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Second fertility preservation surgery for early relapse of seromucinous borderline ovarian tumors

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1. Introduction

Seromucinous borderline tumors (SMBTs) are rare, accounting for 4.8% of borderline ovarian tumors (BOTs). In contrast, 23–70% of SMBTs are associated with endometriosis, and a preoperative diagnosis requires differentiation from endometriotic cysts and malignancies associated with endometriosis (du Bois et al., 2013; Karpathiou et al., 2017; Kim et al., 2010). Since 30% of SMBTs are observed in bilateral ovaries and are predominant in women in their 30 s and 40 s, the choice of fertility-sparing surgery should also be considered (Karpathiou et al., 2017; Kim et al., 2010). Standard surgical procedures (bilateral adnexectomy, total hysterectomy, and omentectomy) are commonly applied to relapse cases after fertility-sparing surgery (Komiyama et al., 2016). We report SMBTs in two cases of early relapse after the first fertility-sparing surgery, which required a second fertility-sparing surgery. The study was approved by the Musashino Red Cross Hospital Review Board and was conducted in accordance with the relevant guidelines and regulations of the Institutional Review Board. We obtained a signed informed consent from all patients.

2. Case 1

A 23-year-old woman with no history of pregnancy presented to the emergency room with lower abdominal pain. She underwent a CT scan and transvaginal ultrasound and was suspected to have a micro-rupture of a 10-cm ovarian cyst, although her pain improved with conservative treatment. As her pain disappeared, she electively underwent laparoscopic right ovarian cystectomy 3 months later. Magnetic resonance imaging (MRI) was performed to investigate the pelvic region prior to surgery (Fig. 1A-C). Her preoperative CA125 level was mildly elevated at 76.1 U/μl. During the surgery, the ovarian tumor ruptured, and the postoperative pathological diagnosis was SMBT stage IC1. Since she wanted to preserve her fertility, we explained the risks to her, and she was followed up carefully without requiring additional surgery. Only two months after the surgery, we found a 3-cm tumor with a 1.5-cm solid nodule in the contralateral left ovary by transvaginal ultrasonography (Fig. 1D-F). The MRI images taken simultaneously did not reveal solid nodules, and the CA125 level was not elevated at 23.5 U/μl. During the follow-up, the ovarian cyst increased to 7 cm, and the CA125 level was elevated at 69.2 U/μl; thus, we decided to perform a second surgery 1 year after the first surgery. Generally, adnexectomy is recommended for relapse cases of BOTs; however, since she strongly desired fertility preservation, we decided to perform a cystectomy. The ovarian tumor was resected without rupture using laparoscopic assistance. The peritoneal cytology was negative, and the pathological diagnosis was SMBT. During the second operation, the abdominal cavity was carefully observed, and no implant was found. She is followed every 3 months with transvaginal ultrasound and blood sampling to measure CA125 levels. One year after the surgery, no relapse of SMBT had occurred, and she had been receiving general infertility treatment.

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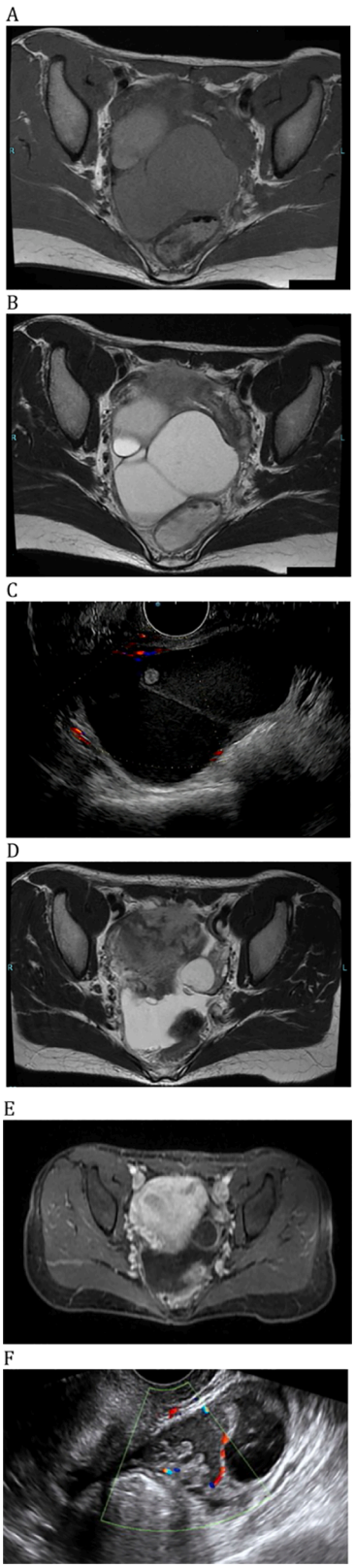

Fig. 1. (A–C) Images taken before the initial treatment: MRI T1 (A) shows an *iso*-intensity multilocular 10-cm right ovarian cyst, MRI T2 (B) shows high intensity, and the transvaginal ultrasound scan (C) shows 5-mm nodules in an ovarian cyst. (D–F) Images taken during relapse: MRI T2 (D) shows an *iso*-intensity monolocular 3-cm right ovarian cyst. MRI T1 contrast (E) shows that the ovarian cyst wall was reinforced, although the nodule was unclear, and the transvaginal ultrasound scan (F) showed 1.5-cm nodules in an ovarian cyst.

3. Case 2

A 33-year-old woman with no history of pregnancy presented to our hospital with menstrual pain. We found an 8.5-cm right ovarian cyst by transvaginal ultrasonography and MRI and suspected an endometriotic cyst (Fig. 2A-C). The CA125 level was mildly elevated at 47.8 U/μl. We performed a laparoscopic right ovarian cystectomy. The ovarian tumor ruptured during the surgery, and the postoperative pathological diagnosis was SMBT stage IC1. Only 11 months after surgery, we found a 2.3-cm tumor with a 0.9-cm solid nodule in the contralateral left ovary by transvaginal ultrasonography (Fig. 2D-F). The solid part was clear on transvaginal ultrasonography, although it was slightly contrasted by MRI. Eight months after the ovarian tumor relapsed, it gradually grew to 4 cm, so we suggested that a second surgery be performed. Generally, an adnexectomy is recommended, although we decided to perform a second fertility-sparing surgery because the patient strongly wanted to preserve her fertility. The ovarian tumor was resected without rupture using laparoscopic assistance. The peritoneal cytology was negative, and the pathological diagnosis was SMBT.

She is followed every 3 months with transvaginal ultrasound and blood sampling to measure CA125 levels. One year postoperatively, no relapse of SMBT had occurred, and she had been receiving general infertility treatment.

4. Discussion

In these two cases, a preoperative diagnosis of endometrial cyst was suspected, and a laparoscopic unilateral cystectomy was performed. The postoperative pathological diagnosis was SMBT, and the FIGO progression stage was stage IC1 due to ovarian tumor rupture during the surgery.

In the case of the postoperative diagnosis of BOT, additional treatment is generally considered for total hysterectomy, bilateral adnexectomy, and omentectomy (Komiyama et al., 2016). According to the Japanese guidelines, if a patient wants to preserve fertility, re-operation should be performed through unilateral adnexectomy, omentectomy, and peritoneal biopsy, or through careful follow-up (Komiyama et al., 2016). However, there have been no definite conclusions regarding re-operation in the case of fertility preservation (du Bois et al., 2013; Fauvet et al., 2004). Raffele et al. reported no difference in relapse rates between patients who have undergone re-operation and those who have not, in the absence of findings other than primary ovarian tumors (Fauvet et al., 2004). Additionally, there are reports mentioning no difference in progression-free survival (PFS) or overall survival (OS) between laparotomy and laparoscopy, and no difference in PFS or OS prognosis between surgical upstaging due to intraoperative tumor rupture (du Bois et al., 2013; Fauvet, Boccara, Dufournet, Poncelet, & Daraï, 2005; Jung et al., 2018). The consensus is that early BOT and salvage surgery after a relapse have good prognoses. In our cases, the patients were diagnosed with SMBT postoperatively, and the attending physician and the patients had a thorough discussion. The patients were then carefully followed up without requiring additional surgery.

A prospective study by Palomba et al. examined patients with bilateral BOT in a group of patients with unilateral adnexectomy and cystectomy or bilateral cystectomy (Palomba et al., 2007). The relapse rate was almost the same in both groups at approximately 60%, and it was reported that the time to relapse was short at 16 months (4–24 months) in the bilateral cystectomy group. Other reports have also shown that the relapse rate is 23% for ovarian cystectomy and 7% for adnexectomy (Suh-Burgmann, 2006). If only cystectomy is performed, and no adnexectomy is added, early relapse may occur and care should be taken. Palomba et al. reported a higher pregnancy rate and shorter time to pregnancy in patients who underwent cystectomy compared to those who underwent adnexectomy (Palomba et al., 2007). However, the pregnancy rate reportedly did not differ between patients who underwent adnexectomy and cystectomy (Delle Marchette et al., 2019).

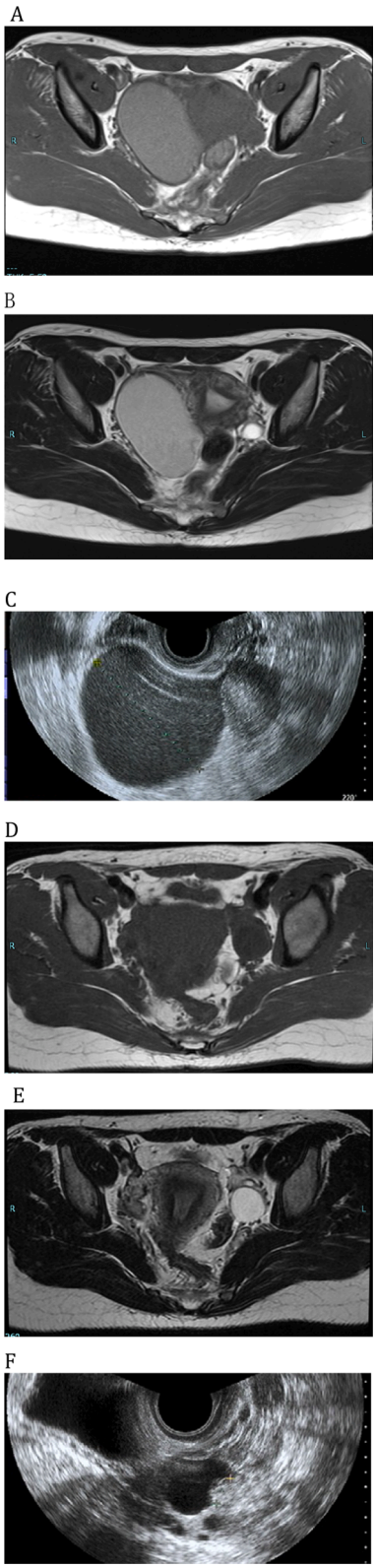

Fig. 2. (A–C) Images taken before the initial treatment: MRI T1 (A) shows a slightly high intensity monolocular 8.5-cm right ovarian cyst, MRI T2 (B) shows high intensity, and the transvaginal ultrasound scan (C) shows no nodules in an ovarian cyst. (D–F) Images of relapse, MRI T1 (D) shows a low intensity 3-cm right ovarian simple cyst, MRI T2 (E) shows high intensity, and the transvaginal ultrasound scan (F) shows 5-mm nodules in an ovarian cyst.

The relapse rate of BOT is reportedly higher in patients who underwent ovarian cystectomy than in those who underwent adnexectomy (du Bois et al., 2013; Palomba et al., 2007; Suh-Burgmann, 2006), although better ovary preservation and higher pregnancy rates are noted in patients who underwent cystectomy (Palomba et al., 2007).

As mentioned above, in cases of cystectomy alone, relapse seems to occur with a high frequency within shorter time frames. Indeed, in our cases, the relapse occurred early at 2 or 11 months postoperatively, although the average time to relapse of BOT is reportedly 4.7 years (Fauvet et al., 2005; Suh-Burgmann, 2006). Preoperative imaging showed no mass on the contralateral ovary and no intraoperative macroscopic abnormality, but SMBT tends to occur bilaterally, and the possibility that the tumor was already latent in the contralateral ovary cannot be denied. Thus, early diagnosis of relapse is needed after fertility-sparing surgery. In our cases, transvaginal ultrasonography, which showed nodules on the cyst wall, made the diagnosis easier. MRI was performed simultaneously, although the solid nodule was unclear. The most common site of BOT relapse has been reported to be the ovary, and follow-up with transvaginal ultrasound after a fertility preservation surgery is useful. The solid nodules of SMBT were faintly enhanced on MRI, and it was difficult to distinguish when the tumor was small. Additionally, since it is difficult to use MRI frequently in terms of medical resources, regular transvaginal ultrasound examinations are convenient and useful.

Adnexectomy is common for patients with BOT who desire fertility preservation. However, BOTs can affect both ovaries synchronously or asynchronously. Nevertheless, despite relapse, BOTs have a good prognosis if they are operable, and no difference in survival rate was found between patients who underwent adnexectomy and cystectomy (Suh-Burgmann, 2006). BOTs may occur in both ovaries in synchronism or asynchronism; therefore, it is necessary to sufficiently explain the risk to patients and to carefully decide between cystectomy and adnexectomy when fertility preservation is considered. There are various opinions, but especially in young people, it may be necessary to select adnexectomy or cystectomy considering the possibility of a relapse in the future, the diameter of the remaining ovaries after surgery, and ovarian reserve. In the present cases, when the second surgery was planned, the patients had a strong desire for fertility preservation. Thus, cystectomy was performed again because the relapse tumors were on the contralateral ovary. After the second cystectomy, there have been no signs of relapse. Both patients are currently undergoing general infertility treatment while carefully following up.

5. Conclusion

BOT after cystectomy is prone to relapse, and the time of relapse may be early. Cystectomy or adnexectomy should be considered carefully when performing fertility preservation, as it can occur in the opposite ovary both synchronously and asynchronously. If a patient opts for cystectomy, we should explain to her that the relapse rate is high, and more careful follow-up is needed. If there is a relapse in the remaining ovary, and the patient strongly desires a second fertility-preserving surgery, cystectomy may be acceptable after a thorough explanation of the risks.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Disclosures

The authors declare no conflicts of interest.

Author contributions

Motoko Kanno: writing of the original draft; Hideki Iwamoto: writing, editing, and review; and Satoshi Umezawa: supervision and review.

All authors critically revised the report, commented on the drafts of the manuscript, and approved the final report.

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