A successful pregnancy after two fertility-sparing surgeries for borderline ovarian tumor*

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ABSTRACT

Low malignant potential serous tumors are the most common subtypes of non-benign serous tumors in the young, usually confined to one or both ovaries. To preserve ovarian function and fertility conservative management can be performed. Although recurrence is higher than that after a completion surgery, the rate of recurrences continues to be debated. Most recurrent diseases are of the same histopathology as the initial tumor and adequate excision of the recurrent tumor can be done.

A 31-year old, primigravid underwent bilateral oophorocystectomy for serous borderline ovarian tumor stage IB. After 3 years she had tumor recurrence and another fertility-sparing surgery consisting of left salpingooophorectomy and contralateral cystectomy was done. Histopathology was a recurrent borderline ovarian tumor. Two years later, she had a spontaneous pregnancy and delivered to a live term baby. This is a reported case of a successful pregnancy after two fertility-sparing surgeries for borderline ovarian tumor.

Keywords: Borderline ovarian tumor, low malignant potential, fertility-sparing surgery, conservative treatment, pregnancy

INTRODUCTION

Low malignant potential serous ovarian tumors accounts for 15 to 20% of non-benign epithelial ovarian neoplasms.[1] This is found in young patients within the reproductive age group and conservative surgery is an acceptable surgical management in order to preserve fertility.[2]

THE CASE

A.S., a 31-year old primigravid was admitted for the first time at 39 2/7 weeks age of gestation (AOG) with a chief complaint of watery vaginal discharge accompanied by abdominal tightening for six hours.

The patient's father and paternal uncle have Diabetes Mellitus. Her brother had Immunodeficiency B. There was no history of cancer in the family.

Personal, social, menstrual, marital and sexual histories were non-contributory.

In 2009, six years before admission at age 26, she had underwent exploratory laparotomy. The right ovary was cystic, 12 x 8 x 8 cm, and the left also cystic, 4 x 3 x 3 cm. Their capsules were smooth, intact and 0.3 cm thin. On cut section, both cysts were unilocular, contained serous fluid, and had multiple excrescences within, with no note of spillage of the ovarian cysts contents intraoperatively. Bilateral oophorocystectomy was done and by frozen section they were serous tumors with low malignant potential. Further procedures done were peritoneal fluid cytology, bilateral pelvic lymph node dissection, para-aortic lymph node sampling, random peritoneal biopsy and infracolic omentectomy. The tumor was staged as IB.

Subsequently, in 2012 at age 29 while on infertility work-up at another institution the left ovary was again cystic. Intraoperatively, the left ovary was converted into a cystic mass 9 x 7 x 6 cm, unilocular, containing serous fluid, with foci of papillary excrescences within the thin walls. The right ovary was 4 x 3 cm with a cystic focus, 1 x 1 cm, unilocular containing light brown fluid. So the patient again underwent exploratory laparotomy with left salpingooophorectomy and right oophorocystectomy. Frozen section of the left ovarian cyst showed tumor recurrence, Papillary serous tumor of low malignant potential and the right hemorrhagic corpus luteum. Further procedure done was omental biopsy. She had follow-up with her physician.

Her last normal menstrual period was on December 4, 2013. She was admitted at 4 weeks AOG due to nausea and vomiting. She was re-admitted at 31 1/7 weeks AOG for control of preterm labor and administration of steroids. She had a total of ten prenatal check-ups. At 39 2/7 weeks age of gestation due to watery vaginal discharge and abdominal tightening she was admitted.

The review of systems was unremarkable.

Upon admission, the patient was conscious, coherent, and not in cardiorespiratory distress. Vital signs were within normal limits. She had essentially normal systemic physical examination findings. The abdomen was globular, with a midline scar measuring 13 cm. Fundic height was

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33 cm. Estimated fetal weight by palpation was 3200 to 3400 grams. On Leopold's maneuver, LM1 was breech, LM2 was the fetal back at the right, LM3 was cephalic, and LM4 was an unengaged fetal head. Fetal heart tones were good. Uterine contractions were noted once in 10 minutes, lasting 30 seconds, moderate in intensity. On speculum exam, the cervix was violaceous, smooth, with note of pooling of clear amniotic fluid. On internal examination, the cervix was 1 cm dilated and 60% effaced. The fetal head was at station -1. There was no palpable bag of waters. Clinical pelvimetry was adequate.

The admitting impression was G1P0; Pregnancy uterine 39 2/7 weeks age of gestation, cephalic, in labor; Prelabor Rupture of Membranes; Serous Tumor with Low Malignant Potential, ovary, Stage IB, Status post Peritoneal fluid cytology, Bilateral oophorocystectomy, Frozen section, Bilateral pelvic lymph node dissection, Para-aortic lymph node sampling, Random peritoneal biopsy, Infracolic omentectomy (2009); Tumor recurrence, Status post Left salpingooophorectomy, Right oophorocystectomy, Frozen section, Omental biopsy (2012). The plan was to monitor the progress of labor and deliver the baby vaginally. Should the need to perform a cesarean section arise due to obstetric indications, an intraoperative assessment of the abdominopelvic organs will be done to determine the status of her borderline ovarian tumor.

Baseline cardiotocography (CTG) was reassuring. Uterine contractions were inadequate and labor was augmented with oxytocin. Ampicillin 2 grams/ IV was given as prophylactic antibiotic. Complete blood count was normal. On the 4th hour of labor, the patient developed low-grade fever with a temperature of 38.1^{o}C. Fetal heart tones were tachycardic at 170 bpm. On internal examination, the cervix was still 1 cm dilated, 60% effaced, with the fetal head still at station -1. Intrapartum resuscitation was done. Repeat CBC showed leukocytosis of 19.1 x 10^{9}/L with predominance of neutrophils (84.3%). After two hours, with the patient still febrile, fetal heart tones still tachycardic, and internal examination the same, an emergency cesarean section was performed for intrauterine infection. She delivered to a live baby boy with a birth weight of 3470 grams (7 lbs 10 oz), APGAR score 9,9 and maturity index of 39 weeks, appropriate for gestational age. The left adnexum was surgically absent (Figure 1). The right fallopian tube was wrapped around the right ovary which was grossly normal, measuring 1.5 x 1.5 cm. There were filmy adhesions between the posterior uterine surface, the left adnexal area and the sigmoid colon (Figure 2). The rest of the abdominopelvic organs were grossly unremarkable on inspection and palpation. Post-operative diagnosis was G1P1 (1001) Pregnancy uterine, delivered term, cephalic, live baby boy, AGA (3470 grams) by Primary Low Transverse Cesarean Section for Chorioamnionitis under spinal anesthesia; Serous Tumor with Low Malignant Potential, ovary, Stage IB, Status post Peritoneal fluid cytology, Bilateral oophorocystectomy, Frozen section, Bilateral pelvic lymph node dissection, Para-aortic lymph node sampling, Random peritoneal biopsy, Infracolic omentectomy (2009); Tumor recurrence, Status post Left salpingooophorectomy, Right oophorocystectomy, Frozen section, Omental biopsy (2012).

The rest of the hospital stay was unremarkable and the patient was discharged stable after three days. The post-oprative course was unremarkable and the patient was advised regular follow-up with a Gynecologic-Oncologist every 3 months for the next two years.

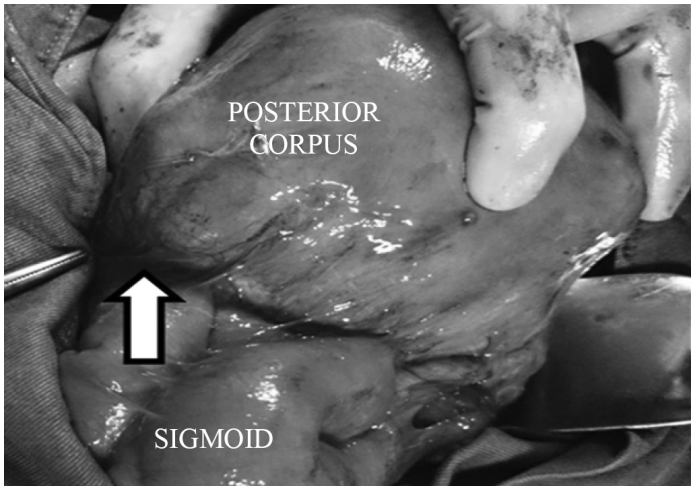

Figure 1. Intraoperatively, the left adnexa was noted to be surgically absent (arrow).

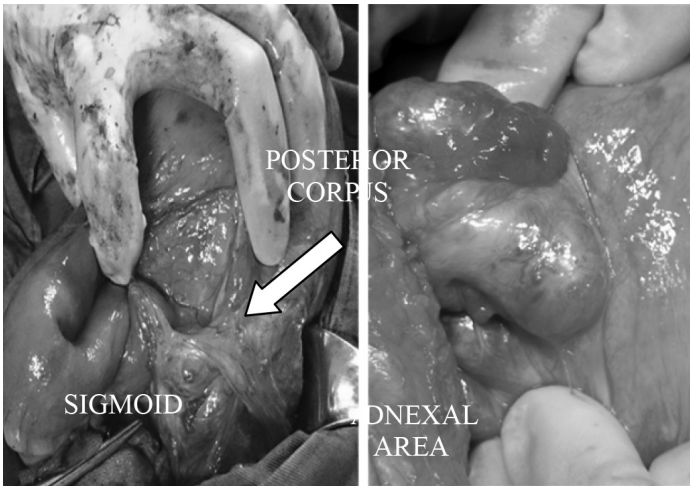

Figure 2. There was note of filmy adhesions (arrow) between the posterior uterine surface, left adnexal area and sigmoid colon.

DISCUSSION

This is a patient who was diagnosed with a serous ovarian tumor. This is a type of an epithelial tumor that accounts for 60% of all ovarian neoplasms. They are thought to arise from the ovarian surface epithelium that is capable of differentiating into Serous, Mucinous, Endometrioid or Transitional epithelium.

The patient underwent two laparotomies, both of which were for ovarian cysts that were diagnosed microscopically as serous tumor with low malignant potential. These tumors account for 15% to 20% of non-benign epithelial ovarian neoplasms. Serous tumors of low malignant potential exhibit epithelial proliferation greater than that seen in their benign counterparts, in the absence of destructive invasion of the stroma.[1]

This type of tumor has a malignant potential of 0.5%. According to Kurman et al., malignant transformation is rare and occurred in only three of 9,533, and one of 76 patients respectively, making the incidence less than 0.5 percent overall.[3] The index patient, no malignant transformation was observed. Her tumor recurrence three years after the initial surgery was still a borderline tumor.

Serous tumor with low malignant potential is the most common subtype, accounting for 25% to 30% among the non-benign serous tumors. The patient was in her third decade of life at the time of diagnosis. A high proportion of women diagnosed with Serous Borderline Ovarian Tumors are young. Approximately 70% of these tumors are confined to one or both ovaries at the time of diagnosis. During the initial surgery, our patient had a bilateral tumor, making her disease a stage IB, which can be found in 20% of patients with serous borderline tumors.[1]

The patient was asymptomatic at the time of diagnosis of the ovarian mass. This clinical presentation accounts for 23% of cases. Patients with ovarian tumors can present with other signs and symptoms namely abnormal vaginal bleeding or discharge, feeling of pressure, fullness, bloating, or swelling in the abdomen, urinary frequency, pelvic and lower back pain, nausea, loss of appetite and a feeling of fullness, indigestion, flatulence, dyspareunia, fatigue and weakness.[4] The patient presented with no sign or symptom attributable to a pelvic mass both in 2009 and 2012.

The diagnosis of ovarian tumor in our patient was an incidental finding on ultrasound as a part of an infertility work-up. This diagnostic modality is the first step in the evaluation of patients with an adnexal mass.[5] The presence of papillae within the cyst was the most common finding ultrasonographically in BOT. However, neither the sonographic features nor the papillae are ultrasound markers of high sensitivity.[6] CA125 may be high in more than half of the patients with BOT. Pre-operative CA125 is elevated in 24% of patients, and CA125 levels are higher in patients with serous borderline malignancy compared to that of the other types of epithelial tumors. For the patient, CA125 was not requested since this is expected to be elevated. CA125 levels peak in the first trimester at five to eight weeks, and soon after delivery. Levels will return to normal values about 10 weeks post-partum.[7,8] Other diagnostic tests may be used such as magnetic resonance imaging (MRI), Positron emission tomography-computed tomography (PET-CT) and computed tomography (CT).[9]

Total abdominal hysterectomy with bilateral salpingooophorectomy (TAHBSO), lymphadenectomy, and omentectomy continue to be the standard surgical management for ovarian cancer. Conservative management defined as the preservation of at least a part of one ovary and the uterus can be considered for early-stage disease to preserve ovarian function and fertility.[10,11] The Society of Gynecologic Oncologists of the Philippines (SGOP) recommend unilateral or bilateral salpingooophorectomy with infracolic omentectomy, peritoneal fluid cytology and complete surgical staging for patients with stage IB ovarian tumor who are desirous of pregnancy.[12] In a study published in 2005, bilateral ovarian cystectomy was recommended as an acceptable surgical management for young patients.[13] Another study proposed two options for patients with bilateral ovarian involvement: salpingooophorectomy or oophorectomy on the side harboring the largest tumor with a contralateral cystectomy, or alternatively, bilateral cystectomies.[11] A randomized trial done by Palomba et. al. in 2007 compared these two conservative treatment modalities. After a follow-up period (81 months), there was no difference between these procedures in terms of the cumulative rate of recurrences. However, the cumulative pregnancy rate and the probability of a first pregnancy were higher in patients treated with bilateral cystectomies compared to those who underwent unilateral salpingooophorectomy and a contralateral cystectomy. This suggests that bilateral cystectomies should be preferred in case of bilateral disease if feasible.[12] Our patient was only a 26-year old nulligravid at the time of her first surgery. Bilateral ovarian cystectomy was done in order to preserve fertility which is in accordance with the primary goal of conservative surgeries. During the initial surgery, our patient had been fully informed of potential oncological and obstetrical outcomes. In retrospect, the performance of a bilateral cystectomy during the initial surgery definitely benefitted the patient, considering that the bigger tumor was from the right ovary, for which a right salpingooophorectomy and a left cystectomy would have been an option. If these were the procedures done, she would have lost her reproductive capacity, since the recurrent tumor three years later developed on the remaining left ovary, for which

a left salpingooophorectomy would have been performed. The performance of bilateral cystectomy during the first surgery indeed gave our patient the opportunity to preserve her fertility and allow childbearing.

Being diagnosed with a stage IB BOT, our patient does not need adjuvant treatment in the form of chemotherapy or radiation therapy. A retrospective study from the Gynaecologic Oncology Group (GOG) analysed 988 adequately staged patients with stage I BOTs who did not receive adjuvant treatment and observed a mortality rate of 0.7% at five years.[14] According to Trope et al., after a review of four randomized studies, adjuvant treatment in patients with stage I disease significantly increases intestinal, neurological, and hematological toxicity without therapeutic benefits.[15] The role of adjuvant therapy in women with advanced stage BOTs is debatable. A meta-analysis of BOTs from Cochrane concluded that current evidence does not show any benefit in the use of adjuvant therapy, whether it is chemotherapy or radiotherapy, independently of the stage or tumor histology.[16]

The patient was advised to have a regular follow-up because of the increased risk of recurrence for patients who underwent fertility-sparing procedures. It was just unfortunate that she did not come back for disease surveillance.[10] The European Society of Gynaecologic Oncology (ESGO) proposed to evaluate such patients every six months during the first three years, and yearly thereafter. Prolonged follow-up to 15 years is required because very late recurrences have been reported.[10] Zanetta et al. followed up 164 women with stage I BOT after conservative surgery of fertility with the use of physical examination, ultrasound and CA125 determination. Physical examination and vaginal ultrasound were done every three months for two years and every six months thereafter. CA125 determination was planned every six months in patients with a serous BOT. The authors concluded that the vaginal ultrasound is the most effective diagnostic technique in this group of patients.[17]

In a local study, the recurrence rate of borderline ovarian tumor was found to be at 13%.[11] The risk of recurrence is reported to be between 0% and 25% in patients who underwent conservative surgery, which was higher than that after a TAHBSO. The patient underwent ovarian cystectomy in 2009 which was found to have a higher risk of recurrence compared with a complete salpingooophorectomy. In 2011, Morice et al. reported that the risk of recurrence for such patients is between 12% and 58%.[10] This risk was also similar in an earlier study done by the same author in 2004, with a risk of 30% to 35% after cystectomy.[1] However, the real impact of performing a cystectomy only, in contrast to doing a salpingooophorectomy, on the increased rate of recurrences continues to be debated by some authors. In a local study done on BOTs, the type of surgical procedure did not show a significant influence on tumor recurrence.[11] Some of the recurrences were observed a long time after treatment of the initial BOT. The latest recurrences were noted 72 months or six years after the initial diagnosis.[10] However, this data does not coincide with the patient's course, having a recurrence after three years only. Surgical management for such patients can usually be done adequately by removal of the recurrent tumor.

Based on the eight series studied by Morice et al, which involved 910 patients seeking to be pregnant, pregnancies have been reported in patients with conservatively treated BOT. The rate of spontaneous pregnancies ranged between 30% and 80%.[10]

The patient was able to deliver to a live full term baby boy at 39 weeks, with a birth weight of 3470 grams, APGAR score of 9,9 by cesarean section, even after two conservative surgeries for her borderline ovarian tumor. This is a reported case of a successful pregnancy in a patient who underwent two fertility-sparing surgeries. In a study done by Smaldone et al., reproductive-age women who underwent conservative surgery for stages IA to IIC ovarian cancers can have successful obstetric outcomes. Out of 52 patients studied, 29 were diagnosed to have ovarian tumors with low malignant potential. Of these 29 patients, 14 were able to get pregnant, accounting for 60% of patients. Eighty five percent (85%) of patients were able to deliver live births. The median birth weight was 3245 grams with good APGAR scores of 9,9. Only one of 29 patients underwent cesarean section. Thus, a high percentage of these patients were able to deliver vaginally, with the history of an ovarian tumor not affecting the mode of delivery. Other identified pregnancy complications were as follows: abortion (7.1 %), preterm birth (28.6%), preterm premature rupture of membranes (7%). There was no reported case of intrauterine fetal demise and congenital anomalies. Neonatal intensive care unit admission was at 7.1%. Conditions such as Gestational Diabetes Mellitus and hypertension were also observed in their study population.[18] All of these were not found in our patient. Although some authors noted associated rapid growth and recurrence of ovarian cancers during pregnancy, in this study, there was no association between pregnancy after conservative management and disease recurrence in a cohort of 52 patients, consistent with other larger studies.[18]

With respect to hormonal contraception, the Center for Disease Control and Prevention has stated that there is no restriction on the use of contraceptive methods. Its use should not be limited by the diagnosis of a BOT.[19]

Thus, the patient was advised to start surveillance

with CA125 ten weeks post-partum.

Is there a need to remove the remaining ovary and perform completion surgery in our patient after her desire of parenthood has been achieved? The answer to this question remains to be controversial. A routine oophorectomy would be unnecessary in 75% to 100% of patients. Furthermore, the majority of those recurrent lesions are BOT and can be easily cured, through a simple surgical procedure. The systematic removal of the remaining ovary thus is not mandatory, provided that the patient will follow up regularly.[10]

SUMMARY

In summary, we are presented with a 31-year old primigravida who underwent two fertility-sparing surgeries for serous borderline ovarian tumor. She was able to conceive spontaneously, and delivered a live birth two years after the second surgery for tumor recurrence. The case presented underlines the fact that such conservative surgeries are feasible for tumors with low malignant potential, with subsequent good obstetric and gynecologic outcomes. ■

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