CORRESPONDENCE

Oocyte Cryopreservation in a Transgender Male Adolescent

TO THE EDITOR: Since the effects of gender-affirming therapy on fertility are unknown, multiple medical societies endorse the preservation of fertility in persons who identify as transgender.[1-3] In transgender male adolescents (with a natal female sex), the pubertal transition to female sex can lead to gender dysphoria, which is often treated with gonadotropin-releasing hormone (GnRH) agonists to prevent pubertal development. This presents a unique clinical challenge of providing effective preservation of fertility without exacerbating gender dysphoria and undesired pubertal development if GnRH agonists are discontinued. In addition, the practicality of cryopreservation of oocytes is uncertain in patients who have not completed puberty. Here, we describe our multidisciplinary approach to cryopreservation of oocytes in a transgender male adolescent who was receiving GnRH agonist therapy and who wished to have genetically related children.

GnRH agonist therapy was initiated when the patient was 14 years of age, when the pubertal stage was classified as Tanner stage 2 (with stages ranging from 1 to 5 and higher stages indicating more advanced pubertal development),[3] and he was referred to a reproductive endocrinologist at 16 years of age. The patient was counseled to discontinue GnRH agonist therapy, given concern that his degree of pubertal development was inadequate to allow effective maturation of oocytes for cryopreservation; however, he opted to continue therapy during the period in which the oocytes were obtained and cryopreserved. Additional discussion detailed the process of future use of cryopreserved oocytes, including the potential use of donor sperm and the role of a gestational carrier.

The baseline gonadotropin levels were consistent with GnRH agonist suppression (serum follicle-stimulating hormone level, 0.89 mIU per milliliter; serum luteinizing hormone level, 0.07 mIU per milliliter). Since he did not want to undergo transvaginal ultrasonography, transabdominal ultrasonography and measurements of serum estradiol levels were used to monitor the patient's response to therapy. Doses of follitropin alfa and low-dose human chorionic gonadotropin were adjusted until the patient had a maximum estradiol level of 1204 pg per milliliter (4420 pmol per liter) on cycle day 30. After induction of oocyte maturation with recombinant human chorionic gonadotropin, five oocytes were retrieved while the patient was under conscious sedation; four mature oocytes were cryopreserved.

Distressing side effects of this process included vaginal bleeding for 7 days after oocyte retrieval and unanticipated breast development, which regressed within 3 months. The patient reported depressed mood and brief passive suicidal thoughts in response to these symptoms. The multidisciplinary team (including pediatric and reproductive endocrinologists, clinicians in adolescent medicine, and psychologists) moni-

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tored the patient for resolution of these symptoms. Testosterone therapy was then initiated as planned. The patient and his parents were satisfied with the process and outcome, although the prognosis regarding his fertility was guarded given the small number of oocytes that were cryopreserved.

This case stresses the importance of education regarding preservation of fertility in transgender youth. This involves a thorough discussion of the risks and benefits of discontinuation of GnRH agonists as well as counseling regarding potential adverse effects.

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Disclosure forms provided by the authors are available with the full text of this letter at NEJM.org.

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Low Incidence of Hospital-Onset *Clostridium difficile* Infection in Sickle Cell Disease

TO THE EDITOR: Patients with sickle cell disease have defects in immune function; they are frequently hospitalized for painful vaso-occlusive crisis and are often given empirical antibiotic treatment for fever in this setting. They also have intestinal dysbiosis.[1] Health care facility–associated *Clostridium difficile* infections might be expected to be more common among patients with sickle cell disease than in other patient populations.

We performed a retrospective cohort study involving adult patients with sickle cell disease who were admitted to Westchester Medical Center in Valhalla, New York, from January 2015 through November 2018. A total of 106 patients (87% of whom were either homozygous for hemoglobin S or had hemoglobin S β+ thalassemia and 13% of whom were heterozygous for hemoglobin S [hemoglobin SC]), representing 365 total consecutive hospital admissions, were included. Patients who underwent allogeneic stem-cell transplantation were excluded from the analysis.

In total, 70% of the admissions were for sickle cell–related complications and 56% were readmissions. There were 54 female patients and 52 male patients, and the median age of the patients was 26 years (range, 17 to 68). The mean length of stay in the hospital was 10.2 days (median, 7; range, 1 to 93). The total number of patient-days in the hospital for this cohort was 3727. Overall, 454 courses of antibiotics were administered during 180 hospitalizations (49%). The total number of days on which antibiotics were administered was 1598, and 1984 units of blood were administered. The most frequently used antibiotics were ceftriaxone, azithromycin, vancomycin, piperacillin–tazobactam, and cefepime.

A Cepheid Xpert *C. difficile* real-time polymerase-chain-reaction (PCR) assay targeting the toxigenic B gene was used to analyze samples from patients who had two or more loose stools in 24 hours in the absence of laxative use. A diagnosis of *C. difficile* infection was made if the PCR was positive in the absence of other conditions that could account for the diarrheal illness. Incidence rates, confidence intervals, and statistical differences were calculated with the use of MedCalc statistical software. Although data on readmissions were recorded accurately during the study period for patients with sickle cell disease, similar data were not available for patients in the hospital-wide group; many hospitalizations over the 4-year study period were readmissions. To allow for this, we opted to consider all admissions as being independent in our calculations of confidence intervals in both groups.

Published data on *C. difficile* infection in hospital-wide populations have shown incidence