Analysis: OB/GYN-Genetics

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ABSTRACT

Ovarian salvage from a patient with brain death is not available and will not preserve viable ova for future reproduction. Previous interest in assisted reproductive technology is only the first step in this process, which requires careful assessment of maternal risks and potential for recurrent genetic disease.

The case of Ms D, described by Laura Guidry-Grimes in this issue of the journal,[1] illustrates the conflict between family members' and patients' desires and the frontiers of medical technology. The ethical question of whether preservation of reproductive potential after death has been critically addressed by Guidry-Grimes, specifically commenting on the "we *can* . . . but *should* we?" quandary. For this family, their interpretation that Ms D had sought preliminary infertility care and expressed interest in surrogacy—in the face of her known severe medical concerns—was that she desired to provide a child of her genetic background to her family, regardless of the outcome of her own life. Even if Ms D had been able to express a well-thought-out desire for this, she had not yet received full counseling with infertility experts to discuss whether her health would allow it. There are maternal health circumstances that can preclude such actions. The lengthy process (two to three weeks) of inducing ovulation and harvesting ova is not easy, and it requires the patient's consent throughout the procedure. Ms D, with her medical concerns, would have been a very high-risk patient for ovulation induction—the fragility of her tissue could have led to ovarian rupture and heavy bleeding, and there would have been similar potential risk in the acquisition of her ovum.

In addition, part of the counseling process of assisted reproductive technology is to clarify what to do with the frozen ova or embryos in the face of death of the mother. Knowing this could have established a clear line of intent and action regarding Ms D's wishes. Her not-unexpected medical complication led to brain death before this happened. Her family's request to harvest ova or ovarian salvage is in line with what they perceived the patient would have desired, but it did not take into consideration that Ms D might not have been considered a candidate for this treatment by assisted reproduction (ART) specialists.

Without such ART guidance, maintaining maternal body/biological support for three weeks in an attempt to stimulate the patient's ovaries would have been unjustified, risky, and of uncertain productivity. Likewise, there are technologic limitations to the success of directly harvesting ovaries and attempting ovarian salvage by that process. There has been very limited success of *in-vivo* ovarian tissue maintenance with subsequent stimulation to produce viable ova. The practice at this time is limited largely to adolescent girls who require chemotherapy that

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could impact their fertility. It is not intended to harvest ova from salvaged ovaries, but instead to support the ovaries briefly until they can be transplanted back into the patient and stimulated later in the patient's life. Ovarian transplant remains a research effort at this time. In addition, no established research program exists that is able to receive a patient's ovaries, maintain them in perpetuity, and stimulate them. Thus, the family's belief that saving the ovaries would save Ms D's reproductive potential is not founded in current medical practice.

Ms D's type of Ehlers-Danlos syndrome is likely Ehlers-Danlos type IV, a defect in the COL3A1 gene. The condition results from pathologic mutations within the gene, that may vary from family to family, and is autosomal dominant in its inheritance; that is, the mutation is passed from an affected person to 50 percent of his or her offspring. Half of Ms D's ova would be expected to have her particular mutation in this gene. Advances in pre-implantation genetic diagnosis have allowed testing of cells of a very early embryo to determine if they carry the deleterious mutation. If Ms D's ova had been harvested and used for embryo development, testing for the mutations prior to the implantation of the embryo would have been a possibility**.** Ms D's family appeared to be accepting of her medical condition and willing to support a child who had her condition. However, this potential had never been addressed with Ms D, and it would be the value that *she* placed on the presence or absence of the mutation that had caused her illness that would be pertinent in this decision. There is a wide variation in choice in these circumstances: some adamantly wish to prevent disease recurrence in their offspring, and others feel prevention is of no importance.

Ms D's fortitude had overcome her many medical challenges during her lifetime. Her family and her long-term partner had been devoted to her and respected her for her strength and determination. They had had the experience of seeing her close to death and, miraculously, pull through. The final worsening of her condition was inevitable—the median age of death of patients with this disease is 48. The family's grief at the loss of this beloved woman was profound, influencing their wishes to hold on to some part of her, even if the technology were not yet available to support it. Similar beliefs regarding procedures such as for cryopreservation or cloning are ethically unsupportable; others, such as private umbilical cord stem cell banking, have capitalized on parental belief in future benefits—only to find that one in 400 to one in 200,000 children can use their own cord stem cells.[2] Advances in medical technology do occur, but embracing them prematurely can lead to costly disappointment. Balancing the "we *can* . . . *should* we" quandary requires a clear understanding of the true possibility of "we *can*."

PATIENT AND FAMILY CONSENT

This case has been anonymized, but no other details have been de-identified or modified. The family provided consent for the patient's case to be used and discussed in this publication, which they believe the patient would have wanted.

NOTES

1. L. Guidry-Grimes, "The Case of Ms D: A Family's Request for Posthumous Procurement of Ovaries," in this issue of *The Journal of Clinical Ethics* 27, no. 1 (Spring 2016).

2. M. Sullivan, "Banking on Cord Stem Cells," *Nature Reviews Cancer* 8, no. 7 (2008): 555-563.