Subcutaneous implantable venous access device erosion through the skin in patients treated with anti-vascula endothelial growth factor therapy: a case series

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Subcutaneous implantable venous access devices (IVADs) are commonly used in oncology practice. They facilitate the administration of chemotherapy, fluids and blood products. The incidence of IVAD-related complications is not uncommon, and includes infection, thrombosis and bleeding. IVAD erosion through the skin has been reported secondary to infection or inexperienced handling. We report three cases of IVAD erosion through the skin in patients treated with anti-vascular endothelial growth factor therapy. Anti-vascular endothelial growth factor agents are increasingly used in the treatment of solid tumors. This class of drugs has been associated with delayed wound healing and thromboembolism. To our knowledge, this is the first case series of IVAD erosion through skin, in patients receiving such therapy.

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Introduction

Implantable venous access devices (IVADs) are widely used in oncologic patients. These devices are convenient, easily accessible and facilitate the administration of chemotherapy or blood products. Several reviews have described various immediate and long-term complications of such devices, including infection, vascular injury, thrombosis and bleeding [1,2]. Erosion through the skin is a rare complication of IVAD and is felt to be related to infection, improper placement techniques by interventionists or improper port handling by medical personnel.

Vascular endothelial growth factor (VEGF) monoclonal antibodies have gained in interest in recent years, and are used in the treatment of different types of cancers.

Bevacizumab is approved by the United States Food and Drug Administration for use in combination with standard chemotherapy in the treatment of metastatic colon cancer and metastatic non-small cell lung cancer. Clinical trials have demonstrated activity of this drug in renal cell carcinoma, prostate cancer and breast cancer.

In a phase II study of patients with metastatic colon cancer, an increased risk of arterial and venous thrombosis was found in the bevacizumab (5 mg/kg) arm, and grade 1 IVAD thrombosis was reported [3]. Delayed wound healing has also been described in patients undergoing major surgery during bevacizumab therapy [4]. We report three cases of Vaxel titanium standard ports, Pressure-Activated Safety Valve (PASV); [Boston Scientific, Natick, Massachusetts, USA] eroding through the skin, in patients treated with anti-VEGF therapy.

Patient 1

A 61-year-old postmenopausal woman, with locally advanced and metastatic estrogen-receptor positive/progesterone-receptor negative and *Her2neu*-negative breast cancer involving bone and soft tissues, was examined. The patient experienced disease progression on endocrine therapy. A PASV port was placed within the right chest wall under fluoroscopic and sonographic guidance without complication. One week later, she was started on paclitaxel (3 of every 4 weeks) with bevacizumab (10 mg/kg) every other week. The patient responded to this treatment; however, 5 months after the initiation of the bevacizumab and the placement of the port, she presented to the clinic with discomfort in her port area. She had no fever or chills. On examination, the metal rim of the port had eroded through the skin and was visible (Fig. 1). The port site was free of swelling, induration or purulent drainage. Bevacizumab was held; the port was removed, and a new subcutaneous PASV port was placed on the same side via the right internal jugular vein. Bevacizumab was resumed 3 weeks later. Three months after placement, the new right chest wall port

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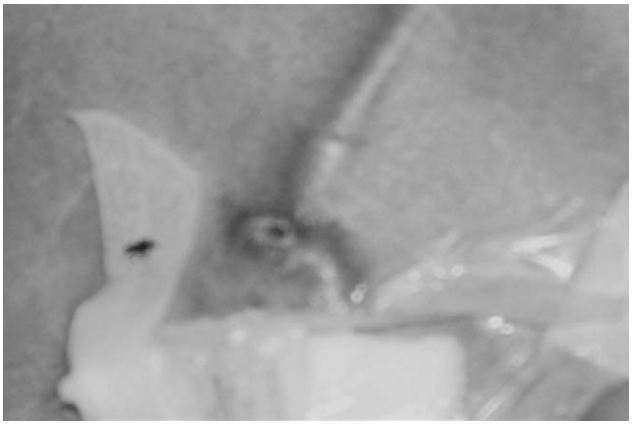
Fig. 1



A picture of the eroded port in patient 1.

again began to erode through the skin. The port was once again replaced, with discontinuation of bevacizumab shortly thereafter.

Patient 2

A 66-year-old woman with hormone-refractory metastatic breast cancer involving the liver had previously received doxorubicin and cyclophosphamide, followed by tamoxifen in the adjuvant setting. After confirmation of metastatic disease, she was enrolled in an investigational protocol. She received docetaxel in combination with axitinib, a small-molecule inhibitor of the receptor tyrosine kinases with picomolar potency against VEGF receptors (VEGFRs) 1, 2 and 3. A right-sided PASV port was placed under fluoroscopic and sonographic guidance, approximately 7 months after initiation of therapy. Treatment was resumed 1 week later. Five months after port placement, and 1 year into the regimen, the metal rim of her port eroded through the skin and became visible. The port was removed and a new one was placed. Treatment with axitinib was discontinued at that time because of disease progression.

Patient 3

A 41-year-old woman with metastatic colon cancer had previously undergone a hemicolectomy and debulking surgery, followed by four cycles of chemotherapy with oxaliplatin, leucovorin and 5-fluorouracil. A right-sided PASV port was placed under fluoroscopic and sonographic guidance. Two weeks later, treatment with oral capecitabine and bevacizumab (5 mg/kg) every 3 weeks was initiated. Two months after initiation of the regimen that included bevacizumab, the patient presented with an opened area around her port site. On examination, the site was nonfluctuant or erythematous. A dehiscence of the surgical incision, which had previously healed well with the metal and plastic part of the port being visible, was found. Bevacizumab was discontinued and her port was removed.

Discussion

Erosion of IVAD is uncommon, accounting for less than 1% of IVAD-associated complication [5–7]. IVAD erosion has been associated with repeated accessing of the port at the same location [8] and with infection. Active patients, in whom repetitive movement can cause the skin to erode, and patients who lose a significant amount of weight seem to be at risk [9]. IVAD placement by an inexperienced interventionist, or poor wound healing early after the port placement, might also increase the risk of skin erosion around the device. VEGF is a highly potent inducer of angiogenesis; it plays a significant role in the neovascularization process involving tumor growth as well as normal wound healing. Treatment with anti-VEGF therapy can lead to slow or incomplete wound healing when administered perioperatively [4].

All three patients in this series received Vaxel titanium standard (PASV) ports. The ports were placed by experienced interventional radiologists under fluoroscopic and sonographic guidance, and were accessed only by experienced oncology nurses. The patients' body mass indices (BMIs) were 19, 20 and 19 kg/m^2. None of these patients experienced significant weight loss around the time of port erosion. In these three patients, port erosion occurred 5, 6 and 2 months after port placement, and all the patients received anti-VEGF therapy within approximately 2 weeks of the port placement. Patient 1 developed a second port erosion after resuming bevacizumab treatment, and the remaining two patients were able to maintain their new ports after treatment with anti-VEGF therapy was discontinued.

As anti-VEGF use increases in the treatment of cancer, there is a growing body of literature related to its adverse effects. To our knowledge, this is the first reported case series of port erosions in patients receiving such treatment. In this series, low BMI might have contributed to the IVAD erosions. The occurrence of this rare complication in three patients at our institution receiving anti-VEGF therapy, in close proximity to the time of IVAD placements, however, raises the possibility that such therapy played a role in the occurrence of this complication. A larger number of patients and an appropriate control population would be required to make more definitive conclusions.

Bevacizumab has a half-life of approximately 20 days. The package insert recommends that the drug be held for 4 weeks before and after surgical procedures. Guidelines for the timing of treatment following minimally invasive procedures are, however, lacking. Controlled studies to

investigate the optimal timing of port placement or other minimally invasive procedures in patients receiving anti-VEGF therapy are needed.

Oncologists, as well as nursing staff, should be vigilant in assessing these devices, and should educate patients to recognize this complication, particularly as the use of anti-VEGF therapies expands.

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