**Aim and background:** The global incidence of cancer is on the rise and with the advancement of cancer care, the survival of cancer patients has also improved. Addressing the fertility needs of survivors is also of paramount importance to improving their quality of life.

**Case description:** We present a case of a young lady with osteosarcoma who was referred to our center for fertility preservation and controlled ovarian stimulation (COS) was done using the antagonist protocol, followed by in vitro fertilization and embryo cryopreservation for future use.

**Conclusion:** Embryo cryopreservation in cancer patients is a well-established method of fertility preservation. In regards to oncofertility, evidence supports a multidisciplinary approach, early referral to a fertility specialist, and individualized discussion on options for fertility preservation without compromising the cancer treatment.

**Clinical significance:** This case highlights the need to include discussions on fertility preservation in oncology patients by the primary care providers and the options available for the patients.

**Keywords:** Cancer, Case report, Embryo cryopreservation, Fertility preservation, Oncofertility.

**International Journal of Infertility and Fetal Medicine (2023): 10.5005/jp-journals-10016-1326**
Fertility Preservation in a Patient of Osteosarcoma

The European Society of Human Reproduction and Embryology. 5 for the patients, this method has been strongly recommended by the nurse staff for assisting in the management of the patient.

Preoperative radiotherapy with neoadjuvant chemotherapy may be a viable option to improve the rates of limb-sparing surgery, especially in patients with large tumor volume or anatomic localization. 4 Cancer can affect female fertility in various ways. Impaired ovarian function at cancer diagnosis may occur if the ovaries are directly involved or metastasis. Chemotherapy and radiotherapy may induce premature ovarian insufficiency (POI). Surgical removal or damage to reproductive organs may also occur. There may be direct and indirect damage due to apoptosis, vascular injury, and focal ovarian cortical fibrosis. The most important factors are the cumulative dose and drug class and alkylating agents like cyclophosphamide have been found to be of greatest risk. 5 The younger the patient, the lesser the risk of ovarian failure as the cohort of primordial follicles is greater. The gonads are very radiosensitive. Damage depends on the radiation field used, the number of treatment fractions, and the cumulative dose. This may cause direct damage to the ovaries’ hypothalamic–pituitary–ovarian (HPO) axis. Exposure to 20–30 Gy or total body radiation of 15 Gy leads to POI. Any radiation beyond 2 Gy can damage half of the primordial follicles. The sterilizing doses are 20.3 Gy at birth, 18.4 Gy at 10 years, 16.5 Gy at 20 years, and 14.3 Gy at 30 years. Radiotoxicity adversely affects the uterus also by reduced vascularity, myometrium fibrosis, and hormone-dependent insufficiency, which causes implantation failure or complications in pregnancy. 6

The best option depends on the type of cancer, the patient’s age, available time, the likelihood of ovarian involvement, and the expertise available. In our case, the patient was young, with a good ovarian reserve and normal semen analysis, so after discussing her options, embryo cryopreservation was decided. Embryo cryopreservation is one of the most well-established methods. 5 Oocyte retrieval should be performed before cancer treatment, as was done in our case. 5 This patient presented in the premenstrual phase, so a controlled ovarian stimulation (COS) with gonadotropin injections to promote multifollicular growth using the antagonist protocol was started. Since this method is short, feasible, and safe for the patients, this method has been strongly recommended by the European Society of Human Reproduction and Embryology. 5 The antagonist protocol followed by freezing all eggs decreases the risk of ovarian hyperstimulation considerably as the doses of GnRH used are lower. Random start protocols and dual stimulation have also been used to maximize fertility preservation outcomes, but the level of current evidence is weak. 5 The oocytes retrieved are then fertilized in the laboratory and are cryopreserved for future use, commonly in their blastocyst phase. Concerns have been raised that COS can promote tumor growth in estrogen receptor-positive cancers, but evidence from early meta-analysis is reassuring. 7 However, stimulation combined with aromatase inhibitor daily to prevent a rise in estradiol levels is recommended and the number of oocytes and embryos retrieved is comparable to standard protocols. 5, 8 The few disadvantages of this method include the following—it is not a viable option for women with aggressive cancer due to the time of 2–3 weeks required for ovarian stimulation, not possible for prepubertal girls, the need for a stable male partner, and ethical issues regarding embryo disposition in case of dispute in future. 9 In postpubertal girls, ovarian stimulation and cryopreservation of mature metaphase II oocytes is an acceptable option, while for more aggressive tumors, cryopreservation of immature oocytes is needed. Prepubertal girls will require ovarian tissue cryopreservation, though this method is considered to be experimental in most countries. Concurrent use of GnRH agonist with chemotherapy or radiotherapy to suppress the HPO axis has been used for a long time, but its efficacy in fertility preservation is not established. 5 Gonadal shielding should be done in case of pelvic or abdominal radiotherapy. 5

In conclusion, the discussion regarding fertility preservation in young adults undergoing treatment for cancer should be a part of the multidisciplinary approach. Cancer treatment should always be made a priority, and fertility preservation options should be tailored according to the patient’s disease, age, and expertise available. Embryo and oocyte cryopreservation are the most established methods currently.

Acknowledgment
The authors are thankful to the patient, the embryology unit, and the nursing staff for assisting in the management of the patient.

Orcid
Manisha Chhetry Ω https://orcid.org/0000-0002-3432-8544
Kunur Shah Ω https://orcid.org/0000-0003-3932-155X

References