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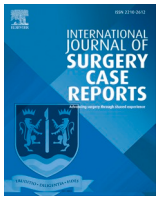

Case report

Successful laparoscopic cytoreductive surgery for multiple (three) advanced recurrences of AGCT in a young woman. A case report

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ABSTRACT

Introduction and importance: Debulking surgery is the main approach for recurrent adult granulosa cell tumors (AGCTs), but the effectiveness of laparoscopic extensive cytoreduction in advanced cases and its impact on quality of life (QoL) remains unclear.

Case presentation: A 34-year-old woman, who had a right adnexectomy for AGCT in 2020, was referred with an 8-month history of a large left ovarian cyst and amenorrhea. Preoperative evaluations indicated a recurrence 18 months post-diagnosis. After discussing her career as a photo model, which required optimal aesthetic outcomes, we opted for total laparoscopic surgery, including radical type A hysterectomy, left salpingo-oophorectomy, pelvic peritonectomy, total mesorectal excision, total omentectomy, and pelvic and lumbo-aortic lymphadenectomy. Pathology confirmed stage 3C recurrent AGCT. After discussions, the patient declined adjuvant chemotherapy and received progestins with close follow-up. Fourteen months later, a positron emission tomography (PET) showed high metabolic activity in the left iliac fossa and right pelvis, confirmed by magnetic resonance as pelvic lymph node recurrence and small intestine involvement. She underwent laparoscopic cytoreductive surgery, including peritonectomy, lymph node metastases removal, and intestinal resection. She recovered with excellent aesthetic results and QoL. She completed six cycles of adjuvant cisplatin (80 mg/m2). Ten months later, following a suspected PET, a diagnostic/operative laparoscopy revealed a miliary peritoneal carcinosis, particularly in Morrison's space.

Clinical discussion: Repeated laparoscopic extensive surgery for recurrent advanced AGCT yielded excellent aesthetic outcomes and effective cytoreduction.

Conclusion: This case supports the safety and efficacy of minimally invasive techniques, emphasizing their role in preserving QoL and body image.

1. Introduction

Ovarian granulosa cell tumors (GCTs) are rare hormone-producing neoplasms originating from ovarian granulosa cells. They consist of two histopathological types: adult granulosa cell tumors (AGCTs), which account for 95 % of cases and primarily affect women aged 50 to 55 years, and juvenile granulosa cell tumors (JGCTs), found in adolescents and young women under 30 years [1,2]. These tumors often produce estrogen, causing related symptoms [3]. Representing <5 % of ovarian tumors, GCTs tend to grow slowly with a generally good prognosis, especially if diagnosed early [4]. Ovarian GCTs typically present as pelvic masses discovered during examinations following vaginal bleeding, the most common symptom, and are confirmed by ultrasonography. Surgery is essential for tumor removal and disease staging. In the early stages, laparoscopic surgery is preferred, and fertility-sparing surgery is an option when the tumor is confined to the ovaries [5]. Despite slow growth, they can recur years after diagnosis [6]. Chemotherapy and radiotherapy may target residual tumor cells and reduce recurrence risk [7]. Close periodic clinical, imaging, and laboratory monitoring are needed to evaluate therapy response and detect

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recurrence early, as recurrence is common, often due to inadequate initial or conservative surgery in younger patients [8,9]. Treating GCT recurrence requires a personalized, multidisciplinary approach based on patient characteristics, overall health, specific tumor characteristics, disease stage, and previous treatment [10,11].

Recurrences can be surgically resolved using extensive cytoreduction [11,12]. Platinum-based chemotherapeutic regimens may be employed to prevent or treat recurrence, whereas radiotherapy may treat localized recurrences or relieve pain [3,10]. Hormone therapies, including aromatase inhibitors and progestins, can control tumor growth and hormonal symptoms. Specific tumor characteristics, such as hormone receptors or actionable mutations, may guide therapy choices and support targeted therapies [13,14].

Although prognosis is generally less favorable than that at initial diagnosis, advancements in therapies and personalized treatment approaches have greatly enhanced survival and quality of life (QoL). It is important to recognize that each patient is unique and requires personalized treatment. In this case, we describe a laparoscopic approach used to remove an extensive abdominopelvic recurrence that occurred 19 months after the initial diagnosis (primary cytoreductive surgery). This surgery was performed at the specific request of the patient, who works as a photo model. A secondary laparoscopic surgery was performed 14 months later due to a recurrence in an ileal loop, followed by a tertiary surgery for a limited recurrence in the abdominal peritoneum. This treatment strategy consistently resulted in excellent aesthetic outcomes and optimal cytoreduction, with the patient remaining disease-free.

2. Case report

The present work has been reported in line with the SCARE criteria [15]. In June 2022, a 34-year-old Gravida 2 Para 2 (first in 2009 and second in 2021) was referred to our department. She underwent a past right adnexectomy in January 2020 for AGCT at another hospital. Later, the patient was not referred for follow-up care, which is why it came to our attention due to an extensive spread of disease. She presented with an 8-month history of a large multilobular cystic left ovarian tumor and amenorrhea. A mobile, nonpainful left iliac fossa neoformation measuring approximately 15 cm was noted on examination. Transvaginal ultrasonography confirmed a multi-septate cystic mass in the left adnexa (doppler color score 3/4) (Fig. 1), with normal uterus morphology and volume. Ultrasound imaging revealed 1–8 cm neoformations in the vesicouterine fold and the Douglas cavity, with heterogeneous components and pathological neovascularization. Serum cancer antigen (CA) 125, CA19.9, CA15.3, Human Epididymis Protein 4 (HE4), and carcinoembryonic antigen levels were within normal ranges; however, estradiol (E2) was very high (580 pg/mL). Preoperative diagnosis suggested possible AGCT recurrence. After comprehensive counseling and consideration of her occupation, which required optimal aesthetic outcomes, the patient requested a fully laparoscopic approach. Given our expertise in this technique, we prioritized the patient for total laparoscopic surgery despite the need for extensive cytoreduction. The patient provided written informed consent for the surgical procedure, publication of this report, and the accompanying images. The overall QoL and sexual function were assessed before surgery using the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC-QLQ-C30) and the Female Sexual Function Index (FSFI) by a dedicated psycho-oncologist working at our Department [16]. The results showed poor QoL and low sexual function levels (see Table 1).

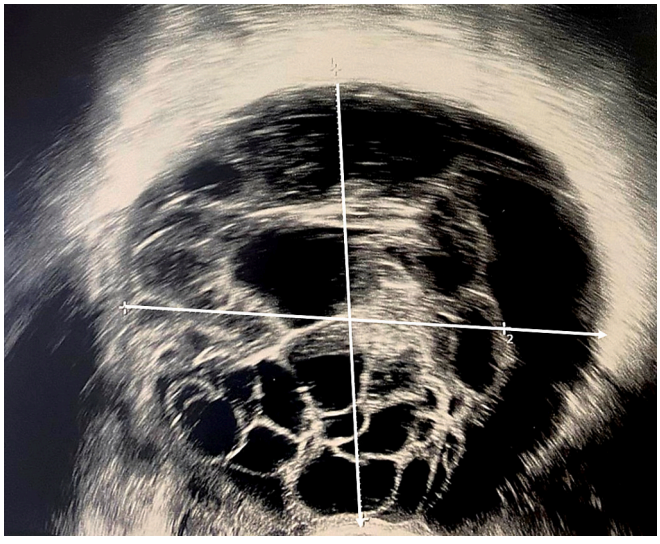

Fig. 1. Transvaginal ultrasonography (US) imaging of ovarian cyst at first admission. The US showed a multi-septate cystic mass in the left adnexa, measuring approximately 12 × 12 cm.

On diagnostic laparoscopy, the tumor originated from the left ovary and appeared as a large cyst with an intact capsule. The uterus had normal volume, while newly formed tissue was noted in the right uterine bladder pouch and less prominently between the pelvic infundibulum and bilateral round ligaments. Lifting the uterus revealed new tissue affecting the rectum, right pararectal douche, and the entire Douglas pouch. Small isolated clusters of tissue were also found in the diaphragmatic peritoneum, Glisson's capsule, and there was extensive metastasis in the omentum. No other signs of disease were observed. An intraoperative frozen section confirmed the pelvic peritoneal tumor as AGCT; therefore, we proceeded laparoscopically as previously agreed with the patient.

An experienced gynecologic laparoscopic surgeon with a strong background in bowel and colorectal surgery for advanced ovarian cancer performed the complete procedure without the assistance of general surgeons. All surgical procedures were performed using LigaSure Maryland Jaw Laparoscopic Sealer/Divider (Covidien, Boulder, CO, USA) and LigaSure Blunt Tip Laparoscopic Sealer/Divider (Covidien). Hemostasis was obtained with BiClamp® LAP and BiClamp® LAP Maryland Forceps (Erbe, Germany). The patient underwent radical type B laparoscopic hysterectomy, left salpingo-oophorectomy, extensive pelvic peritonectomy, total mesorectal excision, total omentectomy, and pelvic and lumbo-aortic lymphadenectomy. For lymphadenectomy and omentectomy, the surgeon positioned himself between the patient's legs with an appropriate monitor aimed from the pelvis toward the head. For omentectomy, the patient was placed in a 15–20° reverse Trendelenburg position.

The pelvic procedure started at the sacral promontory and extended bilaterally along the pelvic brim, following the common iliac vessels. The peritoneal incision was extended laterally toward the hips, allowing the complete removal of the prevesical peritoneum, which contained a 6 × 4 × 4 cm metastasis. Simultaneously, the ureters and uterine arteries were isolated, and pelvic lymphadenectomy and total hysterectomy were performed. Posterolateral peritonectomy was performed above the bilateral ureteral planes ((Supplementary Video 1; https://doi.org/10.5281/zenodo.14261766). In some advanced ovarian cancer cases, we prefer peritoneum and total mesorectal excision over bowel resection when the infiltration of the rectal peritoneum does not surpass the muscular layer. The dissection focuses on removing neoplastic lesions around the rectum. The process included opening the deep subperitoneal space, freeing the lateral peritoneum, and cautiously removing neoplastic lesions using automatic staplers (Echelon Flex™, Ethicon/Johnson & Johnson, Cincinnati, OH, Usa), LigaSure Blant, Meryland, and laparoscopic forceps. Each nodule was separated from the rectal wall, and deeper nodules were excised up to the vaginal fornix (Supplementary Video 2; https://doi.org/10.5281/zenodo.14261766). Uterosacral ligaments were removed from the anterior root. Thermal ablation addressed small diaphragmatic and Glissonian lesions. Blood

Table 1
Evaluation of overall QoL (by EORTC-QLQ-C30) and sexual function (by FSIF) before and after (3 months) each cytoreductive surgery for recurrent AGCT.

Questionnaire	Before the first cytoreductive surgery	After the first cytoreductive surgery	Before secondary cytoreductive surgery	After secondary cytoreductive surgery	Before tertiary cytoreductive surgery	After tertiary cytoreductive surgery
EORTC-QLQ-C30 (overall QoL item)	2	5	3	4	6	7
FSFI	10	20	23.5	17	19.7	17.2

Abbreviations: FSFI, Female sexual function index.

loss was about 300 mL, with no complications during surgery. Total operative time was 300 min, and the patient was discharged on post-operative day 5 following an uneventful recovery.

The final pathological examination confirmed recurrent typical AGCT. The tumor involved the uterine serosa up to the isthmus, left tubal angle, and right parametrium, with vessel emboli and concurrent endometrial hyperplasia. AGCT were also found in the vesicouterine fold peritoneum (6 × 4 × 4 cm), left mesovarium, left pelvic peritoneum, and pre-rectal peritoneum (10 × 7 × 5 cm), with multiple nodules, the largest measuring 4 × 3 cm. Extensive omental involvement was observed, with nodules <2 cm. Metastasis was identified in 2 of 32 right pelvic lymph nodes; the remaining 27 left pelvic and 10 lumboaortic lymph nodes were disease-free. The final stage was determined to be stage 3C, node-positive for AGCT (Fig. 2).

After extensive discussions, the patient opted out of adjuvant chemotherapy due to uncertain results in the literature but agreed to progestin treatment and regular close follow-ups. A positron emission tomography (PET) scan performed 1 month post-surgery showed no signs of cancer. The patient continued with PET scans every 3 months, along with serum E2 and ovarian cancer marker tests. The assessment of overall QoL and sexual function conducted three months post-surgery demonstrated a significant enhancement in both areas (Table 1).

After 14 months, the patient felt well; however, a PET scan revealed high metabolic activity in the left iliac fossa and a large non-specific positive activity in the right pelvis (Fig. 3), with normal serum E2 levels (15 pg/mL). Magnetic resonance imaging confirmed pelvic lymph node recurrence and possible small intestine involvement. Following thorough informed consent, the patient agreed to diagnostic/operative laparoscopy. Surgery included peritonectomy for suspected metastatic areas, removal of likely metastatic lymph nodes from the external iliac vessels measuring 4 cm and from the right inguinal canal entrance (Fig. 4), and wide resection of the intestinal loop with a stapled side-to-side anastomosis. Blood loss was minimal (<50 mL), and the patient recovered immediately, being discharged on postoperative day 4 with normal bowel function. Postoperatively, the patient received adjuvant cisplatin (80 mg/m^2) for six cycles. A PET/computed tomography 1 month later showed no signs of metastasis, and subsequent follow-ups every 3 months with PET scans and tumor marker tests, particularly for E2, remained negative. Overall, QoL and sexual function before intervention were good and did not worsen after surgery (Table 1). After a follow-up of 10 months from secondary cytoreductive surgery, a PET/CT showed suspected abdominal hypermetabolic areas. Then, a tertiary diagnostic/operative laparoscopic surgery showed a miliariform peritoneal carcinomatosis: a peritonectomy was performed. After a follow-up of 6 months (January 2025), a PET/CT showed no evidence of hypermetabolic disease that holds oncological significance (Fig. 5); the patient is currently in good health with excellent QOL and stable sexual function (Table 1) and continues progestin treatment.

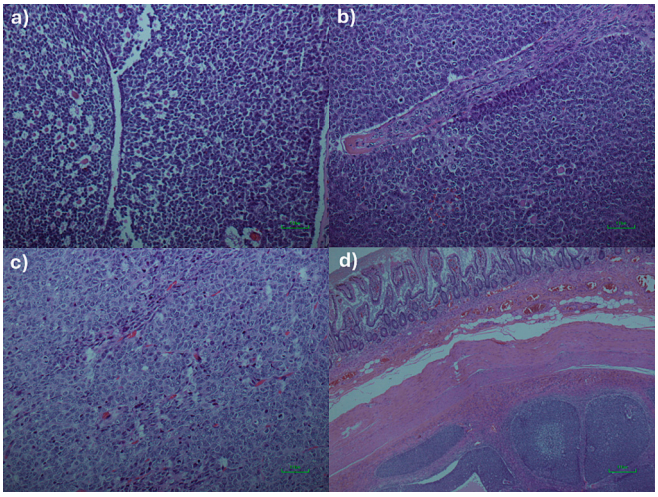

Fig. 2. Final histopathological examination of the first recurrence: a) ovarian localization of adult granulosa cell tumor (AGCT) exhibiting low-grade morphology, characterized by monomorphic nuclei, mild nuclear atypia, no mitosis, necrosis, and hemorrhage) (Hematoxylin-eosin (HE), 40×); b) peritoneal localization of ATCG showing both low-grade and high-grade features (HE, 40×); c) lymph node metastasis of AGCT with high-grade features, including moderate to severe nuclear atypia, apoptosis, karyorrhexis, as well as mitosis, necrosis, and hemorrhage) (HE, 40×); d) Localization of ACGT in the context of the intestinal wall (HE, 10×).

3. Discussion

Our study describes extensive and repeated minimally invasive surgery for thrice-recurrent AGCT. The primary goal of advanced cancer treatment is to prolong life expectancy, typically measured by the Kaplan–Meier survival time after the recommended therapy. Recently, the focus has shifted from only survival to health-related QOL for patients with ovarian cancer, as extensive treatment significantly impacts morbidity in this already debilitating disease [17–19]. This is especially important for younger women diagnosed while still leading active lives [20].

Surgical treatment for gynecological cancer emphasizes preserving the highest quality of health-related life, fostering new avenues and opportunities for minimally invasive surgery for ovarian tumors [21,22]. Herein, we explored critical aspects of minimally invasive techniques for recurrent advanced granulosa cell ovarian cancer in young women, aligning with current literature. Specifically, we examined the importance of laparoscopy as a primary approach for extensive cytoreduction in advanced ovarian cancer, in this case, an AGCT. Minimally invasive and laparoscopic approaches have been proven effective for complex benign neoplasms (e.g., fibromas measuring 1.5–11.0 kg) [23] and certain gynecologic malignancies with high surgical complexity [24,25]. For endometrial and cervical carcinomas, conclusive studies have highlighted the role of laparoscopic surgery. Due to limited prospective survival data, the impact of laparoscopic procedures in advanced ovarian carcinoma remains unclear. However, smaller retrospective case-control [26,27] and rare cohort studies [28,29] suggest that laparoscopic procedures may be technically feasible and achieve cytoreductive quality comparable to conventional longitudinal laparotomy. Additionally, they may be associated with lower perioperative morbidity and improved quality of life. Gallotta et al. [28] described a study involving 58 patients with recurrent ovarian cancer who underwent secondary cytoreductive surgery via laparoscopy. Complete cytoreduction was achieved in 100 % of these cases, although there were intraoperative or early complications in about 17 %

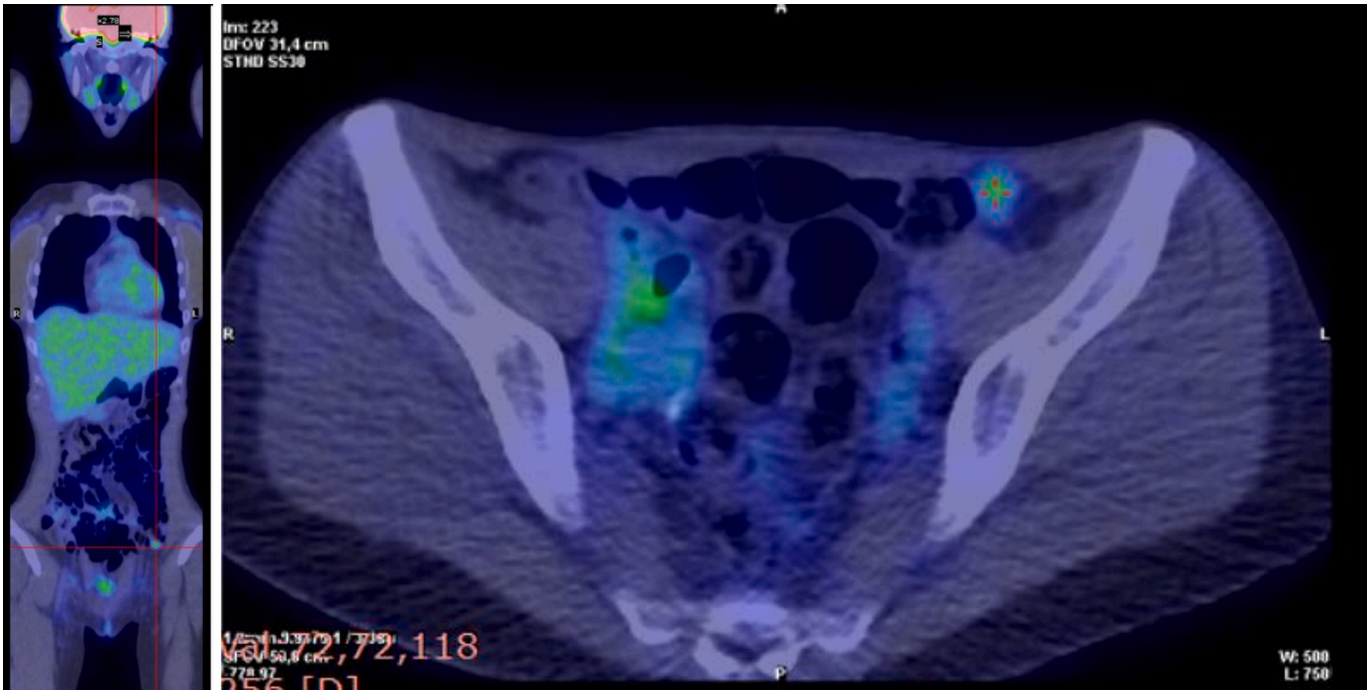

Fig. 3. Positron emission tomography (PET) of the second recurrence: PET scan revealed high metabolic activity in the left iliac fossa and a large non-specific activity in the right pelvis.

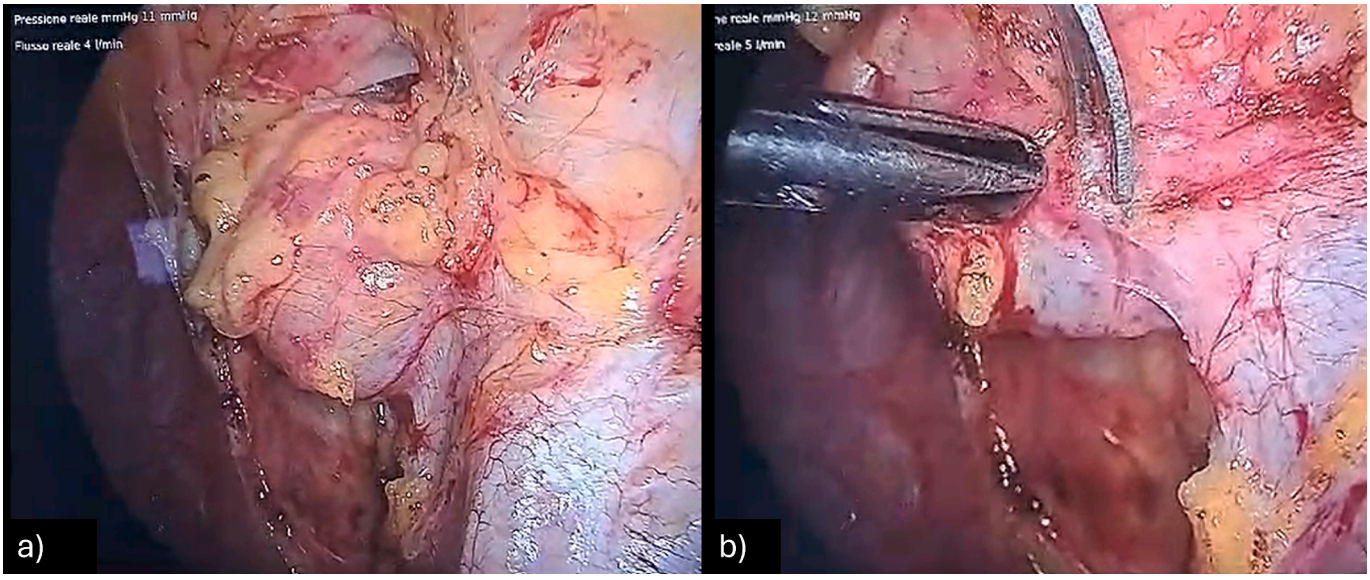

Fig. 4. Intraoperative imaging of the lymph node metastasis localized at the right inguinal canal entrance (a) and its removal with laparoscopic forceps (b).

of the patients.

In the context of laparoscopic cytoreductive surgery for AGCT, it is to note that the presence of residual disease significantly impacts the likelihood of recurrence. Specifically, a study by Gu et al. [30] involving 70 patients with recurrent AGCT found that suboptimal surgical outcomes, regardless of the surgical approach (laparotomic or laparoscopic), are associated with poorer survival rates. Additionally, Mangili et al. [31] highlighted that incomplete surgical staging (hazard ratio 1.23, 95 % confidence interval 1.02 to 2.28) serves as a predictor of recurrence in both univariate and multivariate analyses, while the choice of surgical approach—whether laparoscopic or laparotomy—does not seem to affect the recurrence rate. Supporting this, a meta-analysis [32] indicated no significant difference in overall survival between these two surgical approaches.

Moreover, regarding the role of repeated surgery on recurrence control, Gu et al. report that the residual disease primarily influences the recurrence frequency after each surgery [30]. Given the rarity of AGCT, the benefits and drawbacks of repeated laparoscopic surgery for managing recurrence mainly stem from case reports or small case series [33–35]. The existing literature indicates that this approach is feasible and can successfully achieve complete cytoreduction, allowing for quicker patient recovery and a timely start to adjuvant treatment. Additionally, it may simplify subsequent surgeries for any further relapses. In particular, Groeneweg et al.'s [33] study focuses on the robotic minimally invasive surgery performed on three patients of varying ages who experienced a first recurrence of AGCT. The recurrences observed

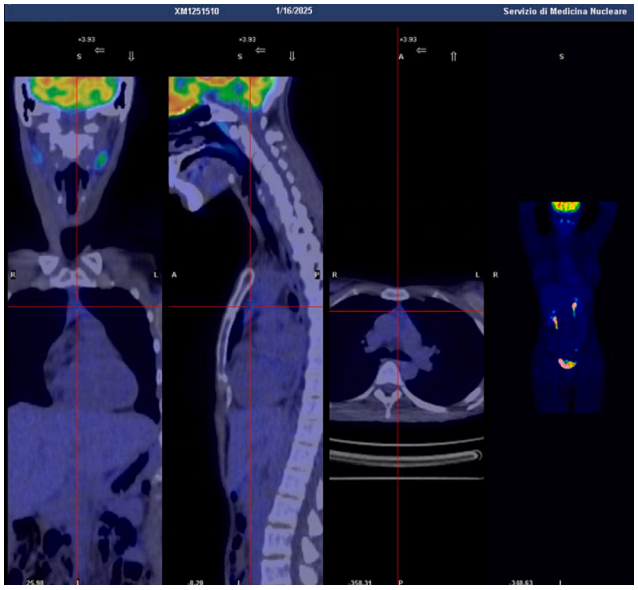

Fig. 5. PET/CT scan at the last follow-up 6 months after tertiary cytoreductive surgery. Images revealed no evidence of abnormal tracer accumulation in the examined body regions that could be associated with high metabolic activity disease locations.

were not due to significant abdominal spread of the cancer; rather, they involved isolated lesions that did not impact the abdominal organs. These lesions were successfully addressed through surface peritoneal surgery, assisted by a general surgeon. García Pineda et al. [34] describe a tertiary surgery for patients with recurrent AGCTs that have returned twice. The first intervention consisted of a laparotomy accompanied by adjuvant chemotherapy. The second surgery utilized minimally invasive robotic techniques to remove a single recurrence located in the sixth segment of the liver, measuring 2 cm. Ohta et al. [35] reported a case of recurrent AGCT occasionally found in the greater omentum, which was resected during a laparoscopic cholecystectomy. Despite the patient having undergone several prior surgeries and positron emission tomography showing no indications of malignancy, they opted to resect the tumor for both diagnostic and therapeutic purposes during the laparoscopic cholecystectomy. These reported cases have described scenarios that do not involve significant surgical extension or complexity.

Additionally, a recent study has shown that tumor morphology can influence various surgical approaches, regardless of the histological diagnosis or disease stage [36]. This finding opens new possibilities for laparoscopic surgery in advanced ovarian cancer, aiming to improve QoL.

In any case, none of these authors addressed the benefits that minimally invasive surgery may provide for QoL protection. We believe that these considerations are crucial when evaluating surgical options for procedures of such high technical complexity. Women with ovarian cancer often face body image challenges because of the extensive and complex nature of cytoreductive surgery [37], impacting family, work, and social roles [17]. Extensive surgery can significantly affect femininity, leading to anxiety regarding sexual interactions and physical pain [38]. Additionally, psychological effects from scarring, stomas, and hair loss can affect women's body image and contribute to psychosexual issues and straining relationships as roles shift from partners to patients or caregivers [39]. Although literature highlights poor QoL and postoperative outcomes, gaps remain in identifying the occupational performance demands for these women. This strain may lead to emotional withdrawal and contribute to anxiety and depression in both patients and their partners.

The current work introduces significant minimally invasive surgical techniques, specifically relating them to the limited findings on QoL, particularly in maintaining optimal body schema. In detail, this study presents a case of a young woman with recurrent AGCT who required minimized aesthetic impact alongside maximizing survival and QoL. After extensive discussions with the patient, maximal laparoscopic cytoreduction was performed multiple times, achieving optimal tumor reduction, as confirmed by several PET scans and specific tumor marker assays postoperatively. Three minimally invasive surgical procedures were conducted, achieving comparable aesthetic and functional outcomes. The patient reported high QoL following the procedures. The patient is currently disease-free and continues her professional activities with satisfaction.

4. Conclusions

This case report primarily focuses on a personalized treatment approach that replaces open surgery and traditional postoperative chemotherapy with multiple laparoscopic procedures for patients with recurrent ovarian granulosa cell tumors (AGCTs). This innovative method offers new insights for similar cases. However, due to limitations in patient data, the clinical implications of the report require further investigation. This approach considers the patient's professional needs and preferences, enabling her to maintain a high quality of life after surgery while achieving favorable survival outcomes. Our work emphasizes the importance of systematically exploring the role of minimally invasive surgery in complex cases of advanced or recurrent AGCTs. This perspective is supported by our case, other case reports, and the limited clinical series available in the literature.

Supplementary data

Supplementary Videos 1 and 2 can be downloaded at https://doi.org/10.5281/zenodo.14261766 (DOI 10.5281/zenodo.14261766).

Institutional review board (IRB) approval

Ethics approval by the Institutional Local Ethics Committee (Ethics Committee of the Sardinian Region) is not required for case reports. Written informed consent was obtained from the patient for publication and any accompanying images.

Clinical trial registration

NA

Consent

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

Guarantor

Antonio Macciò.

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None.

Author contribution

AM contributed to the conception and design of the study, acquisition of data, analysis and interpretation of data, writing the manuscript; VV contributed to acquisition of data, analysis and interpretation of data, drafting the manuscript; GS contributed to acquisition of data, analysis and interpretation of data, drafting the manuscript; SN

contributed to acquisition of data, analysis and interpretation of data, drafting the manuscript; EG, contributed to acquisition of data, analysis and interpretation of data, drafting the manuscript; CM contributed to acquisition of data, analysis and interpretation of data, and writing the manuscript. All authors have reviewed and approved the final article.

Declaration of competing interest

The authors declare no conflicts of interest.

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Data availability

Data are available from the corresponding author upon reasonable request.

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