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CASE REPORT

Use of Bevacizumab in Combination with Chemotherapy in Ovarian Cancer in a Community Practice Setting

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ABSTRACT

Although ovarian cancers tend to be fairly chemo-responsive initially, the difficulty facing clinicians is maintaining or prolonging the duration of disease control. In recent clinical trials, adding bevacizumab to standard chemotherapy and using bevacizumab in maintenance regimens has shown promising results in terms of improving progression-free survival in women with advanced ovarian cancer. In this report, four patients treated with bevacizumab in a community practice setting are presented to illustrate the typical clinical responses that may be achieved by incorporating this targeted agent into the treatment strategy.

Key Words: *Bevacizumab; Drug therapy, combination; Ovarian neoplasms; Treatment outcome*

中文摘要

在社區治療層面上使用bevacizumab聯合化療作卵巢癌的治療

陸凱祖

雖然卵巢癌往往在起初階段對化療有反應，醫生所面對的困難卻是如何維持或延長疾病控制的時間。最近的臨床試驗顯示在標準化療的過程中加入bevacizumab，以及在之後的維持療程當中使用bevacizumab，都可以改善晚期卵巢癌患者的無進展存活期。本文報告在社區治療層面上在四名患者的療程策略中加入bevacizumab之後的典型臨床反應。

INTRODUCTION

The anti-angiogenic agent bevacizumab has been shown in clinical trials to improve progression-free survival when used with standard chemotherapy as first-line therapy for advanced ovarian cancer,[1,2] as well as for treatment of relapsed disease.[3,4] This report describes four patients with ovarian cancer treated with bevacizumab in a community practice setting. The aim of these reports was to illustrate some of the difficulties of treating ovarian cancer, as well as the typical responses obtained by incorporating bevacizumab into the treatment strategy.

CASE REPORTS

Patient 1

In May 2005, a 56-year-old woman underwent a total abdominal hysterectomy and bilateral salpingo-oophorectomy (TAH/BSO) for endometriosis. Approximately four years later, she developed an elevated cancer antigen–125 (CA-125) level (330 kU/L; reference level <35 kU/L), and positron emission tomography / computed tomography (PET-CT) scan revealed a 5-cm pelvic mass. The patient underwent debulking surgery and was diagnosed with adenocarcinoma of the ovary. As debulking surgery

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was judged to be suboptimal, she received six cycles of carboplatin and paclitaxel (CP), which caused good tumour regression. However, in July 2011, her CA-125 level rose again, and a repeat PET-CT showed that she had developed extensive lymph node metastases in the para-aortic, mediastinal, and neck nodes. After completion of six cycles of CP plus bevacizumab, commenced in August 2011, maintenance therapy with bevacizumab was given every two weeks to April 2012. The patient's CA-125 levels declined rapidly and markedly (Figure 1) and the tumours regressed; response to therapy has been sustained to date.

Patient 2

A 43-year-old woman with a right ovarian mass was treated in June 2008 with TAH/BSO plus omentectomy, followed by six cycles of CP. Stage I clear-cell ovarian carcinoma was diagnosed; clear-cell carcinoma is of particular interest in Asia as clinical experience suggests it is more common in Asian women than in western populations. In addition, clear-cell carcinoma is relatively insensitive to chemotherapy and thus has a poor prognosis.[5] Although tumour regression was achieved after the initial chemotherapy, a rise in CA-125 levels to 490 kU/L in August 2010 indicated disease relapse, with diffuse peritoneal metastases found on laparotomy. Neither five cycles of CP nor three cycles of pegylated liposomal doxorubicin (PLD) achieved a clinical response. Multiple peritoneal metastases were visible on CT imaging, with the largest being 7.6 cm in diameter. In October 2011, the patient started treatment with carboplatin, gemcitabine, and bevacizumab for six cycles, followed by maintenance therapy with bevacizumab alone. A good response was achieved, and her CA-125 level declined rapidly and remained low for a prolonged period (Figure 2). A CT scan in January 2012 showed most of the peritoneal and presacral metastases had resolved. A few months later, the patient complained of right upper quadrant (RUQ) discomfort. CT investigation revealed a right perihepatic mass. Chemotherapy was recommenced using irinotecan plus bevacizumab, which has caused a gradual decline in CA-125 levels and relieved much of the RUQ pain.

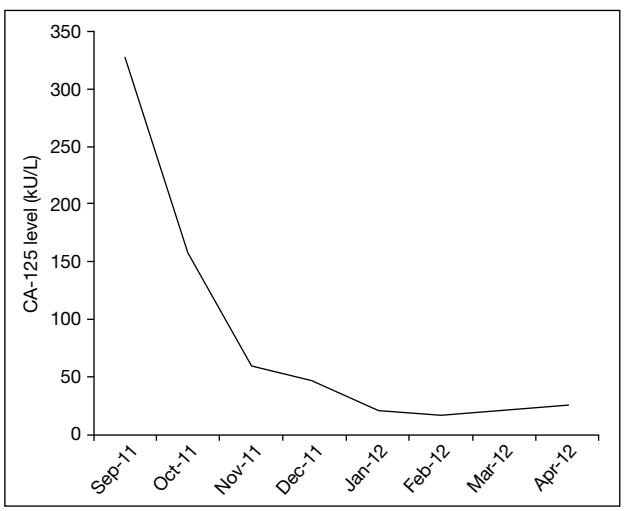

Figure 1. Decline in cancer antigen–125 (CA-125) levels with chemotherapy plus bevacizumab in a patient with advanced ovarian cancer.

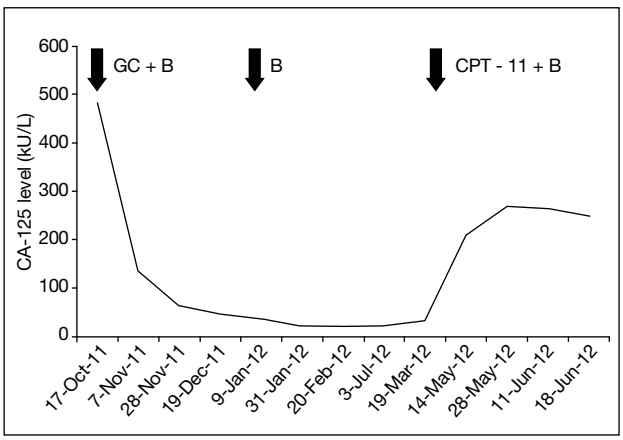

Figure 2. Change in cancer antigen-125 (CA-125) levels in response to chemotherapy plus bevacizumab in a patient with clear-cell carcinoma of the ovary.
Abbreviations: GC + B = carboplatin, gemcitabine, plus bevacizumab; B = bevacizumab; CPT-11 + B = irinotecan plus bevacizumab.

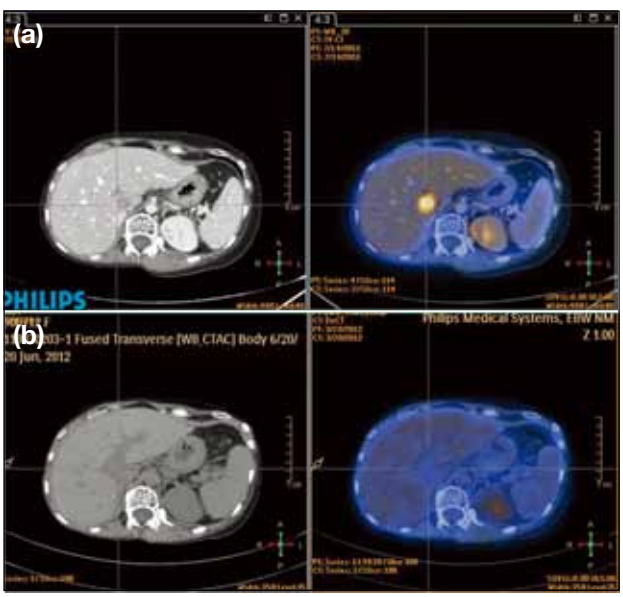

Figure 3. Computed tomography images from (a) July 2011 and (b) June 2012 showing excellent tumour regression after four cycles of carboplatin, pemetrexed, and bevacizumab followed by pemetrexed and bevacizumab maintenance therapy.

Patient 3

A 46-year-old woman was treated in May 2007 for stage III serous cystadenocarcinoma of the right ovary with TAH/BSO plus omentectomy followed by adjuvant chemotherapy (six cycles of CP) to address gross residuals. After abdominal relapse in August 2010, she was treated sequentially with CP, PLD, and gemcitabine. Subsequently, a clinical response was maintained for about one year. In November 2011, the patient developed gross abdominal distension as a result of bowel obstruction and ascites; emergency decompression with colostomy was performed. In December 2011, carboplatin, pemetrexed, and bevacizumab therapy was initiated for this patient. Four cycles of this regimen achieved a good response in terms of both tumour regression on CT scans (Figure 3) and an almost undetectable CA-125 level (from an original level of 830 kU/L). The patient is receiving maintenance therapy with pemetrexed and bevacizumab, and is currently enjoying excellent overall health.

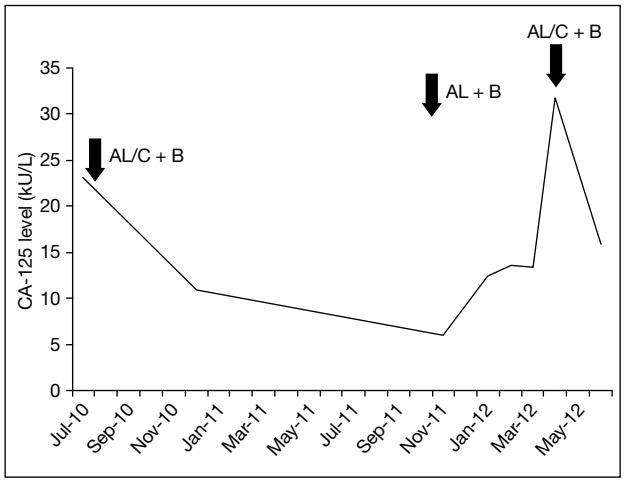

Figure 4. Change in cancer antigen-125 (CA-125) levels in response to chemotherapy plus bevacizumab in a patient with stage III serous ovarian carcinoma.
Abbreviations: AL/C + B = carboplatin, pemetrexed plus bevacizumab; AL + B = pemetrexed plus bevacizumab.

Patient 4

A 49-year-old woman was diagnosed with stage III serous ovarian carcinoma in May 2009 and underwent TAH/BSO and omentectomy. Debulking was considered suboptimal so the patient was given six cycles of CP, ending in December 2009. About six months later, her CA-125 level rose to 25 kU/L and magnetic resonance imaging of the abdomen showed a large lobulated mass in the right pelvic area. The patient was prescribed with carboplatin, pemetrexed, and bevacizumab, and achieved an excellent result with complete clinical and serological responses. She continued with a maintenance regimen of pemetrexed and bevacizumab until May 2012, during which time she was asymptomatic. A CA-125 level rising to 30 kU/L detected in April 2012 prompted the addition of carboplatin to the regimen, which is successfully lowering the patient's CA-125 level.

CONCLUSION

Although ovarian cancers tend to be fairly chemo-responsive initially, maintaining or prolonging the duration of disease control is often challenging. Clinicians in the community setting need to draw upon the experience of clinical investigators in order to utilise the available medications for maximum benefit. Incorporating a targeted agent namely bevacizumab into chemotherapy regimens as well as maintenance regimens has shown promise in terms of prolonging the duration of disease control after relapse in women with ovarian cancer.

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