A 31-year-old female patient presented for treatment of secondary infertility with complaints of irregular menstrual cycles. She had a miscarriage in 2006, followed by two ectopic pregnancies. She had undergone salpingectomy for left ruptured tubal pregnancy in 2009 and was treated with three doses of methotrexate 1 mg/kg on alternate days with folinic acid 0.1 mg/kg for right unruptured tubal pregnancy in 2010. Owing to tubal factor infertility, the patient was advised IVF. Pre-operative investigations done for hysteroscopy in 2012 were suggestive of slightly decreased total leukocyte count of 3370 cells/µL, normal hemoglobin levels of 12.9 g/dL and normal platelet count of 362,000/µL. Hysteroscopy findings were normal, and ovulation stimulation for IVF was started with 150 IU/day of recombinant follicle stimulating hormone. On day-6 of stimulation, she had 14-16 follicles of around 13 mm in diameter and an estradiol level of 785 pg/mL; subsequently, 0.25 mg methotrexate was given to million her pregnancy. On day-10 of stimulation, she developed fever and cough, and complete blood count and peripheral smear with marked leukocytosis were suggestive of acute leukemia. After obtaining the patient's informed consent, 18 oocytes were retrieved. Following intra cytoplasmic sperm injection, 14 eggs were fertilized, and the resulting embryos were cryopreserved. On a referral to a hematologist, a bone marrow biopsy was performed, which confirmed acute promyelocytic leukemia (APL). Literature review suggests this to be the first case of APL reported during the course of ovulation stimulation for IVF.

**KEY WORDS:** Acute promyelocytic leukemia, chemotherapy, embryo cryopreservation, fertility preservation, ovulation stimulation

**INTRODUCTION**

Acute promyelocytic leukemia (APL), a subtype of acute myeloid leukemia (AML), is a rare hematological malignancy with an age-dependent incidence.[1]

Effective cancer treatment regimens have significantly increased survival rates in young patients but have resulted in decreased fertility.[2] However, pretreatment specialized counseling and fertility preservation options have enabled the survivors to attain potential reproductive abilities.[3]

Embryo cryopreservation is a well-established fertility preservation technique. Sufficient time interval prior to initiation of chemo/radiotherapy is paramount to perform ovarian stimulation regimens.[4]

Here, we report embryo cryopreservation in a case of APL incidentally diagnosed during the course of ovulation induction for *in vitro* fertilization (IVF).
of gonadotropin-releasing hormone (GnRH) antagonist was started. On day-10 of stimulation, ovaries had 18-20 follicles, each measuring 16-17 mm in diameter with an estradiol level of 2888 pg/mL. To trigger ovulation and minimize the risks of hyperstimulation syndrome, GnRH agonist was used.

During the course of ovulation stimulation, the patient developed mild rashes on her extremities, which was not evaluated as it was considered insignificant at that point of time. Subsequently, she developed cough and intermittent fever, and when symptoms did not subside with antibiotics, a physician was consulted. A repeat complete blood count was advised, and the reports were suggestive of anemia (hemoglobin: 8.8 g/dL), thrombocytopenia (platelet count: 19,700/µL) and leukocytosis (total leukocyte count: 52,400 cells/mm³). Peripheral smear was indicative of acute leukemia with significant leukocytosis of > 20% blasts. The couple was counseled regarding the adverse effects of leukemia treatment on future fertility and the importance of embryo cryopreservation. After obtaining the consent for oocyte retrieval, 10 units of platelets, 2 units of fresh frozen plasma, and 1 unit of packed cell volume were transfused. Under general anesthesia, 18 eggs were retrieved, and intracytoplasmic sperm injection (ICSI) was performed. Fourteen eggs were fertilized, and the resultant embryos were cryopreserved.

The patient was subsequently referred to a hemat-oncologist. Bone marrow biopsy was suggestive of APL. Based on multicolor analysis, APL was classified as APL French-American-British-M3 variant. Patient was started on chemotherapy after evaluation of renal and liver function tests.

**DISCUSSION**

Ovarian damage due to cancer treatment protocols depends on different factors such as the drugs used, the cumulative dose of drugs, and the age at which the treatment was started. Since the number of ovarian primordial follicles decreases with increasing age, the incidence of infertility is higher in older women compared to young and adolescent cancer patients.  

Acute promyelocytic leukemia, is characterized by abnormal accumulation of immature granulocytes called promyelocytes, which cause fibrinolysis and hemostatic failure. Although the incidence of APL is age specific, the incidence of most other malignancies increases with advancing age. The median age group affected in APL is 30-40 years when compared to AML where age group involved is approximately 60 years and above. Given that APL patients are usually younger than patients with AML, fertility preservation in APL patients prior to beginning treatment for leukemia is crucial.

Rossi *et al.* compared the ovarian reserve in five premenopausal women treated with chemotherapy for AML, with age-matched control group without a history of chemotherapy. The results indicated that the chemotherapy affected the ovarian reserve.

With continuous evolution in assisted reproductive technologies (ART), diverse fertility preservation options are available for reproductive age group women diagnosed with neoplastic diseases. Among the available fertility preservation options, embryo cryopreservation is a reliable and routinely used method. Oocyte and ovarian tissue cryopreservation methods are still in the experimental stage. In embryo cryopreservation, before starting chemotherapy, the patient is subjected to hormone-induced ovulation stimulation protocols to obtain better-quality oocytes. Aspirated eggs are fertilized using ART and resulting embryos cryopreserved either by slow freezing or vitrification. The main advantage of this method is preservation of future fertility and patient reassurance regarding the probabilities of conceiving, irrespective of the fear of attaining permanent amenorrhea, consequent to chemotherapy.

From extensive literature search, we confirm this to be the first case of APL diagnosed and detected during ovulation stimulation cycles for IVF.

Given the increasing incidence of cancer in women of reproductive age, it is paramount to consider fertility preservation techniques as vital aspects of integrated cancer care approach. Though all these methods have ethical and social issues, and many challenges are yet to be resolved, it is the primary role of the oncologist and gynecologist to counsel patients regarding future fertility preservation options and suggests appropriate fertility preservation techniques.

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