

CASE REPORT

Disease-free survival following total pelvic exenteration in localized platinum-resistant recurrent ovarian clear cell carcinoma: a case report

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Abstract

Background: Ovarian clear cell carcinoma is highly resistant to chemotherapy and carries a particularly poor prognosis when recurrence is platinum-resistant. Although surgery is generally not recommended for recurrent epithelial ovarian cancer, aggressive surgical resection may be beneficial in cases of localized recurrence. This report describes a case of platinum-resistant recurrent ovarian clear cell carcinoma treated with total pelvic exenteration and small bowel resection, in which the patient remained recurrence-free for 14 months postoperatively. **Case:** A 37-year-old woman was diagnosed with recurrent ovarian clear cell carcinoma after initial surgery and chemotherapy. Imaging revealed a 70 mm pelvic mass with suspected invasion of the rectum, small intestine, and vagina, with no evidence of distant metastasis. The lesion progressed despite two cycles of gemcitabine-based chemotherapy. As the recurrence was considered localized, the patient underwent total pelvic exenteration with small bowel resection, ileal conduit urinary diversion, and sigmoid colostomy. Pathological examination confirmed recurrent clear cell carcinoma infiltrating the bladder, rectum, sigmoid colon, and small intestine. Genetic panel testing revealed high microsatellite instability and an elevated tumor mutational burden. Fourteen months post-surgery, the patient remained disease-free without receiving postoperative chemotherapy. **Conclusions:** This rare case describes successful long-term disease control in a young patient with platinum-resistant, locally recurrent ovarian clear cell carcinoma, in whom complete surgical resection was achieved through total pelvic exenteration and small bowel resection. This favorable outcome highlights the potential role of radical surgery in carefully selected cases of localized recurrence without evidence of distant metastasis.

Keywords

Ovarian clear cell carcinoma; Platinum-resistant recurrence; Total pelvic exenteration; Small bowel resection; MSI-high

1. Introduction

Ovarian clear cell carcinoma (OCCC) represents approximately 5–10% of all epithelial ovarian cancers, with a higher prevalence of 10–25% reported in the East Asian populations [1]. The recurrence rate of OCCC varies by stage, with rates of 6% in stage IA/IB, 14.6% in stage IC, and up to 54.8% in stage II–IV disease [2]. Recurrent ovarian cancer is classified based on the interval between the end of platinum-based therapy and the next administration of platinum-based agents, known as the platinum-free interval (PFI). A PFI of 6 months or more is defined as “platinum-sensitive recurrence”, while a PFI of less than 6 months is classified as “platinum-resistant recurrence” [3]. Although drug therapy is the mainstay of treatment for recurrent ovarian cancer,

secondary debulking surgery (SDS) may be considered in carefully selected patients with platinum-sensitive recurrence; randomized trials have shown that the survival benefit of SDS is highly contingent upon achieving complete (R0) resection, although trial results varied due to differences in patient selection, surgical selection criteria, and crossover design [4–6]. In contrast, SDS is generally not recommended for platinum-resistant recurrence because of limited resectability, poor prognosis, and the high invasiveness of surgery in this setting [7, 8]. However, several reports have suggested that, in highly selected patients with localized recurrence, aggressive surgical resection may confer survival benefit [9]. Here, we describe a case of platinum-resistant recurrent OCCC treated with total pelvic exenteration (TPE) and small bowel resection, in which the patient remained recurrence-free for 13 months

postoperatively. This case highlights the potential role of SDS in managing localized recurrence, even in platinum-resistant settings.

2. Case presentation

The patient was a 37-year-old woman (gravida 2, para 2), 159 cm in height and weighing 55 kg. Her medical and family histories were unremarkable. At initial presentation, she presented to a local internal medicine clinic with complaints of nausea and lower abdominal pain. Imaging revealed an intra-abdominal mass measuring 100 mm in diameter with partially solid components, accompanied by hypercalcemia (serum calcium: 12.5 mg/dL). Tumor marker levels, including cancer antigen (CA)125 (20 U/mL), CA19-9 (13 U/mL), and carcinoembryonic antigen (CEA) (0.3 ng/mL), were within normal limits. She was urgently referred to a gynecologist with suspected left ovarian torsion and underwent left salpingo-oophorectomy on the same day.

Postoperative pathology revealed primary clear cell carcinoma of the left ovary. Because the initial surgery was performed on an emergency basis for suspected ovarian torsion, and malignancy was not diagnosed preoperatively, systematic lymphadenectomy was not performed at that time. Immediately after surgery, her serum calcium level rapidly normalized. Although formal surgical staging was not performed, combination chemotherapy with paclitaxel (PTX) and carboplatin (CBDCA) was initiated (paclitaxel 175 mg/m² and carboplatin at an area under the curve (AUC) of 6). However, PTX was discontinued during the second cycle because of dyspnea, and CBDCA monotherapy (AUC6) was continued for a total of five cycles. After completion of five cycles of chemotherapy, she subsequently underwent total abdominal hysterectomy, right salpingo-oophorectomy, and partial omentectomy. No macroscopic tumor was detected intraoperatively, no tumor was identified histopathologically, and peritoneal cytology was negative.

Three months after completion of surgery, corresponding to approximately four months after completion of platinum-based chemotherapy, the patient again presented with nausea, and her serum calcium level had increased to 14.1 mg/dL. Pelvic Magnetic Resonance Imaging (MRI) and Computed Tomography (CT) revealed a 70 mm mass centered at the vaginal stump with suspected invasion of the small intestine and rectum (Fig. 1A). Because the recurrence occurred within four months of platinum-based chemotherapy, it was diagnosed as platinum-resistant recurrence. Given the suspected bowel invasion, two cycles of gemcitabine (GEM, 1000 mg) monotherapy were administered; however, the tumor continued to enlarge (Fig. 1B). GEM was selected as second-line therapy because it has demonstrated modest activity in platinum-resistant ovarian cancer, including ovarian clear cell carcinoma, and no specific non-platinum agent has shown clear superiority in this setting. Tumor marker levels remained within normal limits, and no signs of ascites or peritoneal dissemination were observed.

Although invasion into the mesentery of the small intestine, mesocolon, and vaginal wall was evident, the recurrence was considered localized. Multiple preoperative consultations

were held with the patient and her family to discuss the surgical rationale and procedure, the need for permanent colostomy and stoma care, anticipated postoperative quality of life, potential complications, and prognosis. After comprehensive informed consent was obtained, TPE was performed. In addition to TPE, an ileal conduit and sigmoid colostomy were constructed.

The tumor was adherent to and invading the small and large intestines, as well as the vagina and bladder wall. The small intestine was adherent in such a way that overlaid the tumor. To avoid tumor rupture and dissemination, no dissection was performed between the tumor and the invaded organs. Instead, the adherent segments of the sigmoid colon and small intestine were resected. Dissection was performed from the bilateral external iliac vessels to the retroperitoneal space, exposing the anterior bladder and posterior rectum. The bladder, retroperitoneum of the small pelvis, small intestine, and rectum were resected *en bloc* with the tumor (Fig. 2A,B).

Pathological examination confirmed recurrent clear cell carcinoma infiltrating the bladder, small intestine, and sigmoid colon, and all surgical margins were negative. Cancer gene panel testing of the resected specimen revealed high microsatellite instability (MSI-high) and elevated tumor mutational burden (TMB-high). Postoperatively, the patient developed a urinary tract infection, which resolved with antibiotic therapy. She was discharged on postoperative day 33. Fourteen months after TPE, without adjunct chemotherapy, there was no evidence of disease recurrence.

3. Discussion

Despite standard treatment with radical surgery and adjuvant chemotherapy, most patients with epithelial ovarian cancer eventually experience relapse. With each recurrence, sensitivity to platinum-based agents declines, leading to the development of platinum-resistant disease [1]. An optimal treatment strategy for platinum-resistant recurrent ovarian cancer has not yet been established. Non-platinum agents or combination regimens with bevacizumab are commonly used; however, response rates remain low (10–15%), with a median progression-free survival (PFS) of approximately 3 months and a median overall survival (OS) of about 12 months.

Against this background, SDS may be considered a treatment option for localized recurrence [2]. Two phase 3 trials have demonstrated that SDS can prolong OS, but exclusively in patients who achieve complete (R0) cytoreduction [5, 6]. In contrast, although no consensus exists regarding SDS in platinum-resistant cases, studies have shown that complete (R0) resection is associated with significantly improved OS and PFS compared with cases involving residual disease and may confer a survival advantage over chemotherapy alone [9].

Although no established model exists for predicting the feasibility of R0 resection in platinum-resistant recurrence, several factors, including good performance status (PS 0–1), three or fewer lesions, absence of peritoneal dissemination or ascites, low CA125 levels, and no residual disease after initial surgery, may indicate the potential to achieve R0 resection [7]. In this case, the patient was 37-years-old and in good general condition. No elevation of CA125 was observed, and imaging revealed no ascites or peritoneal dissemination. Recurrence

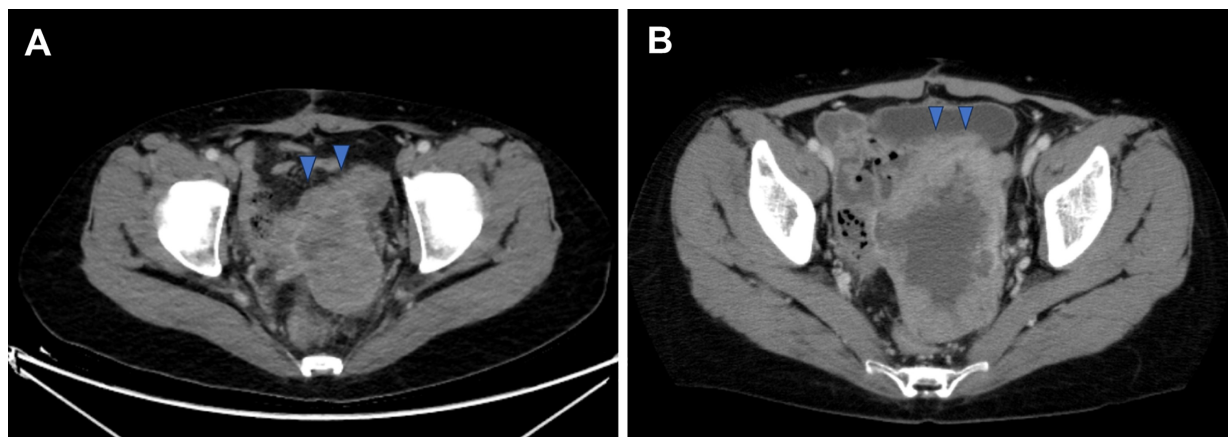


FIGURE 1. Contrast-enhanced computed tomography (CT), axial view. At the site of vaginal stump recurrence (A) and after completion of chemotherapy (B), the lesion had enlarged and exhibited internal necrosis.

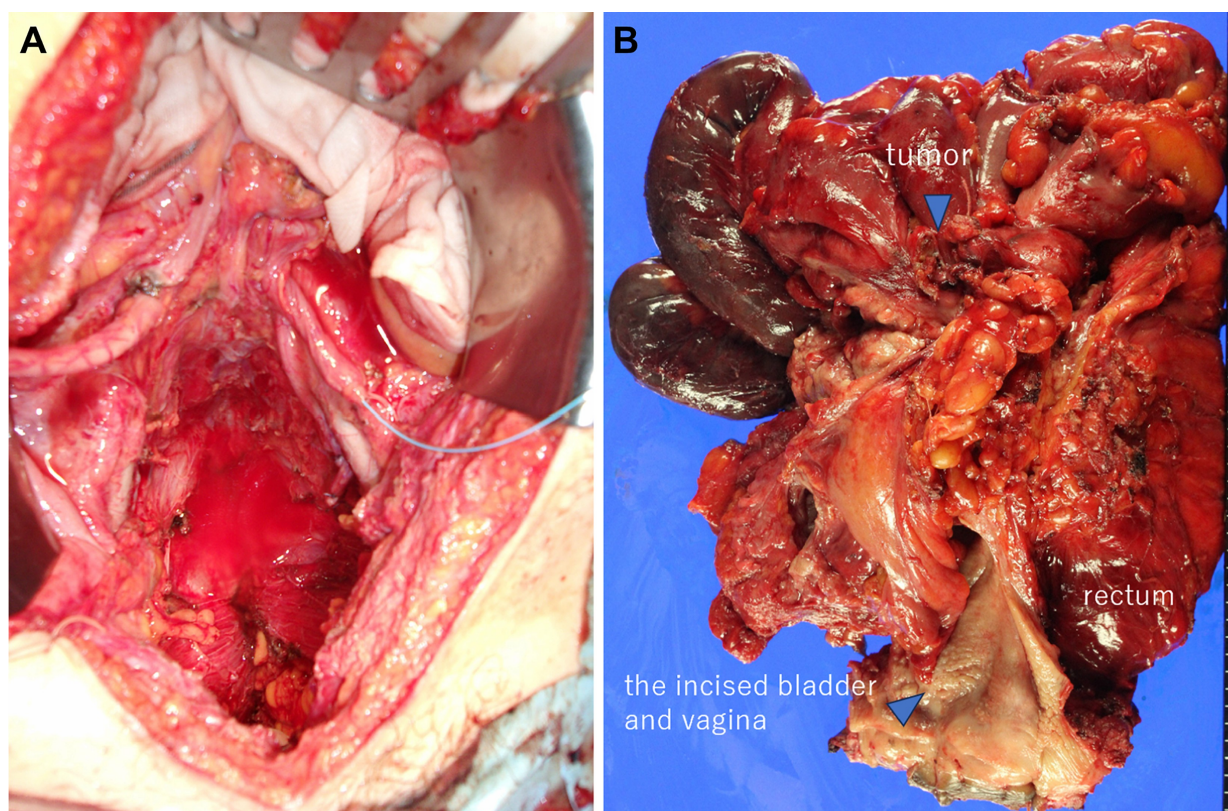


FIGURE 2. Intraoperative findings after tumor resection (A) and the corresponding surgical specimens (B). The bladder, vagina, small intestine, and colon were completely resected *en bloc*, with the tumor indicated by an arrow.

was localized to the pelvis.

TPE aimed at achieving R0 resection can be effective for gynecologic malignancies [10] and requires advanced surgical expertise and cross-disciplinary collaboration [8]. At our institution, these procedures are performed by a multidisciplinary team comprising gynecologic, gastrointestinal, and urologic surgeons, and a previous single-institution series from our center reported no operative mortality among 13 patients undergoing pelvic exenteration [11]. Recent studies suggest that pelvic exenteration, including TPE, may offer meaningful survival in carefully selected patients with recurrent gynecologic malignancies, with R0 resection consistently identified as a key prognostic factor [10, 12–14]. These findings suggest

that pelvic exenteration may be considered for localized pelvic recurrence when complete resection is feasible in experienced, multidisciplinary settings.

Additionally, this case involved clear cell carcinoma, which is highly resistant to chemotherapy compared with other epithelial ovarian cancer subtypes. Reported response rates to first-line platinum doublet chemotherapy range from 22% to 56%, markedly lower than the 70–80% typically observed in serous ovarian carcinoma [15]. In recurrent cases, response rates as low as 6–8% have been reported [16]. Nevertheless, SDS for platinum-resistant recurrence may improve oncologic outcomes by achieving complete cytoreduction and reducing tumor burden.

In this case, postoperative chemotherapy was not administered because R0 resection was achieved. Genomic testing of the resected specimen revealed MSI-high and TMB-high. Although MSI-high status is rare in clear cell carcinoma (approximately 2.3%) [17], immune checkpoint inhibitors (ICIs), such as pembrolizumab, may represent a potential therapeutic option in such cases [18]. Despite the MSI-high and TMB-high status, immune checkpoint inhibitor therapy was deferred because R0 resection was achieved and no evidence of residual disease was observed. These agents were reserved as potential treatment options in the event of future recurrence.

This report is limited by its single-case design, which restricts generalizability. In addition, selection bias is present because the patient had favorable clinical characteristics that allowed R0 resection, and the follow-up period remains relatively short.

4. Conclusions

This case highlights a rare but informative instance of platinum-resistant recurrent OCCC treated with TPE achieving R0 resection. The recurrence was localized, with no evidence of multifocal miliary peritoneal dissemination or ascites. The patient has remained recurrence-free for 14 months after surgery without adjuvant chemotherapy. These findings suggest that complete surgical resection alone may improve prognosis in carefully selected cases.

ABBREVIATIONS

CA125, cancer antigen 125; CBDCA, carboplatin; CEA, carcinoembryonic antigen; CT, computed tomography; GEM, gemcitabine; ICI, immune checkpoint inhibitor; MRI, Magnetic Resonance Imaging; MSI-high, microsatellite instability-high; OCCC, ovarian clear cell carcinoma; OS, overall survival; PFI, platinum-free interval; PFS, progression-free survival; PS, performance status; PTX, paclitaxel; SDS, secondary debulking surgery; TMB-high, tumor mutational burden-high; TPE, total pelvic exenteration; AUC, area under the curve.

AVAILABILITY OF DATA AND MATERIALS

The clinical data that support the findings of this case report are not publicly available due to concerns regarding patient privacy, in accordance with institutional and ethical guidelines.

AUTHOR CONTRIBUTIONS

NK—Conceptualization; Investigation; Writing—Original Draft. SS—Conceptualization; Writing—Review & Editing. AK, CO, HM, TS, YE, SF—Writing—Review & Editing. KF—Writing—Review & Editing; Supervision. All authors were involved in the patient's clinical care. All authors reviewed and approved the final version of the manuscript and take full responsibility for its content.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This is a single-patient case report based on routine clinical care. According to the policy of Fukushima Medical University and in accordance with the Declaration of Helsinki, ethical approval was not required for this type of study. Written informed consent was obtained from the patient for participation in this case report. Written informed consent was also obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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