

Long-term disease-free survival in three ovarian cancer patients with a single relapse

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Summary

Recurrent ovarian cancer with long-term survival is uncommon and often associated with poor prognosis. We report three cases of patients with advanced ovarian cancer who have achieved long-term disease-free survival following a single prior relapse. Case 1 relapsed with a localized bulky tumor and received a complete surgical resection and chemotherapy. Case 2 had a persistent central pelvic tumor after debulking surgery and second-line chemotherapy, and yet achieved excellent control with concurrent chemoradiation to the true pelvis. Case 3 relapsed with paraaortic lymph node metastasis and probable lung metastasis (subsequently negated by positron emission tomography) and received chemotherapy alone. These three patients have since remained disease-free for 13, 12, and seven years, respectively, since their first relapse. We conclude that select patients can obtain long-term disease-free survival after the first relapse by accurate restaging and aggressive multimodality treatment.

Key words: Disease-free survival; Ovarian neoplasm; Recurrence; Treatment outcome.

Introduction

Ovarian cancer is the sixth most common cancer among women worldwide [1]. In Taiwan, ovarian cancer ranks third in incidence among all cancers and is the leading cause of death among gynecologic malignancies [2]. Debulking surgery followed by six courses of platinum-based chemotherapy is the standard treatment. Complete clinical remission can be achieved in > 50% of cases following first-line therapy. However, these responders will relapse within an average of 18 months, and the majority will experience a series of treatments, remissions and recurrences [3, 4]. Thus, management of recurrent ovarian cancer is a great challenge for oncologists.

We report three patients who achieved prolonged disease-free survival following a single relapse of ovarian cancer managed by accurate restaging and aggressive multimodality salvage treatment.

Case Reports

Case 1

A 63-year-old woman was diagnosed in 1993 with Stage IIc epithelial ovarian cancer (EOC) and underwent maximal debulking surgery at a medical center. The tumor was classified histologically as clear cell carcinoma. After six cycles of cisplatin/cyclophosphamide chemotherapy, the patient had no evidence of disease. In 1998, she developed a ventral hernia, and a large mass 17 cm in diameter mixed with solid and cystic components was discovered within the anterior abdominal wall. Another lobulated soft mass of 5 cm was detected in the right abdomen. There was no evidence of metastasis elsewhere. The patient received en-bloc resection of the recurrent tumor involving fascia and muscle of the anterior abdominal wall, part of the

omentum, and a segment of small intestine (mid-ileum), as well as dissection of the paraaortic lymph nodes and appendectomy. Another tumor nodule (6 × 6 × 4 cm) was removed from the right paracolic gutter of the ascending colon and hepatic flexure. No visible residual tumor was noted. After this surgery, the patient was treated with six courses of paclitaxel/carboplatin. The patient has been regularly followed at our clinic with no evidence of disease.

Case 2

A 68-year-old woman was diagnosed in 1996 with Stage IIc EOC and underwent maximal debulking surgery at another medical center. The tumor was classified pathologically as clear cell carcinoma. After four courses of carboplatin/cyclophosphamide, the patient had no evidence of disease.

The patient's serum CA-125 level was found to be elevated in 1999, and second-look surgery found a cul-de-sac mass sized 10 × 10 cm. After three cycles of paclitaxel/carboplatin, the patient was referred to our hospital. She received en-bloc resection of the recurrent mass involving the sigmoid-rectal colon. There was no visible residual tumor except for within the vesicovaginal septum. After this surgery, the patient was treated with six courses of cisplatin/etoposide. In 2000, a tumor of the retro-vesicle region was palpated, and tissue obtained by Tru-cut needle biopsy showed metastatic clear cell carcinoma. The patient was treated with four courses of mitomycin/topotecan and concurrent radiotherapy. The radiotherapy was delivered to the low pelvis by four-field box technique at 4500 cGy in 25 fractions and boosted by intensity-modulated radiation therapy to the gross lesion for an additional 1440 cGy in eight fractions, for a total of 5940 cGy. The patient has been regularly followed and shows no evidence of disease at the time of this report.

Case 3

A 66-year-old woman was diagnosed in 2002 with Stage IIIc EOC and underwent only hysterectomy and bilateral salpingo-oophorectomy at a local hospital. The tumor was classified pathologically as endometrioid adenocarcinoma. After referral to our clinic, the patient received maximal debulking surgery

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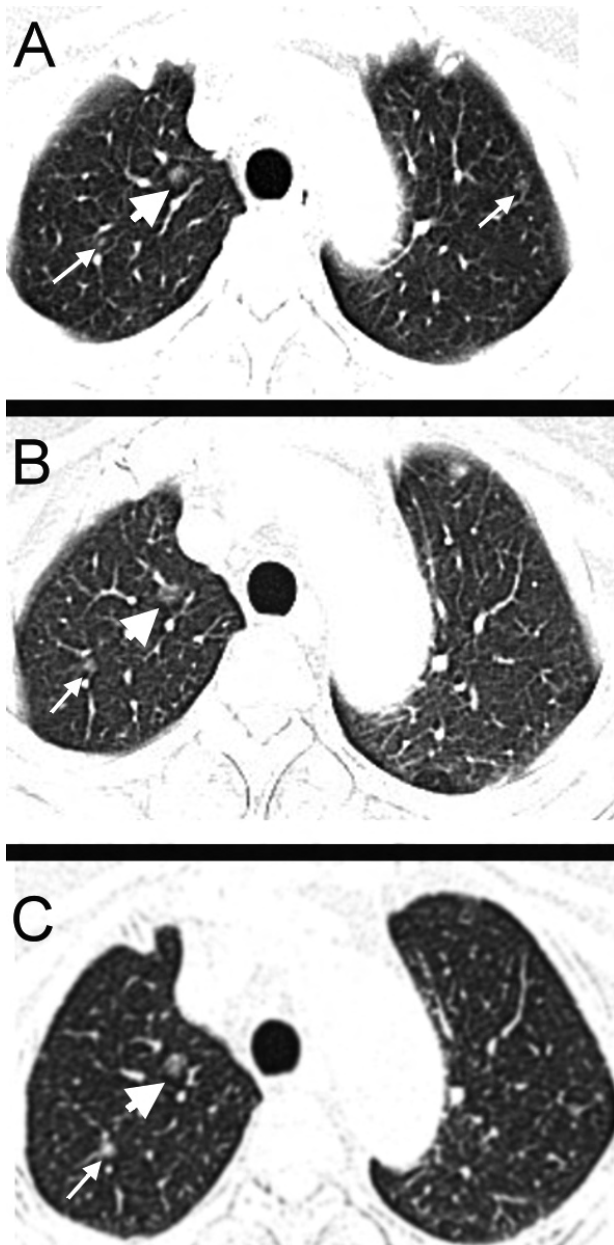


Figure 1. — (a) Multiple faint opaque nodules (arrows) were noted over the bilateral lung field measured by computed tomography (CT) at the first relapse (September, 2004). The largest lesion was located over the right upper lobe (arrowhead) and measured 6.1×5.4 mm. (b) Follow-up CT after treatment (December, 2005) shows multiple stationary lung lesions. The largest residual lesion (arrowhead) measured 6.4×5.8 mm. Serial follow-up CTs were conducted on August, 2007 and March, 2008). (c) Follow-up CT on April, 2011 shows a stationary lesion (arrowhead), which is likely to indicate a persistent granulation lesion resulting from an initial infection without clinical symptoms.

including excision of tumor infiltrating the right periureter, omentectomy, dissection of the bilateral pelvic-paraortic lymph nodes, appendectomy, and biopsies of multiple miliary implants (< 0.5 cm diameter) over the diaphragm, ileocecum,

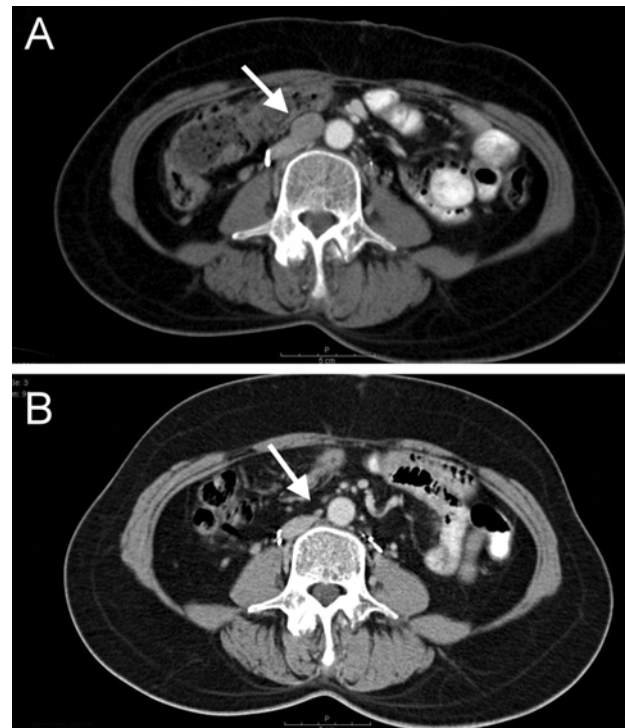


Figure 2. — (a) Enlarged right paraaortic lymph node (arrow) was detected by CT at the first relapse (September, 2004). (b) Follow-up CT after treatment (December, 2005) shows complete remission at the PA region (arrow), and serial follow-up scans on August, 2007, March, 2008, and April, 2011 show that the patient remains in remission.

and rectum. After six courses of paclitaxel/carboplatin the patient had complete remission.

In 2004, she presented with chronic cough and peri-umbilical tenderness and a serum CA-125 level elevated from 8.21 U/ml to 59.13 U/ml. Computed tomography (CT) showed multiple nodular lesions in the bilateral lung field (Figure 1a) and lymph node enlargement in the right paraaortic (PA) region (Figure 2a). F-18 fluorodeoxyglucose (^{18}F FDG) positron emission tomography-CT (PET-CT) showed metastasis of the right paraaortic lymph node at level L-4, of the paraaortic node at the bifurcation at level L-5, and of the right common iliac lymph node, but PET-CT did not show lung metastasis. The patient was treated with six courses of paclitaxel/carboplatin. After these treatments, she achieved complete remission (Figure 2b). She has been regularly followed without evidence of disease in the abdomen, and the lung lesions remain stationary (Figures 1b and c).

Discussion

Recurrent EOC is a chronic and lethal disease. The median survival ranges from 12 to 24 months after recurrence and the primary goal of management is palliation [4]. According to current guidelines, a carboplatin-based combination is strongly recommended for patients with platinum-sensitive disease rather than carboplatin monotherapy, although cumulative toxicity has been considered [5]. Some case reports suggest that aggressive treatment with cytoreductive surgery, chemotherapy, or

radiotherapy could improve survival even in patients with distant metastasis or with bulky tumors, if the therapy is tolerated by the patient [6, 7].

Secondary cytoreductive surgery for recurrent ovarian cancer remains controversial. Factors that affect survival after recurrence have been discussed. It is believed that secondary cytoreduction has a survival benefit in select platinum-sensitive patients. Chi *et al.* [8] suggested using the duration that the patient remained disease-free and the number of recurrence sites as selection criteria for offering secondary cytoreduction. They also suggested that the objective of secondary cytoreduction should be to achieve residual disease that measures less than 0.5 cm, which was associated with a significant survival benefit [3, 4, 8]. The disease-free interval from primary treatment to recurrence was over 50 months for Case 1 and 27 months for Case 2. The two cases had single-site recurrence and received optimal cytoreductive surgery.

The utility of PET-CT in detecting early recurrent ovarian cancer has been demonstrated. PET-CT had greater accuracy and less inter-observer variability than CT alone in detecting lesions in the abdomen (abdomen-pelvis) and in the body overall. PET-CT scanning may therefore have a significant impact on the clinical management of a patient [9, 10]. In Case 3, additional metastatic lymph nodes were detected by PET-CT, and over-diagnosis of lung metastasis was avoided.

Regional extra-peritoneal recurrence of ovarian cancer could be treated effectively by involving field radiation therapy (IFRT). IFRT in combination with optimal surgery can obtain 89% long-term control and 50% 5-year overall survival. IFRT induces less toxicity compared to traditional whole abdominopelvic radiation therapy [11]. Case 2 had excellent control of a persistent central pelvic tumor with concurrent chemoradiation to the true pelvis after the second debulking and chemotherapy.

In conclusion, long-term disease-free survival after the first relapse is achievable by tumor reductive surgery, platinum-based chemotherapy, and/or radiotherapy for selected patients with recurrent ovarian cancer.

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