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Case Report

Successful pregnancy outcome in a woman with malignant bilateral ovarian germ cell tumor

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ABSTRACT

Malignant ovarian germ cell tumors (MOGCT) are rare, accounting for 5% of all ovarian malignancies. In the first two decades of life, almost 70% of ovarian tumors are germ cell tumors and of these one-third are malignant. Bilateral involvement in MOGCT is very rare. This case presented a unique challenge of fertility-sparing surgery in the case of MOGCT. Although fertility-sparing surgery is recommended even in advanced stages if fertility is desired, the bilaterality of disease precluded the option in the index case. Neoadjuvant chemotherapy has been attempted in patients with malignant ovarian germ cell tumors with extensive intra-abdominal disease. Current chemotherapy for GCT has more than 80% chances of menstruation, more than 70% pregnancy rates with no increase in risk of teratogenicity, and less than 10% risk of premature ovarian failure. In our case not only the patient had a successful debulking surgery post NACT without any signs of recurrence, but also had a spontaneous conception with a successful pregnancy outcome with no complications pertaining to prior treatment given.

Keywords: Ovarian tumor, Germ cell tumor, Pregnancy post-chemotherapy

INTRODUCTION

Malignant ovarian germ cell tumors account for only 5% of all malignant ovarian tumors but predominate in the first three decades of life.[1] As they are usually unilateral, surgical resection with adjuvant chemotherapy spares fertility in most cases.[2] Unlike epithelial ovarian cancers, neo-adjuvant chemotherapy is usually not required even in advanced disease in view of the unilaterality of the condition.

Here we present a case of nulliparous woman with a bilateral ovarian germ cell tumor who was successfully managed with neo-adjuvant chemotherapy followed by surgical resection and went on to have a successful pregnancy outcome after a spontaneous conception.

CASE REPORT

A 23 years nulliparous woman was referred to Gynecology OPD of our tertiary care institute with a history of abdominal pain of dull aching, dragging nature radiating to her back for 1 month duration.

There was no menstrual complaint and no significant past history. She was well preserved, with stable vitals and no abnormality in general physical, thyroid, and breast examination. Examination of the abdomen revealed a 24-28 weeks size abdomino-pelvic mass with well-defined margins, firm to hard, slightly tender with irregular surface, and restricted mobility. There were no dilated veins, no scar marks, the Umbilicus was central and inverted and there was no free fluid clinically.

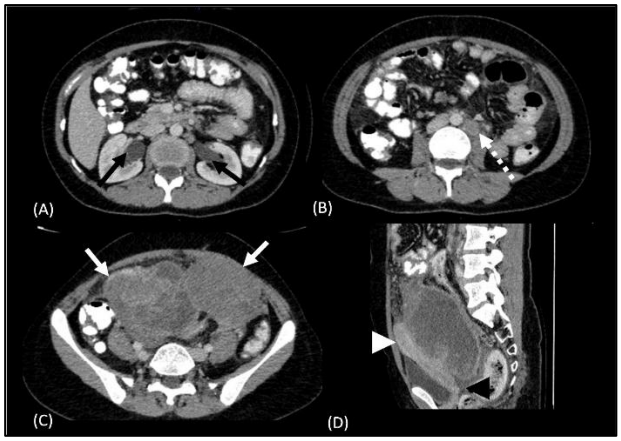

Figure 1 (A-D): Bilateral pelvic masses with enhancing nodular areas likely malignant. Retroperitoneal lymphadenopathy likely metastasis.

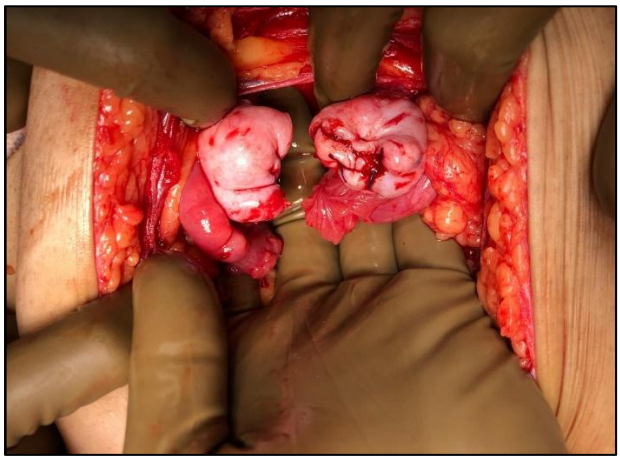

Figure 2: Intra operative image post ovarian reconstruction.

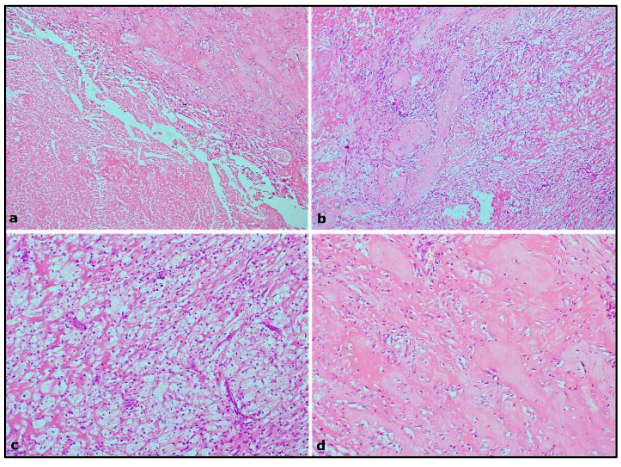

Figure 3 (a-d): Sections from both the ovaries showing extensive chemotherapy related changes in the form of sheets of foamy macrophages, large areas of hyalinization and infarction necrosis. No residual tumor noted (Hematoxylin & Eosin; a, b:10X; c, d: 20X).

USG showed bilateral complex ovarian masses. MRI at our centre revealed large, well-defined, lobulated predominantly solid abdominopelvic masses arising from B/L adnexa, right measuring 12.3×9.1×10.8 cm and left measuring 9.1×9.0×7.2 cm with internal areas of cystic changes/ degeneration (Figure 1).

The most likely radiological diagnosis was epithelial ovarian/ malignant ovarian germ cell tumor. Tumor markers (Table 1) revealed markedly elevated alpha-fetoprotein and hence, a provisional diagnosis of malignant germ-cell tumor was made.

The standard of care was discussed with the patient and family. The scope of fertility preservation seemed unlikely because of bilaterality. Also, the need for post-op chemotherapy, chances of recurrence, and permanent loss of ovarian function at a young age with its associated complications were explained. As the woman was keen for conception, alternate treatment options were considered.

After a thorough review by a multi-disciplinary tumor board and informed consent, 4 cycles of neoadjuvant chemotherapy (Bleomycin, Etoposide, Platinum) were administered which led to a significant decrease in tumor markers. CECT Abdomen (after chemotherapy) revealed well-defined hypoattenuating pelvic mass in bilateral adnexa (right measuring 7.7×7.7×6.4 cm and left measuring 5.2×4.4×5 cm) 30% reduction in tumor size with loss of fat planes with small bowel loops anteriorly and uterus posteriorly.

After a detailed informed consent, the patient was taken up for laparotomy with a midline vertical incision. A large mass on the right side with an unhealthy look of size 7×8 cm was present the same was resected with the reconstruction of normal ovarian tissue.

On the left side, a mass of 5×4 cm was seen with adjacent normal ovarian tissue; the same was resected followed by reconstruction. Bilateral tubes and uterus were normal in morphology. (Intra-op image after reconstruction shown in Figure 2).

The patient had an uneventful post-operative period. Histopathology showed no residual disease in the dissected tissue (Figure 3). The lady was followed up with tumor markers and imaging (Table 2). She resumed her menstrual functions around 3 months post-operatively. She was allowed conception after one year of surgery and had a spontaneous conception after 22 months of surgery.

The antenatal period was smooth with mild hypertension and intrahepatic cholestasis of pregnancy in the 3rd trimester. She had spontaneous labor around 37 weeks POG and delivered a healthy child of 2.6 Kg with no malformations who was adequately breastfed. Currently, the lady is 16 months post-partum with normal menstrual cycles on regular follow-up.

Table 1: Tumor makers at diagnosis and during chemotherapy.

	Initial visit	After 2 cycles of NACT	After 4 cycles of NACT
Alpha feto protein	73100 ng/ml	266.4 ng/ml	40.92 ng/ml
Beta Hcg	34.28 nIU/ml	3.37 nIU/ml	3.1 nIU/ml
LDH	566 U/l	213 U/l	230 U/l
Ca 125	350.8 U/ml	17.25 U/ml	21.1 U/ml
Ca 19-9	0.6 U/ml	NA	NA
CEA	1.47 ng/ml	NA	NA

Table 2: Tumour makers after surgery.

	4 weeks post-op	2 months post-op	4 months post-op	1-year post-op
Alpha feto protein	12.10 ng/ml	8.08 ng/ml	8.72 ng/ml	9.54 ng/ml
Beta Hcg	0.5 nIU/ml	0.9 nIU/ml	1.51 nIU/ml	1.2 nIU/ml
LDH	212 U/l	280 U/l	212 U/l	250 U/l
Ca 125	8.2 U/ml	10.1 U/ml	10.84 U/ml	11.2 U/ml
AMH	0.045 ng/ml	0.056 ng/ml	3.65 ng/ml	NA

DISCUSSION

Surgical resection with adjuvant chemotherapy is the standard of care for malignant ovarian germ cell tumors. Fertility sparing surgery (FSS) is recommended even in advanced stages if fertility is desired. As more than 60% of tumors are limited to one ovary at diagnosis, unilateral salpingo-oophorectomy is usually sufficient. Biopsy of the contralateral ovary is not recommended while hysterectomy has not been shown to impact survival even in advanced stages.[3] The most important condition precluding fertility preservation in germ-cell ovarian tumors is bilateral disease. Hence, we highlight the successful use of neoadjuvant chemotherapy in a young nulliparous lady with a bilateral malignant germ cell tumor in this case.

The use of neoadjuvant chemotherapy in the setting of malignant ovarian germ cell tumors has been reported in literature in patients with extensive intra-abdominal disease (where primary debulking was considered difficult) or in women with poor general conditions for upfront surgery. The largest series of use of NACT in MOGCT has reported its use in 23 patients of stage III-IV GCT who were given NACT for advanced and bulky disease and poor performance status. The outcome was compared to 43 patients receiving standard care at the same time.

All 23 in the NACT group were initially considered unsuitable for FSS in v/o extensive disease. The overall survival and disease-free survival were better in the NACT group with a follow-up of 74 months. While 11 in the standard treatment arm underwent BSO with loss of fertility, 20 women in NACT could undergo successful FSS. During the follow-up, 18 resumed menstrual function while 10 conceived spontaneously (only 10 were married and hence eligible for conception). The authors suggested after the review that in addition to extensive disease and poor GC, NACT must also be considered if initial surgery precludes fertility-sparing in women desirous of fertility.[4] Besides this study, there is another study where NACT has been administered for extensive MOGCT and has shown a favorable outcome.[5]

Loss of ovarian function, temporary or permanent, is a proven effect of chemotherapy and hence, may jeopardize its use. However, the literature is promising in this aspect as the current chemotherapy regime for GCT (BEP) has more than 80% chances of return of normal menstruation, more than 70% pregnancy rates with no increase in risk of teratogenicity and less than 10% risk of POI.[6] The index case also resumed menstruation after 2-3 months of surgery and had a spontaneous conception at 22 months.

CONCLUSION

The index case highlights that neoadjuvant chemotherapy is a promising option in women desirous of fertility with bilateral germ cell neoplasm. The patient is free from disease at 16 months postpartum presently with a healthy child.

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