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CASE REPORT

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Ultrasound-guided laparotomic oocyte retrieval during surgery for fertility preservation in a case of tumor recurrence after a unilateral salpingo-oophorectomy

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Abstract

Case: A 28 year old unmarried woman underwent a unilateral salpingo-oophorectomy and was suspected of having a malignant tumor in the remaining ovary. After consultation with the patient and her family, it was decided to cryopreserve the unfertilized oocytes. In order to reduce the risk of puncturing or rupturing the tumor when performing the oocyte retrieval from the ovary that was affected by the malignant tumor, it was chosen to use direct laparotomic oocyte retrieval during surgery, instead of conventional transvaginal retrieval. In order to further reduce the risk of tumor rupture, an ultrasound was used in the laparotomy field to precisely puncture only the follicle and thus avoid the tumor. A total of 11 oocytes was retrieved and 10 of them were cryopreserved in the MII phase.

Outcome: By using an ultrasound at the same time as the oocyte retrieval, it was possible to avoid the ovarian tumor site. Furthermore, by checking and puncturing the follicles, it became possible to retrieve oocytes from the healthy parts of the ovary with greater precision. The combined use of an ultrasound with oocyte retrieval can be considered to be an effective method because it can be performed relatively easily.

Conclusion: The authors believe that not only macroscopic, but also ultrasonic, methods are useful to reduce the risk of tumor rupture.

KEYWORDS

controlled ovarian hyperstimulation, fertility preservation, oocyte retrieval, ovarian cancer

1 | INTRODUCTION

Female fertility preservation methods can be divided broadly into the cryopreservation of embryos, oocytes, or ovarian tissue. As the cryopreservation of ovarian tissue for patients with gynecological malignancies runs the risk of reimplanting malignant cells and because the relevant technology has now been established, the cryopreservation of oocytes is the more widely applied method in the clinical context. In recent years, there have been successive reports of patients undergoing laparotomic oocyte retrieval during surgery. Particularly in those suspected of ovarian malignancies bilaterally or in the event where there is a possibility of losing both ovaries, malignancy is suspected in the remaining ovary after a unilateral oophorectomy.[1-6] In this article, the case of a patient with a potentially malignant tumor in the remaining ovary following a unilateral salpingo-oophorectomy and who underwent ultrasound-guided

laparotomic oocyte retrieval during resection of the remaining ovary is reported.

2 | CASE REPORT

A 28 year old unmarried woman, gravida 0, para 0, was referred to the authors' hospital for a left ovarian cyst. An irregular papillary protuberant lesion was found in the luminal wall of a cyst that had swollen to a diameter of 10 cm. Thus, an ovarian malignancy was suspected and an abdominal left-sided salpingo-oophorectomy was performed. The findings from the histopathological inspections revealed borderline serous papillary cystadenoma, while the cytodiagnosis of ascites revealed a class II classification. Considering the patient's age and the need for fertility preservation, it was decided to observe her progress instead of additional treatments. Two years after surgery, an enlargement in the remaining ovary was identified. An abdominal contrast computed tomography (CT) examination revealed a multilocular cystic tumor, with a diameter of 9 cm and a solid part in the luminal wall of the cyst (Fig. 1). A malignancy was suspected and it was decided to perform a right-sided salpingo-oophorectomy. As the patient already had undergone a unilateral salpingo-oophorectomy and would lose her fertility by further resection of the remaining ovary, the authors presented the cryopreservation of unfertilized oocytes to the patient, who was unmarried, as an option for fertility preservation. As both the patient and her parents desired fertility preservation, it was decided to conduct the cryopreservation of her unfertilized oocytes. As the oocyte retrieval would be attempted from an ovary that was affected by a malignancy, it was decided to conduct laparotomic oocyte retrieval during surgery, instead of conventional transvaginal retrieval, in order to reduce the risk of puncturing or rupturing the tumor. The risks of tumor rupture were explained to the patient and her family and consent to proceed was obtained. Furthermore, it was decided to use ultrasonography to avoid the tumor and to precisely puncture only the follicle to further reduce the risk of tumor rupture. The patient's anti-Müllerian hormone level before ovarian stimulation was 8.74. The date of oocyte retrieval was scheduled for the same day as surgery and ovarian stimulation was performed by using the gonadotropin-releasing hormone (GnRH) agonist long protocol (Fig. 2). The total dose of gonadotrophin that was administered was 2925 IU. The controlled ovarian hyperstimulation (COH) protocol that was chosen was determined with reference to a fixed stimulation regimen.[7] The patient was prescribed 10,000 IU of human chorionic gonadotropin (hCG) to trigger ovulation at 35 hours before the oocyte retrieval. Just before surgery, a culture medium (human tubal fluid medium) for oocytes was placed in an incubator that was set at 37°C and was transported from the incubation room to the operating room. By the time of the laparotomy, a partial rupture of the right ovarian tumor capsule and a small amount of light-yellow transparent ascites were observed. Prior to the right-sided salpingo-oophorectomy, ultrasound-guided oocyte retrieval was conducted by using a single-lumen ovum aspiration needle (20GA, Bloomington, Indiana, USA). The aspiration was performed manually by using a syringe. For the ultrasound, the ACUSON Freestyle (Siemens, Munich, Bavaria, Germany), a cableless ultrasound diagnostic imaging device, was used. The ultrasound probe was protected with a sterilized cover and the probe was brought into direct contact with the target ovary while checking the follicle within the part of the ovary that was thought to be healthy (Figs. 3 and 4). Furthermore, immediately after the removal of the tumor from the right ovary, the remaining follicles were identified on the excised specimen by ultrasound and additional follicle punctures were performed. A total of 11 oocytes (11 before removal of the ovary and 0 after removal of the ovary) was retrieved. Ten

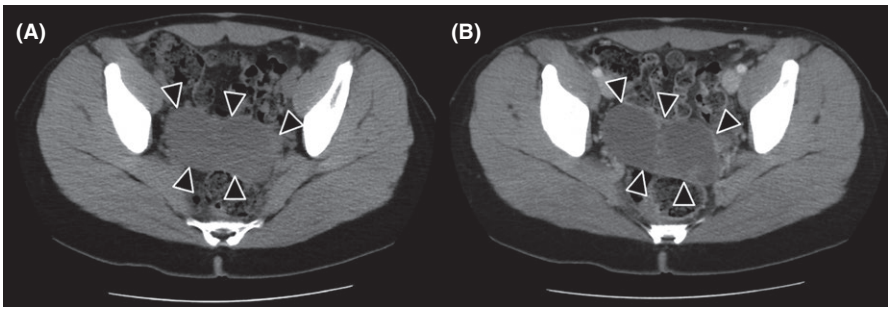

FIGURE 1 Chest computed tomography test (horizontal cross-section). Multilocular cystic tumor with a solid part in the luminal wall of the cyst (▲). (A) Simple and (B) contrast

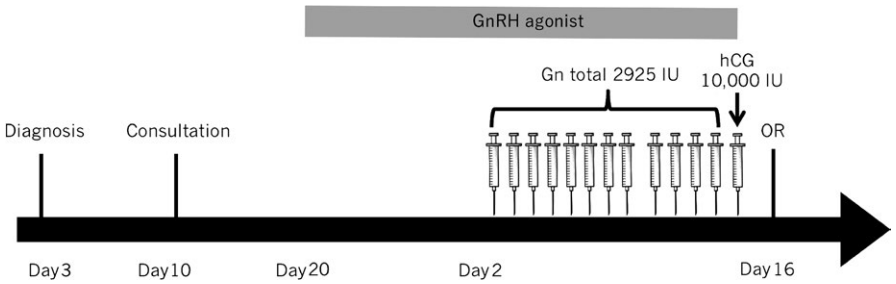

FIGURE 2 Progress from diagnosis to oocyte retrieval. After consultation about fertility preservation, ovarian stimulation was performed by using the gonadotropin-releasing hormone (GnRH) agonist long protocol and the total dose of gonadotrophin (GN) that was administered was 2925 IU. Oocyte retrieval was performed the same day as surgery. hCG, human chorionic gonadotropin; OR, oocyte retrieval during surgery

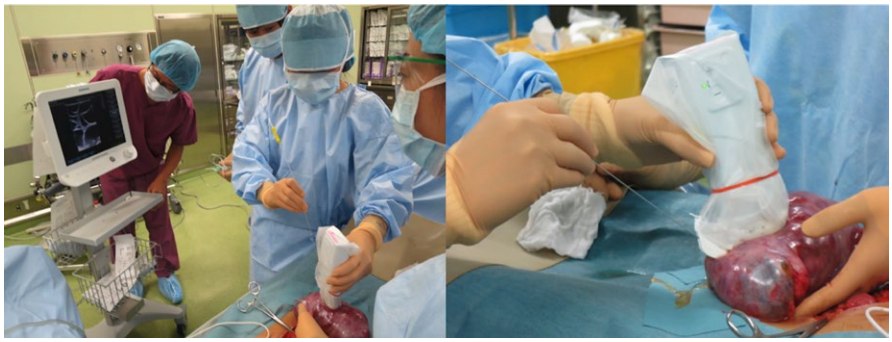

FIGURE 3 Method of laparotomic oocyte retrieval under ultrasound guidance. The ultrasound probe was protected with a sterilized cover and the probe was brought into direct contact with the ovary for puncture while checking the follicle within the part of the ovary that was thought to be healthy

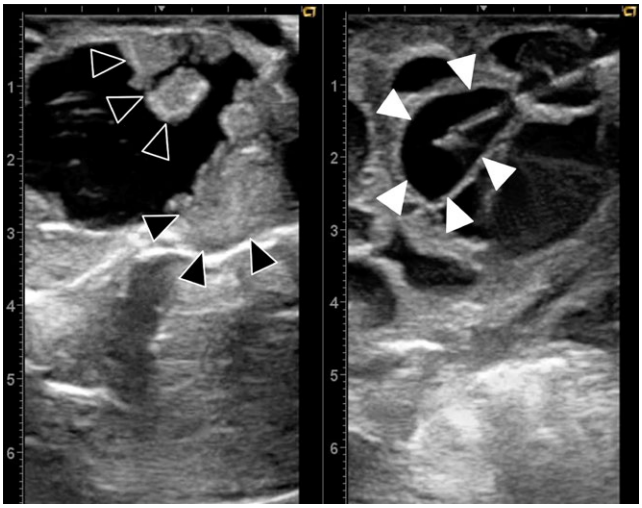

FIGURE 4 Ultrasound image of oocyte retrieval during surgery. By avoiding the suspected tumor sites (▲), only the healthy follicles were able to be punctured (△)

of the oocytes were classified as being in metaphase MII and one was classified as being in the degeneration phase. The cumulus cells were cleaved by using hyaluronidase and then it was removed to confirm the meiosis stage 2 hours after the oocyte retrieval. The 10 mature oocytes were cryopreserved in the MII phase. The finding of the histopathological inspections revealed a borderline serous papillary cystadenoma, while a cytodiagnosis of ascites revealed a Class IV classification. There was no malignancy on histopathological inspection of the retrieved follicular fluid. Considering the pathology results, as well as those of a positron emission tomography (PET)–CT scan that was conducted 1 month after surgery and that revealed no abnormality, chemotherapy was chosen, rather than second-term surgery, with the consent of the patient and her family. She was referred for counseling with a reproductive endocrinologist to fully inform her about fertility preservation. Additionally, it was decided to prescribe her hormone replacement therapy, such as Kaufmann's treatment, until pregnancy was desired.

3 | DISCUSSION

In the field of obstetrics and gynecology, much consideration is given to fertility-sparing surgery in female patients of reproductive age who are affected with borderline ovarian malignancies.[7] However, if a patient is suspected to have bilateral ovarian malignancy or malignant tumors in the ovary that remain after a unilateral oophorectomy for some reasons, the usual standard of care is bilateral oophorectomy or resection of the remaining ovary. In these situations, it is necessary to consider fertility preservation prior to the oophorectomy.

In recent years, surgeons have deployed direct laparotomic oocyte retrieval from the ovary during surgery instead of conventional transvaginal oocyte retrieval in order to reduce the risk of intraperitoneal contamination by cancer cells during the oocyte retrieval from an ovary that is affected with malignant tumors.[1-6] In the present case, a malignant tumor was suspected in the remaining ovary after a unilateral salpingo-oophorectomy. After removing the remaining ovary and having opted to remove the remaining ovary to treat the primary disease, ultrasound-guided laparotomic oocyte retrieval was performed. By using an ultrasound at the same time as the oocyte retrieval, the ovarian tumor site was avoided by using both macroscopical images, as well as ultrasound images. Furthermore, by checking and puncturing the follicles, it became possible to retrieve oocytes from the healthy parts of the ovary with greater precision. No previous study has used ultrasound during this type of surgery. The combined use of ultrasound can be considered an effective method because it can be performed relatively easily, like during amniocentesis or abdominocentesis.

With respect to oocyte retrieval during surgery, whether the oocytes should be retrieved inside the body before the oophorectomy or outside the body after the oophorectomy is not known. Four out of the past six cases that have been published in the literature that involved oocyte retrieval during surgery had the retrieval performed outside of the body after the oophorectomy,[1-3,5] while the remaining two cases had the retrieval performed inside the body prior to the oophorectomy.[4,6] (Table 1). In terms of minimizing the risk of intraperitoneal contamination by cancer cells, oocyte retrieval ideally should be performed outside the body following the oophorectomy. However, although oocyte retrieval after an oophorectomy can shorten the time that is taken between specimen extraction and oocyte retrieval, some studies have suggested that retrieval during surgery interrupts the blood flow to the ovary during the oophorectomy and thus could cause cellular damage and deterioration of the oocyte's quality.[6] Furthermore, a previous report has suggested that there is no significant difference in the prognosis between stage IA ovarian cancer and stage IC ovarian cancer, based on an assessment after ovarian tumor capsule rupture.[9]

TABLE 1 Previously reported cases of intraoperative oocyte retrieval

	Author	Diagnosis	Previous operation	Operation	COH	Oocyte Retrival	Number of oocyte retrived	Number of oocyre cryopreserved	Number of embryo transferred	Pregnancy outcome
Case 1	Huang et al. (2007)	Bilateral serous borderline ovarian cancer	NA	LSO+ROC(II)	NA	Ex vivo	4GV	2 Mature oocytes	NA	NA
Case 2	Fatermi et al. (2011)	Recurrent borderline serous adenocarci-noma	LO(IIC)	RSO	GnRH antagonist protocol	Ex vivo	11 Mature oocyte	7 Zygotes	NA	NA
Case 3	Bocca et al. (2012)	Reccurent borderline serous carcinoma	LSO(IC)	RSO	GnRH antagonist protocol	Ex vivo	14 Mature oocyte	14 Mature oocytes	NA	NA
Case 4	Fadini et al. (2014)	Bilateral ovarian adenocarci-noma	NA	RSO+LOC(IIC)	NA	In Vivo	3GV	3 Mature oocytes	1	No pregnancy
Case 5	Prasath et al. (2014)	Recurrent micropapillary serous carcinoma	RSO+LOC(IIIC)	LO	NA	Ex vivo	4GV	3 Embryos	2	Live birth
Case 6	Kim et al. (2015)	Recurrent immature teratoma	RSO+LOC(IIIC)	LSO	Random start	In Vivo	8 Mature oocytes, 1 immature oocyte	8 Mature oocytes	NA	NA
Case 7	Present case	Recurrent borderline serous carcinoma	LSO (IA)	RSO	GnRH agonist long protcol	In Vivo	10 Mature oocytes, 1 immature oocyte	10 Mature oocytes	NA	NA

COH, controlled ovarian hyperstimulation; GnRH, gonadotropin-releasing hormone; GV, germinal vesicle; LO, left oophorectomy; LOC, left ovarian cystectomy; LSO, left salpingo-oophorectomy; N/A, not applicable; RSO, right salpingo-oophorectomy.

Thus, in the present case, it was chosen to perform the oocyte retrieval prior to the oophorectomy in order to prevent a decline in oocyte quality. In practice, because rupture of the tumor capsule already was confirmed immediately after the laparotomy, there was no change in the International Federation of Gynecology and Obstetrics (2014) classification for staging the ovarian cancer by puncturing the follicle.

Cellular damage and deterioration of the oocyte quality due to interrupted blood flow to the ovary by the retrieval oocytes being performed outside of the body after an oophorectomy needs to be discussed in future studies.

At present, the safety of COH for patients who are suspected of an ovarian malignancy is yet to be established and there is significant room for debate. However, COH is considered to be essential for securing an adequate ovarian oocyte count because only a small number of oocytes can be retrieved and immature oocytes stop growing without COH. In particular, as in this case, oocyte retrieval is possible only after the removal of the remaining ovary after a unilateral salpingo-oophorectomy. Therefore, it is vital to obtain an adequate number of oocytes at a single time point. As a result, 10 unfertilized oocytes could be cryopreserved in this case, thereby indicating that this ovarian stimulation protocol was effective. Adjusted ovarian stimulation also is considered to be effective from the perspective of planning oocyte retrieval in combination with the treatment for the primary disease.

For young women with malignant tumors, it is very important to consider fertility preservation. In particular, malignant gynecological tumors tend to develop directly in the reproductive organ. It is therefore important to consider the possibility of fertility preservation, while selecting the appropriate treatment method. As gynecological oncologists and reproductive specialists cooperate closely and provide prompt consultations, young women with malignancies can be readily informed of the possibilities of fertility preservation. However, in the field of oncofertility, treating the malignant tumor is the top priority.

The present case represents the first case of ultrasound-guided laparotomic oocyte retrieval during the removal of the patient's remaining ovary after the suspicion of a malignant growth in the ovary, despite the patient previously having undergone a salpingo-oophorectomy of the other ovary. Further consideration of the COH method and oocyte retrieval now is necessary in order to reduce the risk of contamination by malignant cells into the peritoneal cavity, while also maintaining a high number and quality of the retrieved oocytes. The method that was used in the present case thus can become a new standard of care. The authors believe that the specific examination of ovarian stimulation methods and oocyte retrieval methods is necessary in the future.

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DISCLOSURES

Conflict of interest: The authors declare no conflict of interest. *Human and Animal Rights*: The research method was approved by the Institutional Review Board of Ethics of Toho University Omori Medical Center, Tokyo, Japan (Approval No. 25-235). Informed consent had been given by the patients and their family and it was confirmed to them that patient anonymity would be preserved. This article does not contain any study with animal participants that was performed by any of the authors

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