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Pregnancy After Fertility Sparing Surgery in Advanced Ovarian Low-grade Papillary Serous Carcinoma: A Case Report

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ABSTRACT

Ovarian Low-grade serous carcinoma (LGSC), a type of epithelial ovarian tumor, is often diagnosed in the advanced stage. Treatment involves surgery and chemotherapy. In advanced stages (3 and 4), removing all tumoral implants with both the uterus and ovaries (debunking surgery) is the first surgical goal. We presented a case of a 38-year-old woman who became pregnant three years after being diagnosed with LGSOC at stage 3c. We resected all tumoral implants, and decision was made to preserve the uterus for her since the patient wanted to be pregnant. The patient underwent surgery, then followed by a standard chemotherapy regime. During the three years of follow-up, there were no signs of tumor return; she decided to get pregnant by egg donation through an in vitro fertilization (IVF) procedure. A cesarean section was done and the twin infants were born in good condition and with good APGAR scores.

Keywords: Ovarian Cancer, Pregnancy, Fertility Preservation, First Trimester, Prediction Model

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1. Introduction

Ovarian cancer, the second fatal gynecological cancer in females, is divided into three main categories: epithelial, non-epithelial, and metastatic **(1)**. Serous ovarian carcinoma, which falls under the category of epithelial ovarian tumors, is the first common type of ovarian cancer and is categorized as low-grade (LGSOC) and high-grade (HGSOC) **(2, 3)**.

LGSOC has a better prognosis than HGSOC and represents 5–10% of patients diagnosed with serous carcinoma **(4)**. Approximately 70% of LGSOCs are diagnosed at an advanced stage, based on the International Federation of Obstetrics and Gynecology (FIGO III–IV). LGSOC stems from epithelial cells of the fallopian tube and, during ovulation, migrates into the ovaries, giving the origin of serous cystadenomas **(5)**. This tumor typically affects the ovarian parenchymal and surfaces as a cystic, solid tumor. The best description of LGSC invasion is the presence of neoplastic cells in the ovarian stroma in a linear dimension or evident desmoplastic. These two characteristics are the best markers of its detrimental incursion **(3)**.

The most prevalent clinical symptoms of LGSOC are abdominal or pelvic pain, bloating, dysfunction of the bowel or bladder, and unexplained weight loss. On the microscopic side, LGSOC is more characterized by mild to moderate atypia, low proliferative index activity, and invasion. Diagnostic methods typically involve clinical examination, including pelvic examination, CA-125 serum marker, ultrasound, or other imaging modalities such as whole-body magnetic

resonance imaging (MRI) or computed tomography (CT) scans of the chest, abdomen, and pelvis **(6, 7)**.

Serous ovarian cancers are also divided into four stages, I through IV, and their treatment strategies are based on surgery and chemotherapy, which are frequently used in conjunction to treat LGSOC patients **(8, 9)**. Depending on the cancer stage upon diagnosis and the size of the infected area (higher stages), removing both the uterus and ovaries may be the first surgical plan, and it can be anticipated that the possibility of pregnancy will be diminished **(10, 11)**.

In this paper, we describe the case study of a woman who was diagnosed with ovarian advanced-stage low-grade serous carcinoma who could be pregnant three years after treatmen.

2. Case Presentation

A 38-year-old woman presented to the Department of Gynecology of Mehr Hospital, Mashhad, IRAN, in June 2020 with a history of new-onset abdominal pain and no pregnancy history. After clinical investigations by a gynecologist, imaging was requested, and images confirmed a bilateral ovarian tumor with peritoneal seeding. The patient is referred to a gynecology-oncologist. A core-needle biopsy under ultrasound guidance from the ovarian mass was done, and LGSCO was diagnosed. The patient was directed to a fertility consultation, where it was determined that preserving eggs prior to surgery was not feasible. An open laparotomy was done. During the procedure, both ovaries were found to have large masses with a tumor-like appearance. These masses were adhered to the pelvic peritoneum, the memo-rectosigmoid, and the omentum. Additionally, the appendix was found to be inflamed. However, the uterus appeared to be normal. Results from diagnostic imaging are shown below (Figure 1).

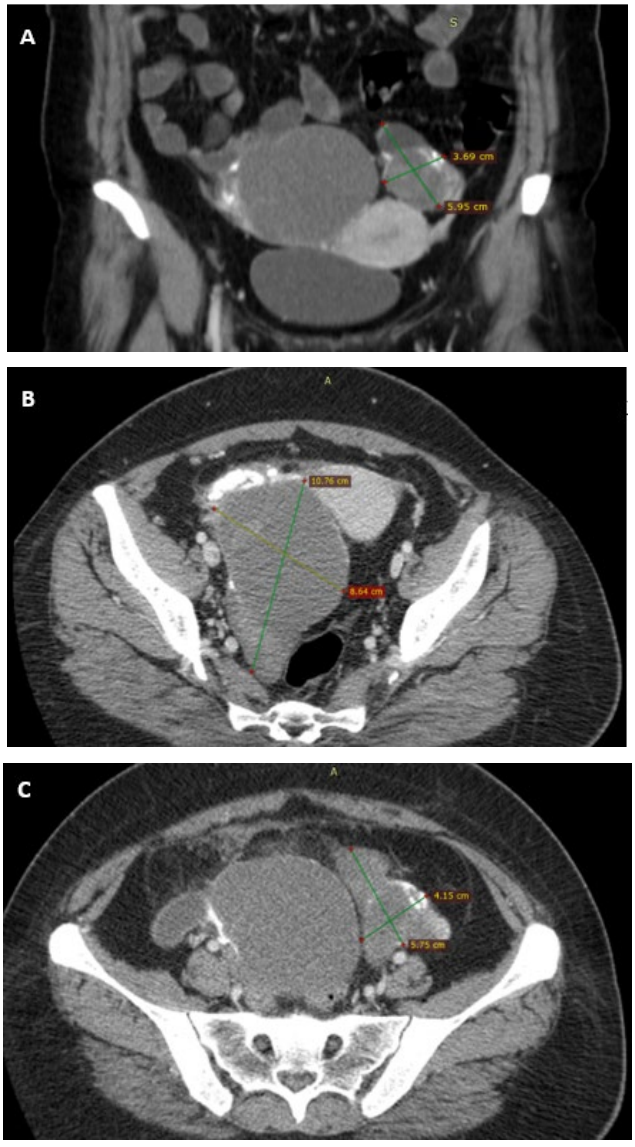


Figure 1. A) Left ovarian mass, B) Right adnexal mass, C) Tumoral omentum involvement

CT scan findings showed a solid septate ovarian cyst with minor calcification in the ovary wall. A massive cyst with internal echo and a solid core with invasion to the right and left adnexa was reported with peritoneal involvement without lymphadenopathy or massive ascites.

Pre-treatment Laboratory tests are shown in Table 1. CA-125 (ECL) was high at the time of diagnosis (256 U/ml).

Table 1. Laboratory blood test results of the patient at the time of diagnosis

Factor	Result	Reference Rang
CA-125 (ECL)	256 U/ml	Up to 35
CEA	2.6 U/ml	Non-smoker: <3.5

Microscopic examinations of ovarian sections revealed numerous micropapillary neoplastic cells with median atypical features. This protection ultimately confirmed the diagnosis of ovarian low-grade papillary serous carcinoma. The microscopic examination results of the specimen are in Table 2, Figure 2. Results were re-checked and confirmed by another pathologist.

Based on the National Comprehensive Cancer Network (NCCN) guidelines, surgery and then systemic chemotherapy are the basic treatment for ovarian cancer in most patients. Surgery is performed to confirm the diagnosis, evaluate the extent of the disease, and remove all visible tumors. Ovaries and uterus removal are advised with debunking other infected organs, but in this case, as the patient was a null-gravida and strongly desired fertility preservation and there was no sign of tumor involvement in the uterine surface, the decision was made to preserve the uterus and the patient underwent through bilateral salpingo-oophorectomy, followed by infracolic-omentectomy, bilateral pelvic lymphadenectomy and removal of all adhesions (to the pelvis and small/large intestine), peritoneal biopsy and appendectomy were completed. After three weeks from surgery, regular chemotherapy treatment with the standard regimen of carbonation (AUC 6) with paclitaxel (175 mg/m2) was prescribed every 3 weeks to 4 cycles.

Regular follow-ups were performed every two to three months to evaluate the possibility of tumor recurrence. Follow-ups contained clinical and physical investigations, abdominal and pelvic imaging, and the evaluation of serum marker CA-125. Fortunately, post-treatment imaging showed no signs of recurrence, which was confirmed by serum tumor marker results. Also, the patient's quality of life was good, so she got pregnant.

For this purpose, she went through the IVF (In vitro fertilization) process after two years of surgery (September 2022), and on the second try, she, fortunately, became twin pregnant with egg donation by IVF. During the pregnancy, the patient took routine supplements, including vitamin D (1000 IU/day), folic acid (1 mg/day first trimester), and ferrous sulfate (27 mg/day during the second and third trimesters), and she was under the close supervision of both oncologist and perinatologist. From the 28th week of pregnancy, she went through every two weeks of examination and check-up. She also received levothyroxine (50 mcg/day) for hypothyroidism from 26 weeks, methyl dopa (250 mg/bid) for her newly diagnosed hypertension from 21 weeks, plus Lever and overpaid insulin for new-onset glucose imbalance from 28 weeks. She also received Aspirin (80 mg/day) and enoxaparin (40 mg/day) until the 33rd week of pregnancy.

Due to two hypertensive crises, she was hospitalized during the 30th and 34th weeks of pregnancy. At the second time, superimposed preeclampsia was diagnosed. As a result of severe preeclampsia, she underwent a cesarean section in the 35th week of her pregnancy.

A cesarean section was performed in the 35th week, and both twins were born completely in excellent condition. The babies weighed 2200 g and 2500 g at birth, with an Apgar score of 9/10.

Table 2. Microscopic findings of different specimens during surgery.

Organ	Findings
Pelvic mass	Involved by ovarian Non-invasive low-grade papillary serous carcinoma
Omentum	Involved by neoplasm
Left and right pelvic peritoneum	Tumor free
Abdominal wall	Involved by neoplasm
Left and right pelvic lymph node	Tumor free
Bladder Peritoneum	Involved by neoplasm
Col du sac	Tumor free
The posterior surface of the uterine	Involved by neoplasm
Appendectomy	Tumor free
Large bowel mesentery	Tumor free
Left oviduct	Involved by neoplasm
Large bowel surface	Involved by neoplasm
Diagnosis: **1-left ovary**	Non-invasive low-grade papillary serous carcinoma
Diagnosis: **Right salpingo-oophorectomy**	Non-invasive low-grade papillary serous carcinoma

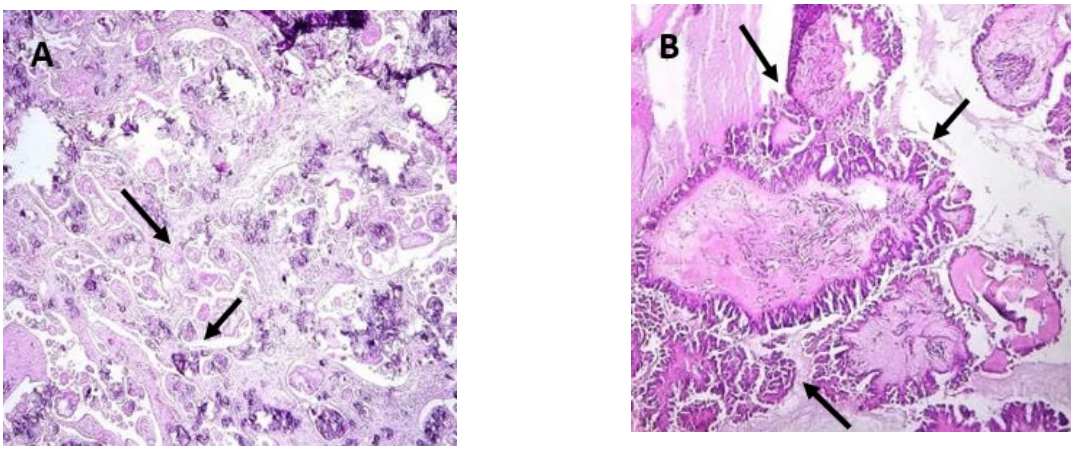


Figure 2. A) Invasive components with multiple sarcomatous calcifications; B) Multiple micropapillary structures with degrees of complexity and cytologic atypia

3. Discussion

The present report describes a woman with a history of LGSOC stage 3c who could successfully achieve pregnancy through a promising surgery method.

LGSOC is an indolent neoplasia commonly in younger patients, which is often asymptomatic or with unspecific clinical symptoms **(12)**. The prognosis of LGSOC can vary depending on factors such as the stage, maximum debunking, and response to the chemotherapy **(4)**. Several studies have identified prognostic markers, including age, body mass index (BMI, higher BMI>35 associated with a higher death rate), and smoking status. Tumor progression is slow, and survival is usually longer than in HGSOC patients **(13)**.

In terms of treatment strategies, LGSOC is less responsive to chemotherapy compared with HGSOC **(11, 14)**, so, secondary or tertiary cytoreduction surgery is more common, as it offers hope that this type of surgery, with no residual disease, can lead to a significant improvement in overall patient survival. In the second line of therapy, chemotherapy, unfortunately, does not yield excellent results due to high drug resistance. Therefore, extensive debunking is always recommended to reduce the risk of recurrence and improve the effectiveness of the treatment

regimen, especially in the advanced stages of the disease **(15)**.

The primary treatment strategies for LGSOC, typically involve maximum cytoreduction surgery followed by adjuvant chemotherapy for some patients. For patients with diseases confined to the ovary, the approach includes bilateral salpingo-oophorectomy, total hysterectomy, and complete peritoneal and retroperitoneal staging. However, in young women with stage I disease that strongly desire fertility preservation, fertility-sparing surgery options like unilateral salpingo-oophorectomy, surgical staging, and endometrial biopsy can be considered. Women with stage IA or IB disease are generally observed after surgery, while patients with stage IC-IIA disease have various treatment options, including observation, systemic chemotherapy, or hormonal therapy.

In patients with advanced disease (stages III-IV), the primary approach is primary debunking surgery to remove all visible diseases. Alternatively, neoadjuvant chemotherapy with interval debunking surgery can also be considered **(16)**.

In certain instances, when the cancer is localized and detected in its early stages, women who desire to preserve their fertility may explore the option of fertility-sparing surgery **(17, 18)**. Since LGSOC often shows limited responsiveness to conventional chemotherapy approaches, alternative treatments such as targeted therapies or hormonal therapies may also be considered **(19, 20)**.

Conservative surgery can also be an option for selected patients who want to preserve their own fertility. So, gynecologic oncologists must balance the risk of fertility preservation and complete surgery **(17, 18)**.

According to the 2007 guidelines of the American College of Gynecology and the 2008 guidelines of the European Society for Medical Oncology, this strategy has been acceptable for patients with stage IA with grade 1 and 2 epithelial ovarian cancer and non-clear cell histology. The European Society of Gynecologic Oncology has recommended that conservative surgery should not be done for patients with grade 3 epithelial ovarian cancer.

4. Conclusion

Due to the disseminated nature of the LGSOC and based on our observation and findings, our case was stage 3c LGSCO, and the decision about preserving the uterus resulted in pregnancy for her. This was an amazing case, as despite the vast metastasis of the tumor to the abdominal cavity, the uterus was preserved. Patient survival for 3 years was good, and no sign of recurrence was seen. We obtained verbal consent from the patient to report on her case.

5. Declarations

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Ethical Considerations

Written informed consent was obtained from the patient for publication of this manuscript and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

Authors' Contributions

All authors contributed to the conception and design of the work, as well as the acquisition and interpretation of data. All authors have reviewed the manuscript and given their approval for publication.

Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

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Consent

Written informed consent was obtained from the patient to publish this case report.

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