Spontaneous rectovaginal fistula during bevacizumab therapy for colon cancer

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Dear Editor:

In October 2011, a 61-year-old female presented with a painless rectovaginal fistula. Nine years ago she underwent a right colectomy due to ascending colon cancer. Follow-up revealed hepatic metastasis treated initially with chemotherapy folinic acid–fluorouracil–irinotecan (FOLFIRI)/FOLFOX within a clinical assay followed by metastasectomy in June 2003. In September 2004 and due to a lung metastasis, treatment of FOLFIRI and cetuximab was started with partial response and being resected in March 2006. In July 2007, another lung lesion was diagnosed and again resected. In February 2008, she presented an unresectable systemic disease (lung and liver) starting bevacizumab plus FOLFIRI due to persistence of residual neurotoxicity. Partial disease control was gained after six courses and withdrew after 12 courses of chemotherapy. In March 2009, the disease again progressed and the same treatment was reintroduced with a partial disease control after other six courses. These courses were intermittently administered until October 2011. The reasons for this intermittent regime were twofold: due to drug-toxicity and on patient demand. After the last six courses of FOLFIRI and bevacizumab, she complained in October of 2011 of foul-smelling discharge from her vagina without other symptoms. At exploration she presented a low rectovaginal fistula with no

evidence of local tumor in rectum and vagina. No history of trauma was related. A full thickness endoanal repair was performed in November after withdrawal of bevacizumab 4 weeks before. She denied a colostomy.

Bevacizumab is the most common antiangiogenic agent used for treatment of metastatic colorectal cancer. Gastrointestinal or spontaneous bowel perforations and postoperative fistulae have been related to this drug.

Rectovaginal fistulas have been associated with prior rectal cancer surgery. The double-stapling technique for rectal anastomosis and a partial vaginectomy increases the incidence of the disease. Radiation in rectal cancer is another source of rectovaginal fistula with a 0.3 to 6 % incidence. Gynecologic surgery in ovarian cancer treated with bevacizumab, especially if there is rectovaginal nodularity, seems to increase the risk of perforation or fistula formation and have been lately reported. A very recent study identified nine patients (4.1 %) out of 222, having six patients with rectal cancer, one with synchronous colorectal cancer, and two with colon cancer. Two thirds had anal fistulas and one third colovesicular fistulas. Cessation of bevacizumab led to fistula healing in six cases, but three required fecal diversion. In this paper, development of fistula appeared soon after initiation of bevacizumab. Spontaneous healing after bevacizumab withdrawal has been reported in other papers too.

Therefore, the particular aspects of this case are: surgery of a right colon cancer 9 years ago and no radiotherapy; long history of systemic disease with intermittent courses of bevacizumab since 2008 until presentation of a spontaneous rectovaginal fistula. Timing of fistula development is more likely secondary to bevacizumab therapy although the appearance of a rectovaginal fistula is late.

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