A Novel Indication for Oocyte Cryopreservation Prior to Autologous Hematopoietic Cell Transplantation for Refractory Multiple Sclerosis

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Background

Multiple sclerosis (MS) is an immune mediated inflammatory diseases of the central nervous system characterized by focal ovoid like lesions of demyelination seen on MRI(1,2). The etiology of MS is unknown, however inflammation followed by CNS demyelination and axonal degeneration are known to be part of the pathologic processes that lead to the disease (1). The mean age of onset of MS is 28-31 years old and tends to affect women more often then men with a ratio of 2.3:1 (3,4) . Other risk factors associated with MS include vitamin D deficiency, smoking, and certain viruses (5). The pattern of the disease can be classified as either Relapsing or Progressive depending on whether the patient has periods with or without symptoms (6). MS is diagnosed clinically with MRI used to support the diagnosis. In cases where the diagnosis isn't clear the McDonald diagnostic criteria can be applied (2). The life expectancy is reduced 7-14 years compared to the general population with increased deaths from infection, cardiovascular disease, respiratory disease, and suicide (7). Treatment can be divided into acute flairs, chronic, and symptomatic. The acute flairs are generally treated with steroids or plasma exchange, while the chronic disease is generally treated with disease modifying therapy (DMT)(5). No known treatment cures MS or completely prevents progression, however, which has led to many novel therapies. One of the promising therapies being explored for the past 2 decades is autologous hematopoietic cell transplants (AHCT).

AHCT is the process of collecting stem cells from either the peripheral blood stream, destroying the cells in the body with either radiation or chemotherapy, and then reestablish blood cell production by reintroducing the collected stem cells. AHCT can be divided into 3 categories: myeloablative, nonmyeloablative, and reduced intensity conditioning (RIC). These categories are differentiated whether the medicine employed is expected to result in pancytopenia (myeloablative), lymphopenia but minimal cytopenia (nonmyeloablative), or does not fit into either category (RIC). AHCT has been used for the treatment of multiple

Background Continued

Myeloma, lymphoma, and plasma cell disorders (8). AHCT almost always leads to infertility. Studies show infertility in >98% of patients receiving myeloablative stem cell transplant (9). One study showed that out of 37,362 patients who received a stem cell transplant, 232 of those patients (.6%) were successful in becoming pregnant. 30 of those 232 patients used assistive reproductive techniques (ART) to conceive (10). This high infertility rate is likely secondary to treatment-related gonadotoxicity (9). Even in Patients who have gonadal recovery, the spontaneous pregnancy rate is <15% (11). Because of the high rate of infertility secondary to gonadotoxicity, oocyte retrieval and cryopreservation should be considered for any patient undergoing AHCT treatment for MS and desires future fertility.

Case

The patient is a 24-year-old G0P0 who presented for fertility preservation with a past medical history of depression, anxiety, nephrolithiasis, and MS refractory to traditional medical therapy. She was referred to a tertiary care center to undergo AHTC over the summer for treatment of her MS. After thorough counseling on options, medications, and risk, the patient decided to proceed with oocyte cryopreservation.

The patient was started on combined estrogen/progesterone birth control for 3 weeks in preparation for initiation of controlled ovarian hyperstimulation, with baseline transvaginal ultrasound (TVUS) demonstrating an endometrial stripe of 6mm and E2 of 22. Patient received daily Follistim 150IU/Menopur 75IU on cycle day 1 to 6, followed by Follistim 150IU alone on cycle day 7 to 9. Ganarelix 250mcg was given on cycle day 6 to 9. Serial TVUS were performed on cycle days 5, 7, and 10 demonstrating appropriate follicular development. E2 levels on cycle day 5, 7, and 10 were 1100, 2497, and 4930, respectively. The decision was made to proceed with trigger with Lupron on cycle day 10 for oocyte retrieval on cycle day 12. Ultrasound guided needle

Case Continued

aspiration was performed under conscious sedation on cycle day 12 with retrieval of 12 oocytes, or which 11 were mature and underwent cryopreservation.

Discussion

This report demonstrates a case of successful oocyte retrieval in a patient planning to receive AHCT treatment for MS who desires future fertility. The need for fertility planning is well known for patients undergoing stem cell transplant for other indications; however, upon journal review the author notes this is a novel use of ART for this clinical scenario. One can assume that the same guidelines, complications, and fertility rates would be the same as other indications, but as AHCT treatment for MS becomes more prevalent further research should be carried out on the subject. As with the other indications for stem cell transplant, any patient who desires future fertility and is undergoing stem cell therapy for MS should be referred to a reproductive endocrinologist prior to receiving therapy.

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