Nasal Septum Perforation in a Bevacizumab-Treated Patient with Metastatic Breast Cancer

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A 54-year-old woman with hormone-sensitive, HER-2/neu-normal, metastatic breast cancer developed progression of disease after 6 years of sequential hormone-targeted therapies and one line of chemotherapy with capecitabine. One year ago, she began weekly paclitaxel (70 mg/m²). Eight months later, bevacizumab (Avastin®; Genentech, Inc., South San Francisco, CA), 10 mg/kg every 2 weeks, was added based on data suggesting a superior response rate and longer disease-free survival from this combination in metastatic breast cancer [1, 2].

After 2–4 cycles of bevacizumab in combination with paclitaxel, our patient developed rhinorrhea, nasal irritation, occasional blood-streaked discharge, and alopecia of the nasal passages. After the sixth cycle of bevacizumab with chemotherapy, she incidentally noted a “hole in her nose.” Her symptoms had increased to include nasal congestion, epistaxis, and rhinorrhea, which led to frequent nose blowing. Her past medical history included rosacea, benign positional vertigo, Raynaud’s phenomenon, and prior breast cancer treatment as mentioned above. Her family history is remarkable for a mother with premenopausal breast cancer and a brother with colorectal cancer. She denied use of nasal sprays or cocaine. She was without signs or symptoms of infection and denied recent travel or trauma/instrumentation of the nasal passages.

Anterior rhinoscopy and examination by a head and neck surgeon revealed a large perforation involving the anterior inferior portion of the nasal septum (Fig. 1). The upper septum strut and the columellar strut were intact. A computed tomography scan of the sinus confirmed this defect (Fig. 2). There was no radiographic evidence of acute sinusitis, inflammation, or mass.

Vascular endothelial growth factor (VEGF) is a proangiogenic molecule that has been implicated in several steps throughout normal and pathologic angiogenic processes [3]. Bevacizumab, a humanized monoclonal antibody directed against VEGF, has significant activity against many solid tumors [4–8]. Bevacizumab is associated with a 1% risk for bowel perforation in gastrointestinal malignancy, and this has been reported in several women undergoing treatment for ovarian cancer [5, 9]. Similarly, a greater number of wound-healing complications has been observed in patients undergoing major surgery during bevacizumab treatment [10].

Nasal septum perforation is rare [11], although its possible association with bevacizumab use has been described once before in the literature [12]. Our case report is the second reported occurrence and supports the potential association among bevacizumab use, concurrent chemotherapy, and nasal septum perforation. The nasal septum is vulnerable to perforation when mucosal irritation or laceration exposes underlying avascular cartilage. Nasal cartilage relies upon the overlying mucoperichondrium for its blood supply and nutrients. Several risk factors for nasal septum perforation have been described, including traumatic injury, cocaine abuse, inhaled irritants, inflammatory states (Wegener’s granulomatosis, tuberculosis), and infections (tuberculosis, abscess); however, our patient lacked these typical risk factors.

Our patient received aggressive supportive measures with humidified air, intranasal saline spray, lubricant, and antihistamines. Bevacizumab was discontinued and her symptoms are slowly improving. Our management differed from that of the previous report of bevacizumab-associated nasal septum perforation, in which a patient with colon cancer continued to receive chemotherapy in combination with
bevacizumab. Chronic complications of nasal septum perforation can include audible whistling on inspiration from turbulent airflow through the defect, collapse of the nasal bridge from large anterior defects, and a sensation of nasal congestion resulting from impaired turbulent airflow. The appropriate treatment modification of bevacizumab and/or chemotherapy in the setting of nasal septum perforation is unclear; however, a conservative approach in this patient led to wound healing and symptomatic improvement.

We hypothesize that chemotherapy in combination with bevacizumab has contributed to the nasal septum defects described. Alopecia associated with taxane therapy may impair an otherwise intact mucosal defense mechanism. Nasal irritation and rhinorrhea resulting from chemo-therapy can be exacerbated by frequent nose blowing and mechanical tissue trauma, leading to mucosal abrasions. Angiogenesis-dependent wound healing is impaired in the setting of anti-VEGF therapy, which in turn leads to increased irritation, epistaxis, and perforation of the exquisitely vulnerable, avascular, nasal cartilage.

As increasing numbers of patients are receiving bevacizumab, oncologists should be aware of this potential bevacizumab-associated complication.

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DISCLOSURE OF POTENTIAL CONFLICTS OF INTEREST
The authors indicate no potential conflicts of interest.

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