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## Case Report

# Mucinous carcinoma recurrence after fertility preservation surgery

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## ABSTRACT

Benign ovarian tumours occurs in 7% of women in reproductive age group. The average age of onset for borderline ovarian tumours is ten years younger than that of ovarian cancers. Considered the very good prognosis following an adequate surgical staging in early epithelial ovarian cancers (EOCs), the FPS for women of childbearing age group has become an argument of debate in last decades. 25% of the EOCs are diagnosed in early stages, 14% of those early stage patients are under age of 40 at the time of diagnosis. Fertility preservation is widely accepted in early stage epithelial ovarian cancers, germ cell, sex cord stromal tumours. Based on data, fertility sparing surgery in EOCs recommended in stage 1A, grade 1 and 2 and favourable histologic types (endometrioid, mucinous, low grade serous and clear cell carcinomas) ovarian cancer. Above stage 1A, grade 3, high grade serous and clear cell tumours decision process about FPS should be individualised, weighing a slightly higher risk of recurrence with fertility goals. Correct surgical staging is mandatory and oncological safety should be primary importance. Survival rates in oncological patients have been steadily increasing now a days due to the effectiveness of novel oncological treatments like surgery, chemo and radiotherapy. However, these treatments impair the reproductive ability of the patients and may cause premature ovarian failure in females and azoospermia in males. A multidisciplinary approach with oncology, reproductive endocrinology may be of utility to help these patients to achieve their fertility goals in future.

**Keywords:** Fertility preservation surgery, Epithelial ovarian cancer, Reproductive age group

## INTRODUCTION

Epithelial ovarian cancers is the second most common cause of death from a gynecological cancer. Borderline ovarian tumors account for 15% of all epithelial ovarian malignancies.<sup>1</sup> Epithelial ovarian cancers (EOCs) is the most lethal of malignant ovarian tumors. Clinicians have been reluctant to perform fertility sparing surgery in certain group of patients with stage 1 epithelial ovarian cancers including those with poorly differentiated tumors and clear cell carcinomas.<sup>2</sup> In early EOCs, 5 years survival rate ranges from 70 to 100% for stage 1 and 50 to 95% for stage 2. A thorough surgical staging is crucial to address appropriate treatment and guarantee optimal survival. Less extensive surgical procedures may fail to detect extra ovarian spread of disease. Several papers reported on the

risk of unrecognized occult disease, with a 30% risk of upstaging on restaging surgery. 25% of EOCs are diagnosed in early stages, in that 14% of those early stage patients are under the age of 40 at the time of diagnosis. These women are potentially interested in preserving their fertility.<sup>3</sup>

While faced with the diagnosis of any cancer, reproductive aged women have to face the possibilities of never conceiving a child with their own eggs. Preservation of fertility in men may be easier with banking of sperms before treatment but for women, storage of gametes is technically very complex with limited success.<sup>4</sup> As some approaches to fertility preservation may require modification in the timing of a patients treatment and cannot be implemented once systemic therapy has begun,

integration of fertility issues into initial discussions about cancer treatment is essential.<sup>5</sup> Embryo storage is ideal for an adult woman in a stable relationship as it is an established technique which has been available since the mid 1980s. IVF offers a success rate of approximately 30% per cycle (dependent on age) and this is similar to the natural conception rate that is achievable by healthy couple without assisted reproductive techniques.<sup>6,7</sup>

In women who wish to preserve their reproductive function, FSS is the treatment of choice where feasible. This includes resection of the tumor through conservative surgical procedures like ovarian cystectomy, unilateral salpingo-oophorectomy (USO), recently ultrasound guided ovarian wedge resection (UGOWR) in trend. In women with bilateral ovarian involvement USO, ovarian cystectomy, bilateral ovarian cystectomy may be indicated. In these cases, where peritoneal washings, omentectomy and peritoneal biopsy is performed, women would be considered having undergone a complete staging of a disease. The predominant risk associated with FSS, recurrence of the disease which is reported to be between 5-34%.<sup>1</sup> Evidence also suggests that recurrence is 2-4 fold higher compared to radical surgery. For this reason individualized and carefully planned surgical management is very important.

This can only be approached with the multidisciplinary team consist of surgical oncologists, medical oncologists, radiation oncologists, reproductive health specialists and embryologists during the development of treatment plan. Algorithm for early referral and timely interventions for fertility preservation in young patients with cancers (Figure 1).<sup>8</sup>

## CASE REPORT

A 26 years old nulligravida, presented to our setup with abdominal pain and distension for 3 months with loss of appetite and weight. She had been married for 7 years, evaluated for primary sub-fertility 4 years ago, given ovulation induction twice and discontinued treatment due to family commitments. She had regular menstrual cycles with normal flow. 2 years back during evaluation of subfertility, a cyst was found in right adnexa with normal CA-125, hence proceeded to DH with laparoscopic right adnexal cystectomy (6.5×5 cm) done (May 2018). Intra-operatively cyst was accidentally punctured and mucinous fluid was suctioned out. Cyst wall sent for HPE. Report came out to be borderline mucinous tumor of right ovary (endocervical type) with focal intraepithelial carcinoma. After discussion with medical board, patient opted for fertility preservation surgery (August 2018).

Intra-operative findings- uterus, left ovary, appendix and POD normal. FPS proceeded to right salpingo-oophorectomy, right pelvic and para-aortic lymphadenectomy, omentectomy, appendectomy, peritoneal fluid and contralateral ovarian fluid sampling taken for cytology. HPE came out to be benign cyst of right

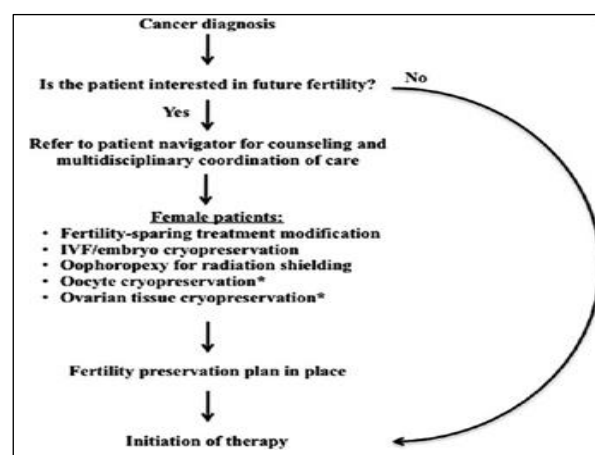
ovary, all other samples negative for malignancy. Since there was breach in capsule during primary surgery, she was staged as 1C3, advised 3 cycles chemotherapy after oocyte retrieval (Figure 2).

Ovulation induction with HCG trigger, oocyte retrieval done. ICSI was done with 7 eggs and 5 embryos (8 cell stage) were obtained and frozen. She had completed chemotherapy in November 2018 and up to November 2019 patient was on 3<sup>rd</sup> monthly follow up with ultrasound and CA125 that was normal. Frozen embryo transfer was done with 2 embryos after 1 year of chemotherapy, but failed. Now 3 embryos remaining. Because of COVID pandemic, patient lost her follow up for past 1 year. Now presented with abdominal pain and distension. Her general examination and vitals stable. On per abdomen, a soft non tender, firm mass of 24 weeks size occupying hypogastric, right and left iliac fossa, umbilicus, lumbar region with varying consistency, no guarding and rigidity, no free fluid. On per vaginal examination, cervix pointing forwards, uterus retroverted and deviated to right, left forniceal fullness was present, no POD nodularity, same adnexal mass palpable (more on left side) (Figure 3).

While investigated her Hg 10.4, Pl 2.41, PCV 31, RFT, LFT, TFT, Coagulation profile was normal, CA125 14.4 IU/ml, CEA 2.18 ng/ml. MRI abdomen pelvis-complex ovarian mass of size 22×18×11 cm well defined, thick septations, solid components seen within the lesion. Ovaries not made out separately, probably malignant origin. Upper GI scopy- normal study. PET-CT- active malignant ovarian lesion with increased metabolic activity in solid component of the lesion. Radical surgery (November 2020) proceeded to total abdominal hysterectomy, left salpingo-oophorectomy, left pelvic and para-aortic lymphadenectomy, appendectomy.

## HPE report

Mucinous carcinoma grade 2. As per medical oncologist advice now patient is on 3<sup>rd</sup> monthly follow up.



**Figure 1: Algorithm for early referral and timely interventions for fertility preservation in young patients with cancers.<sup>8</sup>**



**Figure 2: MRI image showing abdominopelvic mass.**



**Figure 3: Intra-operative pictures of mass lesion.**

## DISCUSSION

3 to 14% of epithelial ovarian cancers occurs in younger age group. Younger women more likely to present with early stage and low grade. Survival without chemotherapy is 94% in stage 1A, 92% in stage 1B, 84% in stage 1C. Fertility preservation did not have any adverse effect on survival in early stage disease. It can be offered to women with stage 1A-1C disease. Recurrence rate ranges from 4-28%. Antagonist or random start protocol are generally used in patients awaiting chemotherapy due to time constraints. These do not alter the oocyte or embryo yield. It is essential to assess the ovarian reserve prior to stimulation. In stage 1A disease where chemotherapy is an adjuvant may not be needed. Fresh or frozen embryo transfer doesn't make any difference in pregnancy outcome. In stage 1C disease, chemotherapy with taxanes or platinum based agents are used. Here preservation of embryos done and then followed by chemotherapy usually preferable. After one year of chemotherapy, embryo transfer should be done. Reproductive function and ill effects of surgical menopause can also be prevented by FPS in early epithelial ovarian cancer.

If a patient is currently planning to become pregnant, she should be informed about an elevated postoperative risk of infertility due to low ovarian reserve, possible tubal factors

and elevated risk of recurrence especially in the first 24 months of post-surgery. If a woman wishes to become later, oocyte cryopreservation after hormonal stimulation and/or embryo cryopreservation are conceivable options. The main clinical factors associated with disease relapse are advanced age at diagnosis, preoperative elevation of CA125, presence of invasive implants and micropapillary histology. Recurrence rate after FPS in BOTs are higher compared to radical surgery, however after completion of desire of conception surgical second look with removal of uterus and contralateral ovary remains debated. For mucinous BOT several authors suggest completion of surgery because many mucinous tumors relapsed as invasive ovarian tumors.<sup>8-10</sup>

## CONCLUSION

In early stage mucinous carcinoma, fertility sparing surgery may be an acceptable option for younger women. But concerns regarding sub optimal surgery remain there. One major concern with FPS is very small or microscopic focal involvement of the normal looking uterus and contralateral ovary. Previous studies shown that contralateral ovary involvement during surgery and recurrence in contralateral residual ovary is low. Women with a diagnosis of BOT should be referred to onco-fertility cent prior to performing FPS in order to assess the reproductive status and to plan future post treatment conception. In these patients a routine follow-up evaluation should be done with clinical examination, ultrasound and serum markers. Surgical management of relapse depends on disease localisation and histology. Fertility preservation techniques like oocyte/embryo cryopreservation availability, patient can be a biological mother even after radical surgeries.

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