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CASE REPORT

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A case report on second fertility-preserving surgical management for early recurrence of borderline ovarian tumor in a young woman

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Abstract

Borderline ovarian tumors (BOTs) have low malignant potential and favorable prognoses. The group of patients most affected by BOTs are women of childbearing age; therefore, fertility-sparing surgery is considered the first choice of treatment for young patients. Several studies have reported that conservation treatment was associated with a higher recurrence rate; however, data on the treatment and clinical management of patients after relapse are scarce. A 19-year-old woman was admitted to our hospital for two weeks due to unexplained abdominal distension. Palpation of the uterus showed no significant abnormality, but an ultrasound examination revealed abdominal effusion and a solid cystic mass in front of the uterus. Since the patient wanted to preserve fertility, she underwent fertility-sparing procedures, including abdominal right adnexectomy and excision of the left ovarian mass. Histological examination confirmed stage III serous BOTs (desmoplastic non-invasive implants associated with ovarian serous borderline tumor). After the surgery, the patient had normal menstruation. After 20 months, the patient experienced a recurrence of serous type BOTs (stage IIIC; serous carcinoma, non-invasive, low grade, ICD-O: 8460/2), and a second fertility-sparing surgery was performed. Presently, although no disease recurrence was detected at the last follow-up, the patient had no menses for six months and had not yet completed childbirth. In young women diagnosed with BOTs, fertility preservation surgery might be associated with a high risk of recurrence, especially for those with advanced staged disease. Clinically, pregnancy should be recommended as early as possible after surgery, and long-term follow-up is required.

Keywords

Borderline ovarian tumors; Fertility-sparing surgery; Recurrence; Case report

1. Background

As a unique histological and clinical entity, borderline ovarian tumors (BOTs) have low malignant potential and present as intermediate lesions between benign cystadenomas and invasive carcinomas [1]. BOTs account for 10–20% of all epithelial tumors of the ovary and are characterized by atypical epithelial hyperplasia without stromal invasion [2]. It is generally detected in young women of reproductive age, with approximately one-third of cases diagnosed before the age of 40 [3]. The two main subtypes of BOTs are the serous and mucinous subtypes and have favorable prognoses, with 5 and 10-year survival rates of 95% and 90%, respectively [4]. Therefore, fertility-preserving surgery is considered for patients who desire pregnancy. However, a recent study indicated that fertility-preserving surgery could increase the risk of recurrence [5], especially for patients diagnosed with stage II and above BOTs. Therefore, determining the clinicopathological characteristics of patients prone to recurrence, identifying those who require fertility-preserving surgery and formulating individualized follow-up plans have become the important focus for clinicians to improve patients' outcomes.

BOTs are mostly asymptomatic in the early stages and can mimic the symptoms of invasive ovarian cancer, which includes abdominal swelling, nausea, vomiting and weight loss, making preoperative diagnosis difficult [6]. The management and follow-up of BOTs are challenging for clinicians, and few clinical studies have addressed these issues in recent decades. Furthermore, guidelines on BOTs management are poorly developed owing to a relative lack of evidence. A recent study suggested that although BOTs had a good clinical outcome in terms of prognosis and biological characteristics, shorter disease-free survival should be considered, especially in patients with micro-tumor infiltration identified by histopathological evaluation following fertility-preserving surgery [7]. In addition, conducting long-term follow-ups is

necessary. Here, we report the case of postoperative recurrence in a young female patient with BOT who underwent fertility-sparing surgery. The patient provided informed consent, and the study protocol was approved by the ethics committee of our hospital.

2. Case presentation

A 19-year-old woman, who was gravida 1 para 0, presented to our hospital on 02 November 2019, with unexplained abdominal distention for two weeks. Physical examination revealed a normal development. An abdominal examination revealed a bulging abdomen with positive mobile turbid sounds but no significant abnormality upon palpating the uterus and bilateral adnexa. Transabdominal ultrasonography showed a small uterus with a large amount of fluid in the abdominal and pelvic cavities, with cystic masses measuring 134 mm × 95 mm and 10 mm × 80 mm detected in the anterior part of the uterus (Fig. 1). Magnetic resonance imaging (MRI) showed a cystic and solid mass in the lower abdomen and pelvis, which was considered to be an adnexal tumor lesion (Fig. 2A–D), suggestive of ovarian cystadenocarcinoma with local peritoneal metastasis. No abnormalities were observed in routine blood biochemical tests. However, her serum levels of cancer antigen (CA125, reference range: <35 U/mL) and human epididymal secretory protein (HE4, reference range: 0–140 pmol/L) were 2685.0 U/mL and 456.5 pmol/L, respectively.

Since the patient was young and not yet childbirth, she opted for fertility-sparing surgery. Thus, on 13 November 2019, the patient underwent laparoscopic exploration, abdominal right adnexectomy, left ovarian mass excision, pelvic lesion resection, and pelvic catheterization. During the surgery, a large amount of fluid (approximately 5000 mL) was found in the abdominal cavity (Fig. 3A). An uncapsulated cauliflower mass of size: 10 × 9 × 7 cm was observed in her right ovary. Additionally, a 15 × 13 × 12 cm encapsulated mass was observed in her left ovary, and no obvious abnormality was observed in the appearance of the fallopian tube (Fig. 3B). Further, we observed bilateral appendages adhered to the pelvic floor intestinal canal and extensive miliary metastases in the pelvic peritoneum, transverse septum and greater omentum, with no macroscopic lesions in other abdominal organs. Subsequently, the resected right appendage was collected for pathological examination.

The tumor tissue showed classic serous BOTs changes with multi-level branching papillae (Fig. 4A), and the cells were stratified with hyperchromatic nuclei, moderate atypia and mitoses (Fig. 4B). In addition, a cribriform arrangement of tumor cells was observed in the micropapillary region (Fig. 4C), and the cells showed moderate atypia with mitoses (Fig. 4D). The results of our pathology report suggested that all these lesions were histologically non-invasive implants and confirmed the presence of stage III serous BOTs.

Postoperatively, the patient was treated with hyperthermic perfusion combined with normal saline, docetaxel and lobaplatin from 14 November to 16 November 2019, and she had an uncomplicated postoperative recovery. She was asymptomatic, was discharged on the 5th postoperative day (18 November 2019), underwent follow-up every six months for tumor markers (CA125 and HE-4) assessment, and had a normal menstrual cycle after surgery.

However, 20 months after the treatment, the patient visited our hospital for examination on 18 July 2021, due to abdominal pain and diarrhea for 10 days. Abdominal B-ultrasound showed no obvious abnormalities in the liver, pancreas and spleen, but there was effusion in the abdominal cavity (approximately 22 mm). Subsequent ultrasound scans revealed mixed echogenicity in both the left ovary and the pelvic region (Fig. 5). MRI revealed a new cystic solid mass in the left ovary, measuring approximately 52 mm × 33 mm × 60 mm, with partially unclear borders. DWI, T1WI and T2WI showed high, slightly low and high signals (Fig. 6A–C). A solid part was observed and the separation was significantly strengthened on contrast-enhanced scanning (Fig. 6D). Additionally, the CA125 level (48.770 U/mL) was elevated; thus, we considered a postoperative recurrence of BOT.

Since the patient still wanted to preserve fertility, she was given fertility-sparing surgery after being advised of the potential risks. On 20 July 2021, she underwent laparoscopic left ovariectomy, electrocautery of the pelvic lesions, greater omentum resection, pelvic adhesion release, and thermo perfusion tube placement. During the operation, the left ovary was found to be enlarged (diameter, ~5 cm), and a milky white celiac lesion was observed inside the swelling (Fig. 7A). A cauliflower-like lesion of about 2 × 1 cm in size was observed protruding from it (Fig. 7B), and multiple membranous adhesions were found on both sides of the bowel and lower abdominal wall (Fig. 7C), as well as on the liver surface and anterior wall of the upper abdomen. After surgery, some normal tissues were preserved in the left ovary (Fig. 7D). Peritoneal effusion volume was approximately 100 mL. An intraoperative frozen section of the left ovary revealed BOT with a localized pattern of micropapillary growth and moderate atypia (Fig. 8A,B). In addition, the immunohistochemical results for p16 and P53 were positive and wild-type, respectively (Fig. 8C,D). At the time of recurrence, the diagnostic criteria for low-grade non-invasive serous carcinoma were met, which has a poorer prognosis than typical serous BOTs.

The operation was successful, and the patient received three treatments of intraperitoneal hyperthermia after the operation. Her tumor markers were subsequently followed every two months, and CA125 and HE-4 levels were within the normal range at the latest follow-up. However, the patient has had no menstruation since the second surgery (six months by the time of writing this report).

3. Discussion

Fertility-sparing surgery is the first choice of treatment for patients with BOT who have fertility preservation needs because BOTs are common in women of childbearing age and have a good prognosis [8]. However, compared with radical surgery, conservation surgery has a higher recurrence rate (approximately 5%), but most of them do not become malignant, and postoperative recurrence can be re-treated by surgery without affecting overall survival [9]. This study reported the BOT recurrence 20 months after fertility preservation surgery in a 19-year-old female patient initially diagnosed with stage III

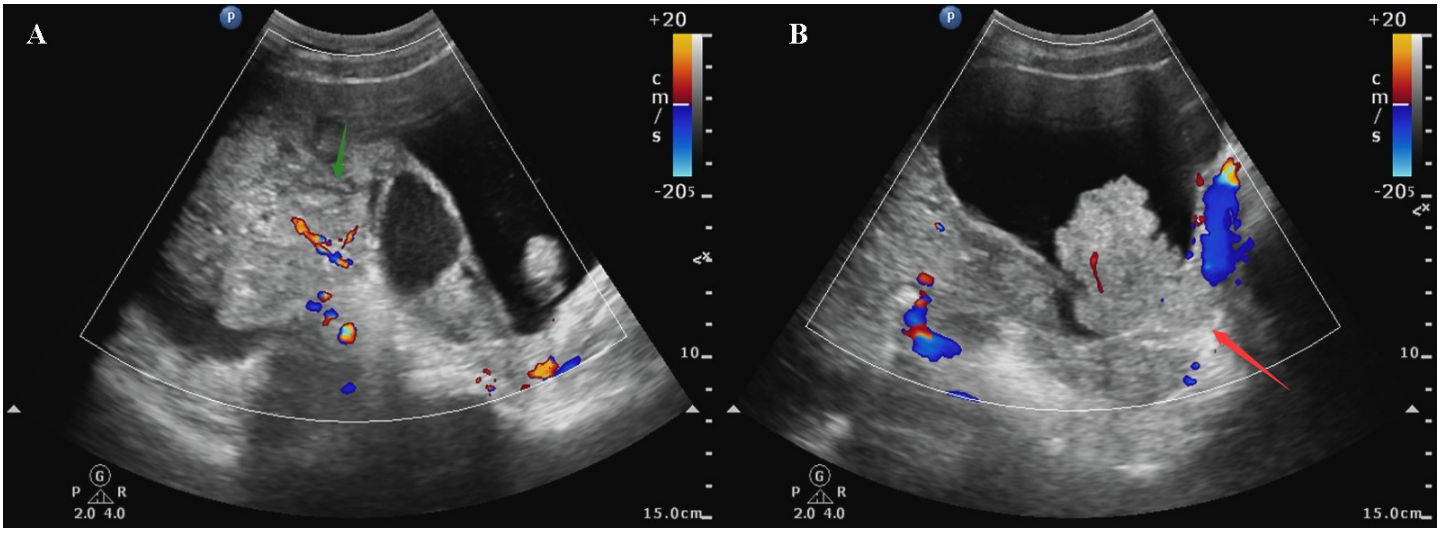

FIGURE 1. Color doppler ultrasound features of the serous borderline ovarian tumors (BOTs). Detected cystic solid masses in the anterior part of the uterus. (A) 134 mm × 95 mm on the right (green arrow). (B) 10 mm × 80 mm on the left (red arrow).

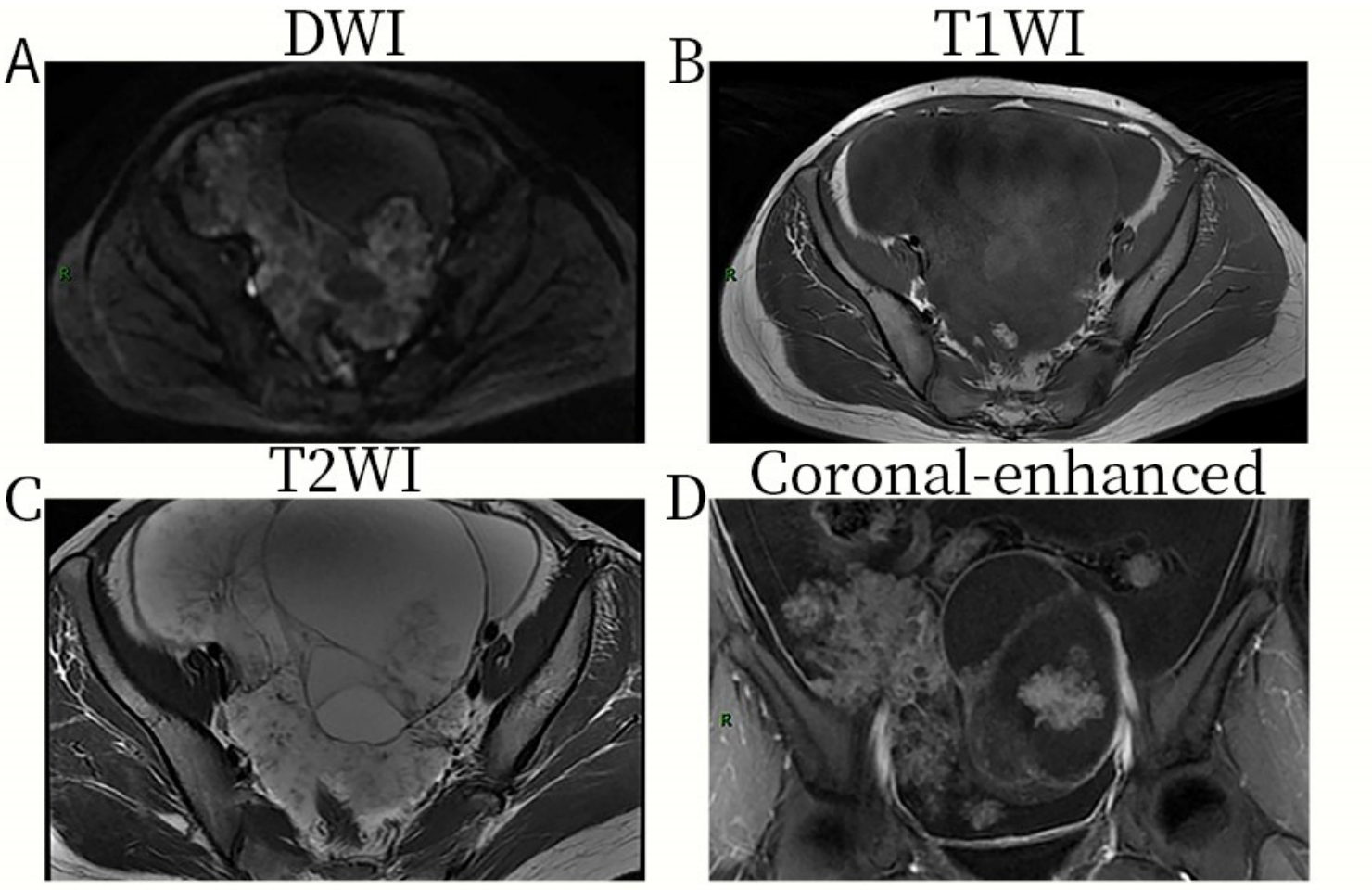

FIGURE 2. MR images at initial diagnosis. (A) Diffusion-weighted Imaging (DWI) shows a low signal in the cystic component and an enhanced signal in the solid component. (B) T1 Weighted Imaging (T1WI) shows a low signal in cystic and solid components. (C) T2 Weighted Imaging (T2WI) exhibits a high signal in the cystic component. (D) Coronal-enhanced scan of the solid part is obviously enhanced, with an enhanced septal line.

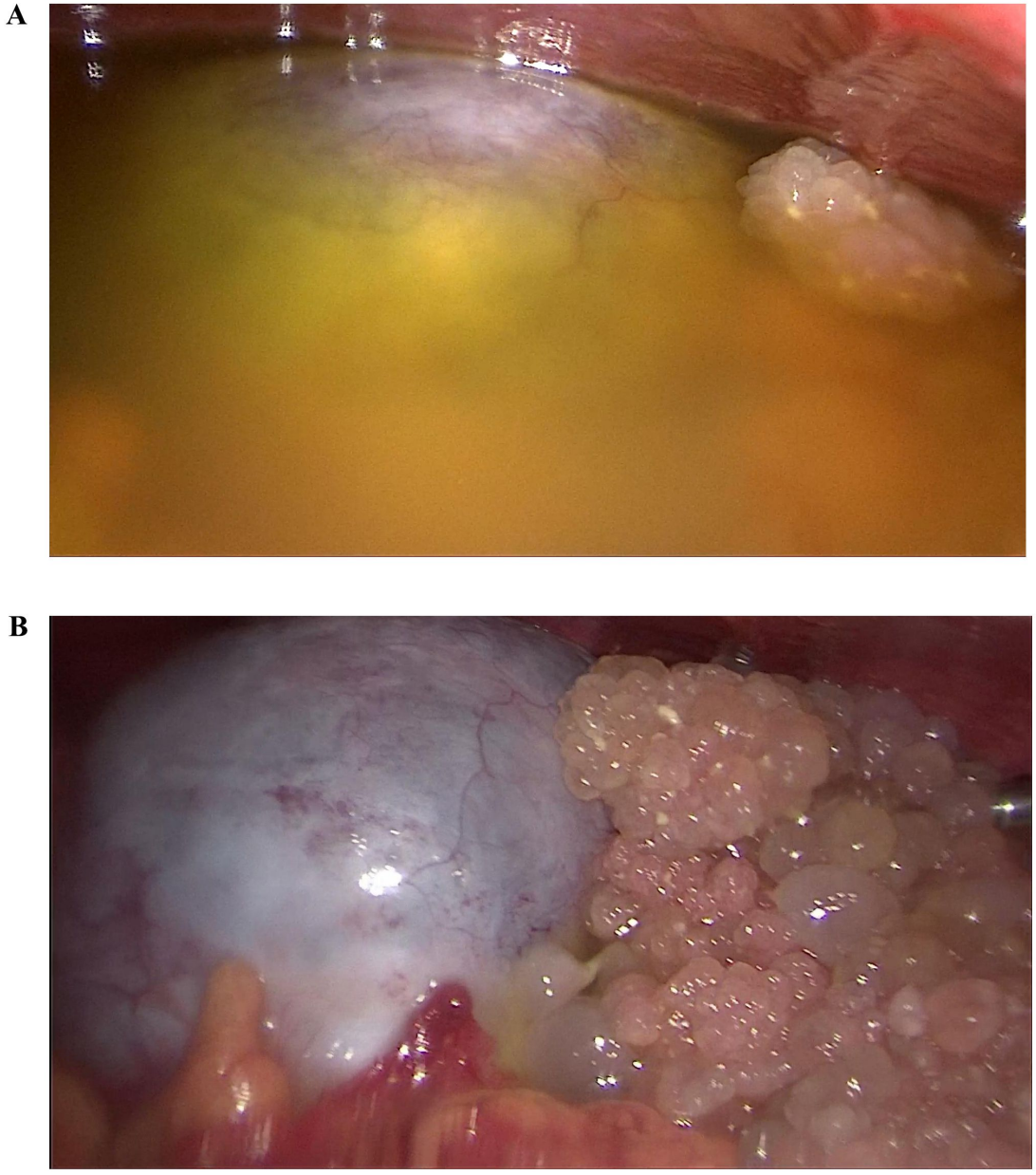

FIGURE 3. Extensive miliary metastases in the pelvic peritoneum. (A) A large amount of ascites was detected in the abdominal cavity. (B) Left ovary with intact capsule mass and right ovary with cauliflower-like mass.

serous BOT.

The most common histopathological types of BOTs are serous and mucinous, among which serous BOTs account for approximately 50% of all BOT cases [10]. Fang *et al*. [11] reported that patients with serous BOTs at an advanced stage (≥stage II) had shorter recurrence intervals and higher recurrence rates. In addition, micropapillary tumors were found to be associated with a higher incidence of recurrence [12]. A previous study indicated that both micropapillary and fertility-preserving surgeries were considered risk factors for recurrence in patients with serous BOTs [13]. Falcone *et al*. [14] recruited 91 patients with stage II-III serous BOTs undergoing fertility-sparing surgery and found that 53.8% of the patients experienced at least one recurrence, with a median time to first relapse of 22 months. Moreover, a small number of relapsed patients might develop malignant transformation [15]. Similar to these studies, we observed a short-term recurrence (approximately 20 months) after fertility preservation surgery in this case. Considering that our reported patient was young and had fertility needs, a second fertility-sparing surgery was performed. A recent meta-analysis revealed that secondary fertility-sparing surgery is a safe procedure for stage I patients with reproductive needs, as it resulted in high pregnancy and live birth rates after surgery; however, the benefits and risks of a second surgery should be carefully weighed for patients with advanced stages [16]. Therefore, for those who need fertility preservation, the treating surgeons showed detailedly inform them about the potential risks of high recurrence rate and the need for more careful follow-up.

In regard to reproductive outcomes, the most important topic for patients after fertility-sparing surgery, a previous study showed that conservative treatment effectively preserved fertility and allowed natural pregnancy, with a cumulative spontaneous pregnancy rate of 50–60% after surgery [17].

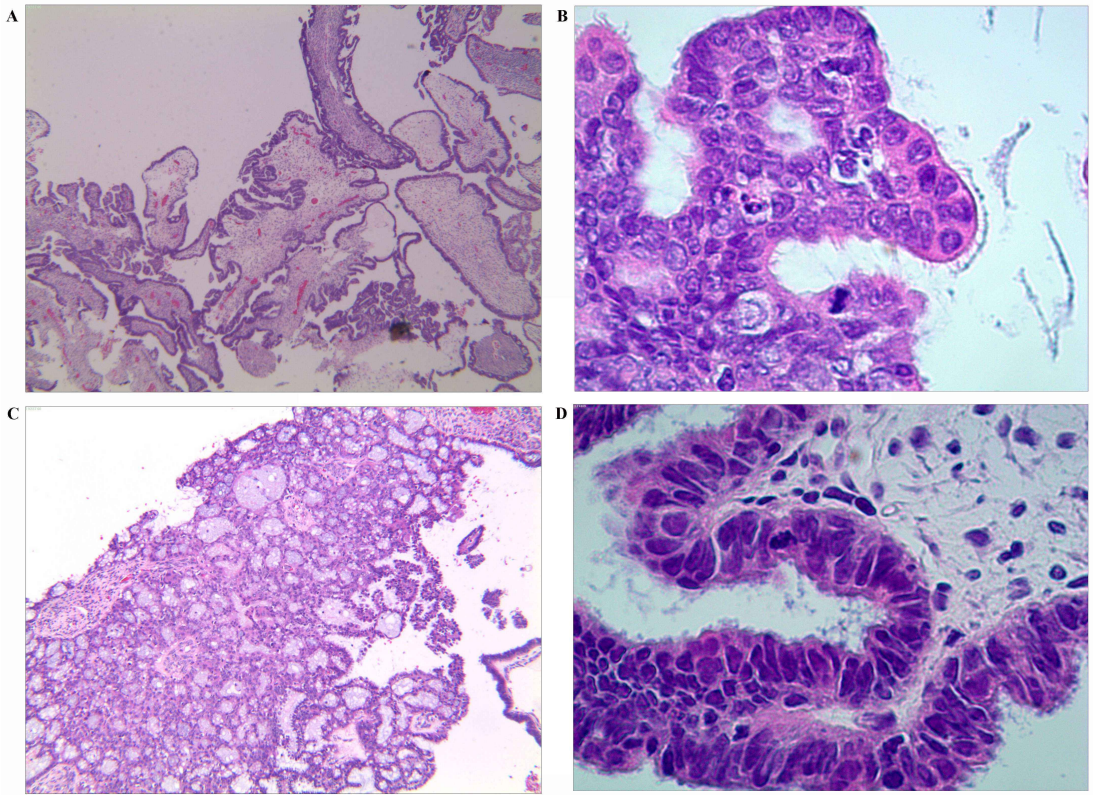

FIGURE 4. Hematoxylin-eosin (HE) staining images of the right ovarian tumor adnexa. (A) The tumor tissue was characterized by serous BOTs, and the cells are arranged in a multi-level branched papillary pattern (40× magnification). (B) Partial enlargements of the (Fig. 4A) and cells are arranged in layers with hyperchromatic nuclei, moderate atypia, and mitotic figures (200× magnification). (C) The micropapillary area shows tumor cells arranged in a cribriform pattern (40× magnification). (D) Partial enlargements of the (Fig. 4C) and cells are moderately atypia with visible mitoses (200× magnification).

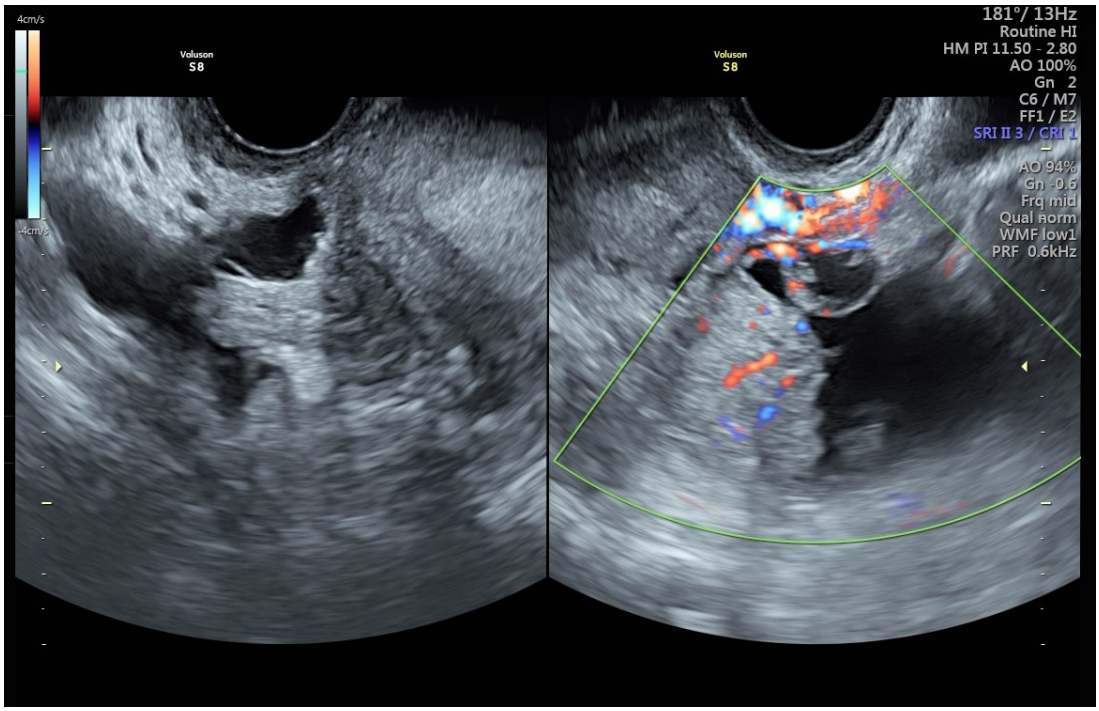

FIGURE 5. Transvaginal ultrasound scan of the relapsed BOT lesions. Examination showing mixed echoes of the left ovary with a pelvic effusion of 22 mm.

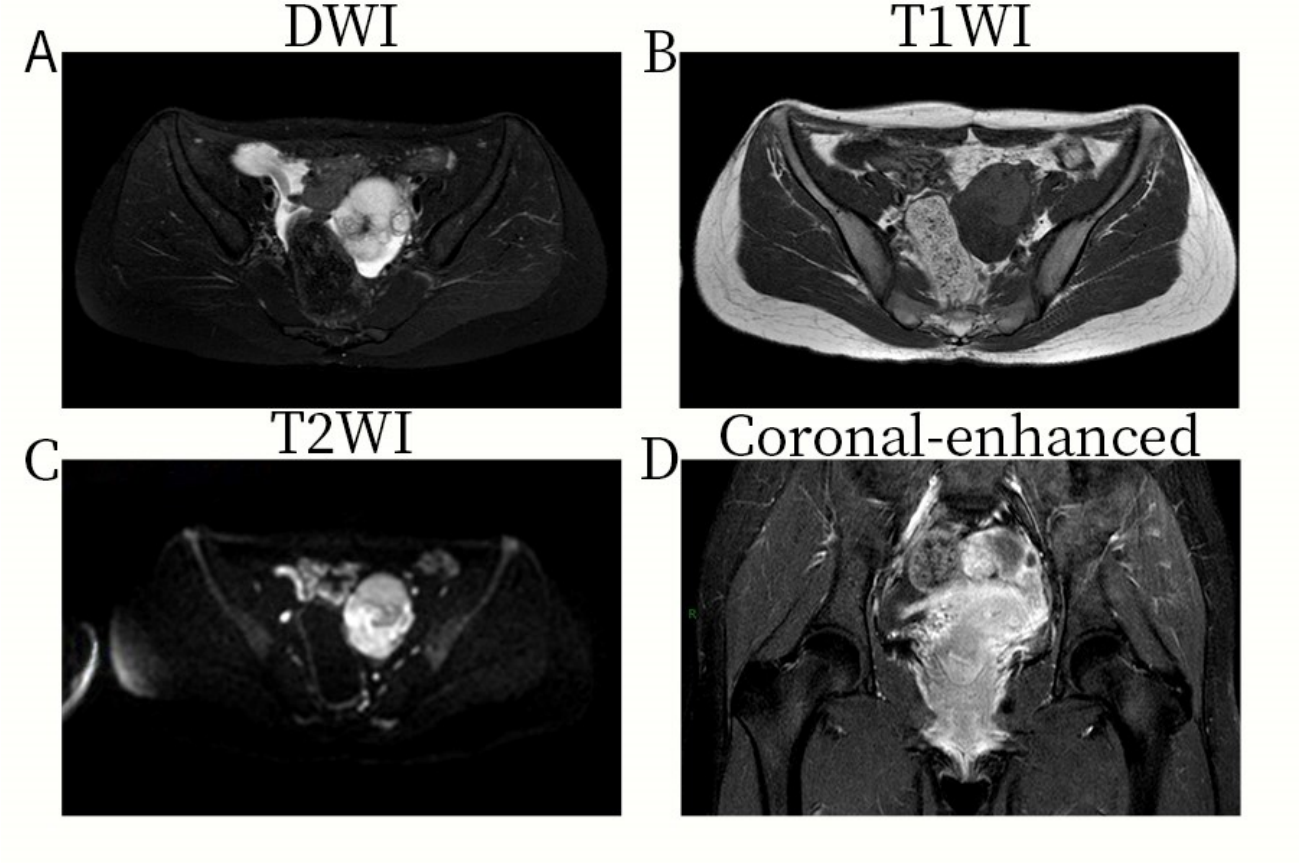

FIGURE 6. MR images for this case at the time of recurrence. (A) Diffusion-weighted Imaging (DWI) shows a high signal. (B) T1 Weighted Imaging (T1WI) shows a slightly lower signal. (C) T2 Weighted Imaging (T2WI) shows an enhanced signal. (D) The enhancement scan reveals a solid portion and significant enhancement of the separation.

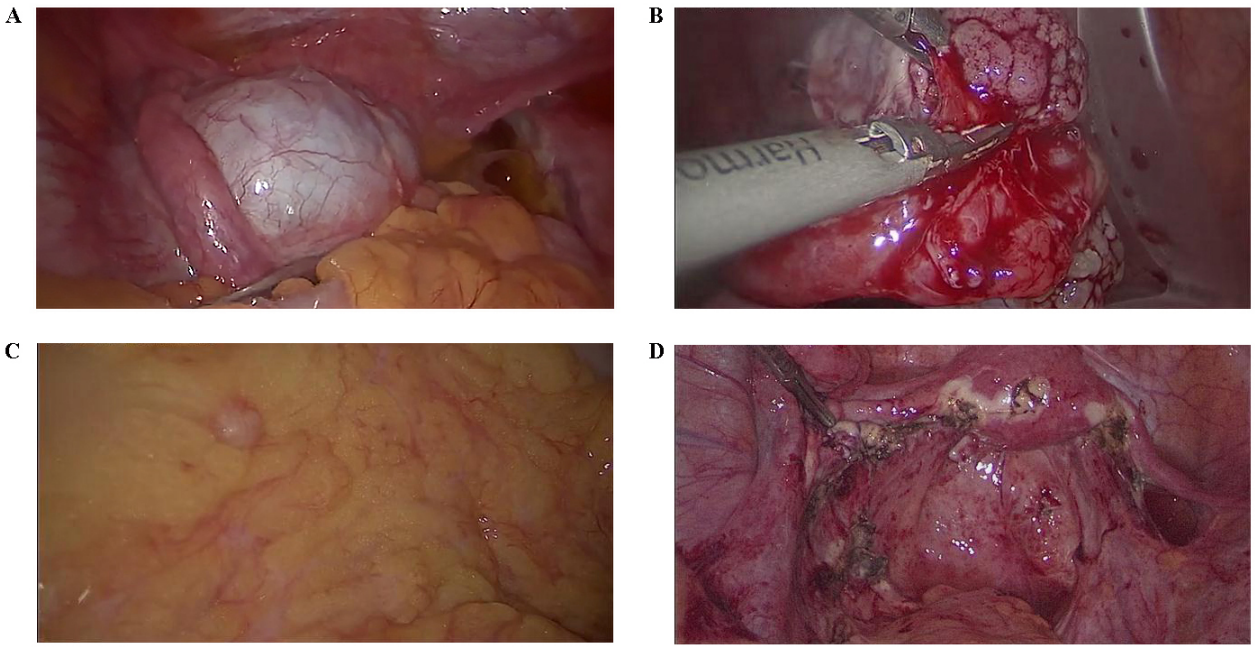

FIGURE 7. Images of the lesion during the second fertility-preserving surgery. (A) The right ovary and fallopian tube were absent, and the left ovary was enlarged to a diameter of about 5 cm. The left fallopian tube and ovary were still clear. (B) A milky white moose-like lesion was seen on the left ovary, and a cauliflower-like lesion of size 2 × 1 cm was visible within the capsule after exfoliation. (C) A peanut-sized milky white lesion can be seen on the left greater omentum. (D) After surgery, some normal tissues were preserved in the left ovary.

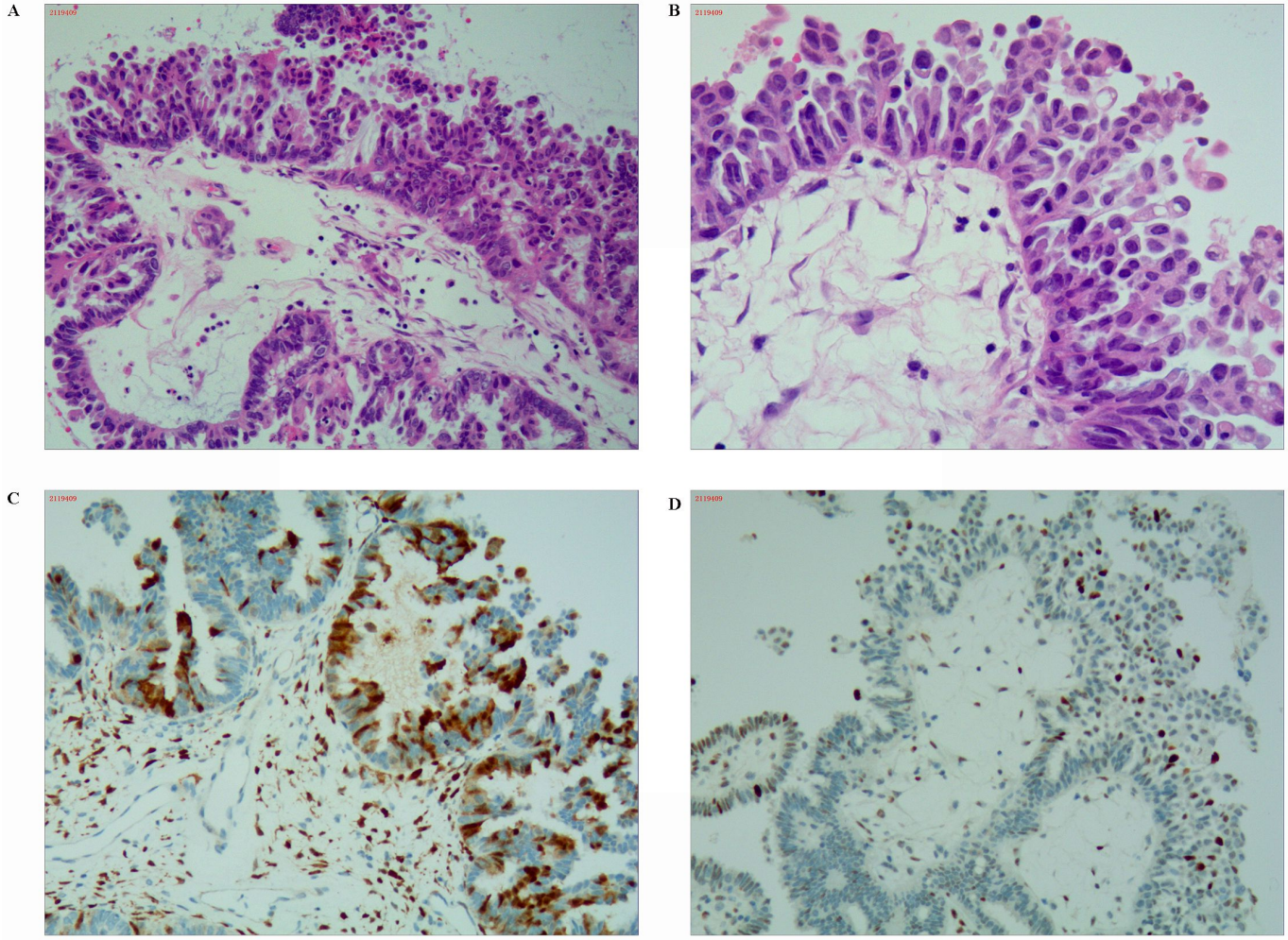

FIGURE 8. Histopathological staining images of left ovarian tumor adnexa. (A) The cells grew in a micropapillary pattern with elongated papillae and fewer microvascular axes (100× magnification). (B) Partial enlargements of the (Fig. 8A) and cells are moderate atypia (200× magnification). (C) The immunohistochemical image for p16 was positive (100× magnification), and that for (D) P53 was wild-type (100× magnification).

However, each additional ovarian surgery performed after recurrence may carry a risk of reducing ovarian reserve and inducing premature ovarian failure, while a conservative treatment does not appear to completely preserve fertility [18]. In a study comprising 52 women of reproductive age, Chevrot *et al*. [19] found that 26% of the patients required assisted reproductive drugs to become pregnant after surgery. In our case, although the patient had normal menstruation after the first surgery, she still did not have her menstruation six months after the second surgery. We speculate that this might be due to damage to ovarian function caused by reperfusion therapy after recurrence. Therefore, if a patient wants to become pregnant, it is necessary to wait for the recovery of ovarian function.

Several studies have assessed obstetric outcomes in BOTs cases treated with fertility-sparing surgery. Johansen *et al*. [20] surveyed 213 women with BOTs in Sweden who underwent fertility-sparing surgery and found that 23% of the women had successful delivery after surgery, with a mean interval of 32 months from surgery to delivery. They also indicated that 9% of the patients received assisted reproductive treatment, of whom eight achieved delivery. In five Korean patients who underwent fertility-sparing surgery, Song *et al*. [21] found that they all had normal menstrual cycles, four conceived spontaneously, and one conceived after two cycles of ovulation induction with clomiphene citrate, with a median interval of 15 months between tumor treatment and pregnancy. Taken together, depending on the histological type of BOT, age, risk of recurrence and duration of pregnancy after fertility-sparing surgery may be important factors to consider in these patients. Generally, it might be preferable to conceive immediately after the procedure when circumstances allow [22].

In addition, assisted reproductive techniques should be considered when the likelihood of natural conception appears low after conservative surgery. A previous study indicated that *in vitro* fertilization pregnancy demonstrated good clinical outcomes in patients with BOTs after preservation surgery, with a pregnancy rate of 63.5% [23]. Thus, for young women diagnosed with BOTs, enhanced follow-up and tumor fertility counseling are necessary, especially for those with advanced-stage disease [24]. In our reported case, the patient did not undergo oocyte cryopreservation. Thus, at follow-up, patients should be advised to cryopreserve ovarian tissue, oocytes, or embryos as soon as possible.

4. Conclusion

In summary, fertility-sparing surgery may be a feasible strategy for patients with BOTs; however, it may be accompanied by a high risk of recurrence. Therefore, clinicians should consider the patient's fertility needs and perform intensive follow-up before making a final decision. For this group of young female patients, it is advisable to conceive immediately after surgery or undergo oocyte freezing in permissible circumstances. However, additional research is required to support this recommendation.

AVAILABILITY OF DATA AND MATERIALS

The data presented in this study are available on reasonable request from the corresponding author.

AUTHOR CONTRIBUTIONS

BCS—performed the operation. BLZ and CZS—involved in the acquisition of data and preparing the figures. JYW and CZS—conceived, designed the research and wrote the manuscript. YLW—contributed substantial advice help to polish the language. XFL—assisted in explaining pathology problem. YZ—conducted the project and revised the whole manuscript. All authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This research was approved and supervised by the Hospital Ethics Committee of the Affiliated Hospital of Guangdong Medical University (PJKT2022-082). The patient provided signed informed consent. In addition, written informed consent was obtained from the patient to publish this case report and all of the accompanying images.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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