



Case Study of Postpubertal Adolescent Female Undergoing Ovarian Tissue Cryopreservation and Oophorectomy Prior to Gonadotoxic Therapy

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60.1 Assessment and Diagnosis – 548

60.2 Management – 548

60.3 Operative Considerations – 548

60.4 Outcome – 549

Review Questions and Answers – 549

References – 550

Case Presentation

A 14-year-old female living in South Africa presented with a history of 7 months of worsening right lower back pain and progressive neurological symptoms including radiating pain, numbness, and tingling down her right leg. The initial MRI performed revealed a bony lesion involving the right iliac bone, right SI joint, and right sacrum associated with a large soft tissue component (9.6 × 8 × 8.4 cm). The imaging was concerning due to a malignant process requiring further evaluation. The family transferred care to a tertiary pediatric hospital in the USA where diagnostic testing was completed.

60.1 Assessment and Diagnosis

Ultrasound-guided core biopsies of the mass were positive for CD99+ small round blue cells. RT-PCR analysis of the cells was positive for the EWSR1-FLI1 fusion transcript, confirming the diagnosis of Ewing Sarcoma. A single metastatic lesion was noted in the in the left sacrum. CT chest was negative for metastatic disease.

Ewing Sarcoma (ES) is the second most common malignant bone tumor of childhood/adolescence. ES is a chemo- and radiosensitive tumor. Treatment consists of both systemic treatment (chemotherapy) and local control (surgical resection or radiation therapy). The management of local disease depends on the anatomical location of the tumor as well as the associated risks and benefits of each treatment modality. Large pelvic tumors, in particular, are not typically amenable to surgical resection [1].

60.2 Management

The treatment plan included neo-adjuvant chemotherapy followed by radiation therapy (55.80 Gy) with adjuvant chemotherapy. Chemotherapy would consist of alternating cycles of vincristine, doxorubicin, cyclophosphamide (8400 mg/m²), ifosfamide (63,000 mg/m²), and etoposide every 14 days. The radiation therapy field would include the right pelvis as well as the focal lesion identified in the left sacrum.

Infertility is a known side-effect of both alkylating agents and radiation to the ovaries or pelvis. The cyclophosphamide equivalency dose

(CED) of this treatment is 23,772 mg/m². Based on a CED of 23,772 plus radiation therapy to the pelvis, her risk for ovarian failure is greater than 80% [2–4].

Fertility preservation counseling was initiated once diagnosis was confirmed. The family met with the Advance Practice Registered Nurse (APRN) to discuss risk of infertility and preservation options. Oocyte harvesting and oophorectomy were discussed with the family as standard fertility preservation options. Ovarian tissue cryopreservation was presented as an investigational procedure [5]. Oocyte harvesting was not available at the pediatric institution and required transfer of care to reproductive medicine specialists at a partnering adult hospital. Both ovarian tissue cryopreservation and oophorectomy would be performed at time of routine venous port placement and bone marrow aspirate and biopsy.

The family decided to proceed with ovarian tissue cryopreservation and oophorectomy. They understood oocyte harvesting is standard of care and ovarian tissue cryopreservation was considered experimental. The family stated they based their decision on a desire to start treatment as soon as possible due to increasing pain. Delay of treatment initiation for fertility preservation is a concern often expressed by families at the time of cancer diagnosis [6]. Additional concerns identified were the intensity of the stimulation process for oocyte harvesting as well as invasive ultrasounds required to monitor oocyte maturation. Potential for ovarian insufficiency from gonadotoxic treatment was also a worry for the mother. The reports of restoration of hormone function from transplanted tissue also factored into the family's decision to pursue OTC [7].

60.3 Operative Considerations

Most girls undergoing potentially sterilizing therapy will receive symmetric exposure to both ovaries. Therefore, in most cases, either ovary can be removed at the discretion of the surgeon during laparoscopic oophorectomy for cryopreservation. If diagnostic laparoscopy confirms normal bilateral fallopian tubes and ovaries, the right ovary is often removed out of convenience due to the proximity of the sigmoid colon to the left ovary. An exception is for girls who are expected to

receive asymmetric pelvic radiation. In this patient's case, the primary tumor involved the right hemipelvis, and the radiation field was anticipated to disproportionately affect the right ovary. Therefore, in discussion with the radiation oncologist, the decision was made to perform a laparoscopic right oophorectomy in the usual fashion and oophoropexy of the left ovary. This was accomplished using a single laparoscopic suture between the mesovarium and the peritoneum overlying the iliac vessels to suspend it out of the pelvis. The goal of oophoropexy was to minimize the radiation exposure of the contralateral ovary.

60.4 Outcome

The patient went home on the day of surgery and had an uncomplicated postoperative course. Chemotherapy was initiated on the fourth postoperative day.

Clinical Pearls

- Calculating potential for infertility includes assessment of chemotherapy, both high-risk medications and cumulative dosing, radiation, and surgical risks.
- Determination of fertility preservation options requires discussion between medical oncologist, radiation oncologist, and surgeon.
- Family may choose an experimental fertility preservation option if the standard procedure will delay onset of treatment or if the investigation option offers a perceived benefit not provided by standard therapy.
- In girls receiving potentially sterilizing therapy who will undergo asymmetric pelvic radiation, laparoscopic oophorectomy for cryopreservation should remove the ovary anticipated to receive the higher radiation dose.
- Concurrent laparoscopic oophoropexy can be used to suspend the contralateral ovary out of the pelvis and minimize its radiation exposure.

Review Questions and Answers

- ❓ Q1. Which patient is at highest risk for infertility due to treatment?
- (a) Four-year-old female receiving vincristine, doxorubicin, dactinomycin, and 10.8 Gy radiation to the right flank for treatment of Wilms' tumor
 - (b) Twelve-year-old female receiving 18 Gy cranial radiation and cyclophosphamide 1000 mg/m² for treatment of acute lymphoblastic leukemia
 - (c) Twenty-year-old female receiving 55 Gy radiation to the right thigh for treatment of synovial cell sarcoma
 - (d) Fifteen-year-old receiving cyclophosphamide 8400 mg/m² and 54 Gy to the right hip for alveolar rhabdomyosarcoma
- ✔ A1. (d)
- ❓ Q2. What factors may influence the decision regarding ovarian tissue cryopreservation?
- (a) Urgency to start treatment
 - (b) Patient's age
 - (c) Standard therapy versus investigational
 - (d) All of the above
- ✔ A2. (d)
- ❓ Q3. In which of the following patients is there a side preference for laparoscopic oophorectomy for cryopreservation?
- (a) Two-year-old female with neuroblastoma of the right adrenal gland
 - (b) Eleven-year-old female with recurrent AML undergoing stem cell transplant
 - (c) Fourteen-year-old female with alveolar rhabdomyosarcoma of the retroperitoneum in the right hemipelvis
 - (d) Four-year-old female with metastatic but local stage I Wilms' tumor
- ✔ A3. (c)

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