

# Spontaneous rectovaginal fistula during bevacizumab therapy for ovarian cancer: a case report

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**B**evacizumab is a monoclonal antibody that targets the vascular endothelial growth factor receptor. It has been reported to improve overall survival in metastatic colorectal cancer.<sup>1,2</sup>

Two recent phase II studies have reported that bevacizumab is active in patients with recurrent ovarian cancer.<sup>3,4</sup>

However, bevacizumab is associated with some side effects. Gastrointestinal or spontaneous bowel perforations and delayed postoperative fistulae have been described for metastatic colorectal cancer.<sup>5</sup> Few data are available on its use as an adjuvant treatment for ovarian cancer. No cases of fistulae have been described with the use of bevacizumab for ovarian cancer.

Here we report the first case of a rectovaginal fistula occurring 2 months after debulking surgery with colorectal resection in which bevacizumab may have contributed to the fistula formation.

## CASE REPORT

A 45-year-old woman was referred under suspicion of ovarian cancer. Apart from a conservative hysterectomy, she had an unremarkable medical history. Physical examination, sonography, and a computed tomography (CT) scan showed an ovarian tumor with voluminous ascites and peritoneal carcinomatosis. The CA-125 serum

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Recent studies have demonstrated efficacy of bevacizumab for recurrent ovarian cancer, but few data on its use and gastrointestinal potential complications when administered as adjuvant chemotherapy after cytoreductive surgery are available. In this study, we report the first case of a rectovaginal fistula in this indication.

**Key words:** antiangiogenic chemotherapy, bevacizumab, colorectal resection, ovarian cancer, rectovaginal fistulae

level was 7000 U/L. The patient underwent initial laparoscopy, which confirmed the possibility for optimal cytoreductive surgery. We performed a posterior pelvicotomy with terminoterminal anastomosis, bilateral salpingo-oophorectomy, appendectomy, omentectomy, right diaphragmatic peritoneal stripping, bilateral pelvic and paraaortic lymphadenectomy, cholecystectomy, and small bowel resection. During the course of the surgery, a cuff vaginal resection was carried out. At the end of the surgery, the patient had no residual disease.

Histology showed a stage IIIC ovarian cancer with metastatic involvement in 10 of the 43 nodes removed.

The oncological committee recommended adjuvant chemotherapy with bevacizumab.

The first course of chemotherapy was administered 35 days after surgery and the second at 50 days. After 2 cycles of bevacizumab, the patient complained of passing flatus and feces per vagina. Clinical exam and CT scan revealed an obvious rectovaginal fistula (Figure). There was no evidence of local recurrence. The third course of chemotherapy was done without bevacizumab. The rectovaginal fistula healed spontaneously.

## COMMENT

In a review of the literature on late bowel complications with treatment with bevacizumab,

**FIGURE**  
Rectovaginal fistula on CT scan



Air pocket in the vagina (white arrow).

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TABLE

## Clinical characteristics of patients with delayed anastomotic complications under treatment with bevacizumab

Reference	Cancer type	Surgery	Radiotherapy	Evolutive disease	Local recurrence	Anastomotic fistula	Interval between surgery and complication (mo)	Duration of bevacizumab (wk)
August et al <sup>6</sup>								
Case 1	Rectum	Yes, anastomotic leak	Yes	Yes	Yes	Yes	26	6
Case 2	Rectum	Yes	Yes	Yes	No	Yes	33	20
Case 3	Rectum	Yes	No	Yes	No	Yes	5	14
Wolf et al <sup>7</sup>								
Case 1	Rectum	Yes	Yes	Yes	Yes	Yes	3.5	6
Case 2	Rectum	Yes	Yes	Yes	Yes	Yes	4.5	2
Adenis et al <sup>8</sup>	Rectum	Yes, anastomotic leak	Yes	Yes	No	Yes	30	3
Ley et al <sup>9</sup>	Rectum	Yes, posterior vaginectomy	Yes	Yes	No	Yes	32	24
Present case	Ovary	Yes, posterior vaginectomy	No	No	No	Yes, spontaneous healing	2	4

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zumab (Table), perforations or fistulae have been reported for colorectal cancer but not for ovarian cancer. In the 7 published cases of late gastrointestinal complications, 2 risk factors were identified: progressive local disease<sup>6-9</sup> and radiotherapy. A review article<sup>10</sup> reports 16 perforations in 298 ovarian cancer patients. As observed for colon cancer, all the patients had progressive disease. Perforations may be caused by necrosis of the tumor with weakening of the intestinal wall.

Two particular aspects of our case report deserve special mention. First, there was no evidence of local active disease. Second, the patient did not receive radiotherapy. Therefore, the fistula could not be related to the risk factors reported in colon carcinoma. The only risk factor of rectovaginal fistulae was the opening of the vagina during surgery. However, postoperative anastomotic leakage usually occurs soon after surgery; the largest series to study rectosigmoid resection for ovarian cancer<sup>11</sup> reported that the mean interval was 19 days (range, 4-32).

Some authors recommend a free interval of at least 30 days between surgery and bevacizumab treatment.<sup>5</sup> Our patient received the first course at 35 days, and there

was no rectovaginal fistula when chemotherapy was initiated. Therefore, the use of bevacizumab seemed to be the most evident risk factor.

In light of this complication, some precautions should be proposed: first, the initiation of bevacizumab treatment should be delayed until the second cycle of chemotherapy, as is recommended in some clinical trials. Second, an ileostomy may be proposed for dysfunction of the distal colorectal anastomosis, as has been suggested by Richardson et al<sup>11</sup> for selected patients after rectosigmoid resection for ovarian cancer.

In conclusion, this case report raises the issue of the specific risk of chemotherapy with bevacizumab for ovarian cancer patients with bowel resection. ■

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