



## Case Report

## Abdominal wall perforation in a patient with recurrent epithelial ovarian cancer after bevacizumab treatment

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## ABSTRACT

Bowel perforation is a rare but well-described complication of bevacizumab, a VEGF monoclonal antibody. However, bevacizumab associated abdominal wall perforation is a more serious complication. In here, a patient with recurrent epithelial ovarian cancer developing both bowel and abdominal wall perforation after bevacizumab treatment is reported with review of the literature to point out the clinical significance of this rare complication. To our knowledge, this is the first case with bevacizumab associated abdominal wall perforation.

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## 1. Introduction

Bevacizumab is a recombinant humanized monoclonal antibody against vascular endothelial growth factor (VEGF) leading to angiogenesis inhibition.<sup>1</sup> Hypertension, proteinuria, bleeding, thrombosis and delayed wound healing are well-known side effects.<sup>2</sup> Gastrointestinal perforation is the most serious adverse effect with an incidence rate of 15%.<sup>3</sup> However, abdominal wall perforation following bevacizumab containing treatment is almost rare. To our knowledge, it has not been reported anywhere else.

## 2. Case report

A 48-year old female with pelvic mass underwent a major surgery for ovarian cancer. Total abdominal hysterectomy, bilateral salpingo-oophorectomy, pelvic & para-aortic lymphadenectomy, omentectomy, segmental colon resection with end to side anastomosis and appendectomy were applied for optimal surgery.

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Pathology revealed stage IIIc papillary serous ovarian cancer. Following two courses of adjuvant chemotherapy with carboplatin and paclitaxel, she was operated twice within three months for intra-abdominal abscess and vesicovaginal fistula, respectively. Therefore, she could not have completed adjuvant six courses of carboplatin and paclitaxel. After a sixteen months of disease free survival, she had multiple intra-abdominal nodal recurrence. She received carboplatin and pegylated liposomal doxorubicin for a total of 6 courses and had stable disease for eleven months. Thereafter, she had multiple liver metastases with high level of Ca125 (1660 U/ml). She was given topotecan & bevacizumab (topotecan 4 mg/m<sup>2</sup> on day 1 and 8, bevacizumab 10 mg/kg on day 1, every 3 weeks). After a total of 6 courses, she had stable disease with a Ca125 level of 400 U/ml. She was admitted to the hospital with fever and cough after a week. On physical examination, the temperature was 38.8 °C, the arterial blood pressure was 100/60 mmHg and the heart rate was 144 beats/min. She had widespread candidal plaques in the oral cavity and bilateral basal crepitant rales. Laboratory studies revealed neutropenia and thrombocytopenia. A chest radiography showed bilateral consolidations on lower lobes. The cultures of the blood and sputum both yielded *Escherichia coli*. After a week of antibiotics, she had sudden onset of severe abdominal pain. On abdominal computed tomography, there was fluid accumulation with air-fluid levels in the left upper quadrant of the abdomen. Bowel perforation with formation of intra-abdominal abscesses was suspected inspite of no contrast



**Fig. 1.** Massive necrosis of suprapubic area involving the entire skin thickness and stool-like secretion.

agent outside of the bowel lumen. On the second day, physical examination revealed a suprapubic skin defect with a diameter of  $25 \times 10$  cm and malodorous stool-like secretion (Fig. 1). Because of rapid deterioration of vital signs leading to the diagnosis of sepsis, she was referred to the Intensive Care Unit. Transverse colon perforation with a diameter of 2 cm was seen on abdominal exploration. It was repaired with a prophylactic colostomy. The cultures of the blood and abdominal abscess grew various organisms including *Escherichia coli*, *Bacterioides fragilis* and *Candida albicans*. She was given antifungal therapy with antibiotics. However, she died after 2 months of follow-up despite these efforts.

### 3. Discussion

Bevacizumab, a monoclonal immunoglobulin G1 antibody targeting VEGF has anti-angiogenic activity in various types of solid tumors including ovary.<sup>4,5</sup> Bowel perforation is an uncommon but well-documented adverse effect of bevacizumab. It has been established that the highest incidence of bevacizumab-associated bowel perforation is observed in the patients with ovarian cancer.<sup>6</sup> Predicting risk factors associated with bowel perforation in ovarian cancer patients treated with bevacizumab remains a challenge. Potential risk factors are bowel obstruction, bowel involvement on computed tomography, bowel resection during primary surgery, history of treatment with inflammatory bowel disease, platinum-resistant disease and number of previous chemotherapy

regimens.<sup>7–10</sup> Our patient had no inflammatory bowel disease, bowel obstruction or bowel involvement. However, operation for intra-abdominal abscess and vesicovaginal fistula might have been risk factors for bowel perforation.

The mechanism of bevacizumab-induced bowel perforation is unclear. However, anti-VEGF effects of bevacizumab on bowel perfusion, direct bowel involvement or the regression of normal blood vessels leading to an increased possibility of cell damage, necrosis, and perforation might have been possible mechanisms.<sup>10</sup> Our patient had both bowel and abdominal wall perforation simultaneously. We consider that the mechanisms of abdominal wall perforation are presumably similar to those in gastrointestinal perforation. Formation of enterocutaneous fistula after bowel perforation might have contributed to bowel and abdominal perforation. To our knowledge, our patient is the first case who developed abdominal wall perforation after bevacizumab treatment. We consider that the clinicians should be aware of this fatal complication of bevacizumab, especially in those with recurrent epithelial ovarian cancer.

### Conflicts of interest

The authors indicated no potential conflicts of interest.

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