat infertility has been around for over two decades.[3] It is widely used and inspires little debate in secular bioethics (though some religious groups remain opposed to IVF).[4] Furthermore, PGD has previously been used in conjunction with IVF to identify embryos affected by severe genetic disorders such as sickle cell anemia and cystic fibrosis.[5,6] Used in this way, PGD permits at-risk couples to have unaffected children without having to face the difficult decisions about abortion that in utero prenatal diagnosis raises. Because its goal is to avoid severe illness and discomfort, PGD is generally accepted for this purpose.

The current case, then, is unique because PGD was used to select a child in part to benefit a third party (his sibling). Assuming that IVF to treat infertility and PGD to avoid the birth of a child with a severe genetic abnormality are ethically acceptable, there are several potential arguments against this new use of PGD. First, some might raise the Kantian objection that, because the child was created for another's benefit, he was treated as a mere means rather than as an end in himself. A related concern is that the child, by virtue of the circumstances of his conception, might not be valued appropriately. Third, this use of PGD might represent the first step towards "designer genetics,"[7] whereby children are selected on the basis of trivial traits like athletic ability. And finally, it might constitute the beginning of a journey down a different slippery slope, this time towards the selection of children who can serve as sources of spare parts, even at risk to themselves. For example, children might be conceived in order to donate kidneys or other solid organs. We will tackle each of these objections in turn.

Was this child created merely as a means to an end? Not necessarily. While it is of course plausible that a couple might conceive a child only to serve as a stem cell donor, there is no inherent reason why the child could not be wanted by the family in his or her own right. Indeed, in the current case, the investigators only agreed to perform the procedure for couples who had

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expressed a wish for additional children anyway.[2] And whether children conceived for this purpose will, in general, be less valued than other children is an empirical question for which there can be no a priori correct answer. It is equally plausible that such children will be more loved as a result of the special circumstances surrounding their birth.

What of the argument that this use of PGD represents a step towards designer genetics? Perhaps so, but any use of PGD—including its use to prevent severe illness such as cystic fibrosis—represents such a step. The line between "severe" conditions that warrant PGD and milder conditions for which its use would be inappropriate will, of course, prove difficult to draw. For example, would the use of PGD to avoid the birth of a child with congenital deafness be acceptable? There is likely to be considerable controversy on this question.[8] What about avoiding the birth of a child with a hereditary cancer susceptibility mutation such as in BRCA1 or p53? What about short stature? Clearly, we have already had to address these questions; the recent case does not force us to confront the issue of designer genetics for the first time.

The final concern, that PGD for HLA-matching begins a slide down the slippery slope towards the "manufacture" of infants for spare parts, is the most challenging. We are in fact taking a step down that road. This forces us to address the questions raised by all slippery-slope arguments: can we identify what constitutes "too far," and then can we trust ourselves to stop before we get there? I suspect we can. Collecting cord blood is unique because it involves no risk to the donor. In contrast, when harvesting the organ involves risk (as with kidney transplant), we will recognize the line and refuse to cross it. Indeed, we already refuse to permit young children to serve as solid-organ donors. As one reporter asked rhetorically, "is the potential for abuse in some circumstances reason not to pursue research that can be lifesaving under the right circumstances?"[2]

Ultimately, then, I must conclude that if we accept IVF as fertility therapy and PGD to avoid the birth of a severely affected child, the current case raises no intractable new ethical concerns. It harms no one, including the child thus conceived, while offering the prospect of considerable benefit to the affected sibling. And while it represents a step onto the slippery slope of creating infants for spare parts, I am confident that we will stop before we get ourselves into trouble. Additional questions, such as whether the procedure ought to be covered by third-party payers, remain. But on the central ethical issue before us, I believe that we remain on firm and comfortable ground. OS

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