Gonadal function in pediatric Fanconi anemia patients treated with hematopoietic stem cell transplant

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Supplemental Methods

Fertility Preservation Services

Fertility preservation services were offered to all patients planning to proceed with HSCT from 2014 onwards. Individualized fertility counselling was provided to each HSCT recipient by members of our reproductive fertility team. Fertility preservation services included embryo freezing, oocyte freezing, and ovarian tissue cryopreservation (OTC) for female patients and sperm cryopreservation or testicular tissue cryopreservation (TTC) for male patients. Fertility preservation services were offered to all HSCT recipients prior to the initiation of chemotherapy. The standard work-up included reproductive hormone assessments, including serum AMH levels for female patients to evaluate ovarian reserve. Due to the known risk of infertility risk in patients with FA, even patients who did not proceed with HSCT were offered fertility preservation services if they met specific criteria.

Reproductive hormone assessments and hormone replacement therapy

Annual routine reproductive hormonal evaluations are conducted for all patients with FA at CCHMC beginning age 11 years old. LH, FSH, estradiol, and AMH levels were measured in female patients. LH, FSH, testosterone and inhibin B levels were measured in male patients. Pre-pubertal females and males were defined as those patients without any signs of secondary sexual characteristics, specifically breast buds for girls and testis volume $\leq$3 mL for boys. Pubertal status was reviewed for each patient included in the study by our endocrinologist based on clinical exam findings and reproductive hormone assessments. The lower limit of detection for our clinical serum AMH assay was 0.003 ng/mL, any concentration below 0.003 ng/mL is considered to be undetectable. Serum inhibin B levels in male patients were also collected as markers of spermatogenesis and fertility recovery. Hormone replacement therapy (HRT) and duration of use was recorded in patients. Each patient's reproductive hormone levels

were recorded and included in the data analysis to evaluate longitudinal changes before and after HSCT. Hormone assessments (with the exception of serum AMH and inhibin B) were not recorded for females and males receiving estrogen or testosterone therapy to avoid reflecting the effects of the therapy. One patient who was undergoing gender transition was not included in the reproductive hormone analysis but is discussed separately.

HRT was offered as treatment to patients who met criteria for POI and testicular failure under the guidance of our endocrinologist. HRT was also offered to female diagnosed with POI for the prevention of osteoporosis. Treatment with HRT was offered under the discretion of our endocrinologist after weighing the benefits and risks of HRT and taking the patient's medical history under consideration to ensure there were no contraindications against use of HRT.