Hepatic Artery Dissection in a Patient on Bevacizumab Resulting in Pseudoaneurysm Formation

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ABSTRACT

Interventional radiologists are frequently encountering patients with colorectal cancer that are being treated with bevacizumab. This therapeutic agent is associated with a potentially increased risk of adverse events when invasive procedures are performed while patients are on therapy. The current case report reviews a complication related to planning angiography for radioembolization with Yttrium-90 microspheres in an individual on bevacizumab and subsequent management of the patient.

KEYWORDS: Radioembolization, complications, bevacizumab, colorectal cancer

CASE REPORT

This 53-year-old man with metastatic colorectal cancer was referred for evaluation for radioembolization with Yttrium-90 microspheres. He had progressed on oxaliplatin- and irinotecan-based regimens and presented with bilobar disease that was isolated to the liver (Fig. 1). He was not considered to be a surgical candidate based on clinical comorbidities. At the consult, he was taking bevacizumab (Avastin[®], Genentech, South San Francisco, CA) as he had maintained stable disease with this agent as monotherapy over several scans.

At the consult, treatment with both chemoembolization and radioembolization with resin-based microspheres (SIR-Spheres[®], Sirtex Medical, Lane Cove NSW, Australia) were reviewed with treatment planning, number of visits, outcomes, and toxicities discussed. The patient strongly preferred outpatient therapy and elected to proceed with radioembolization. He was averse to stopping his bevacizumab, which he was receiving on an every other week basis. The plan was

made to perform his mapping arteriogram toward the end of the second week after he received his dose.

During the mapping arteriogram, we first selected the superior mesenteric artery (SMA) and then the celiac artery, performing digital subtraction angiography (DSA) from each location (Fig. 2A-B). We intended to select and embolize the gastroduodenal artery (GDA) with coils using a 4 French Cobra catheter. The catheter did not initially select the GDA and at the expected location of the proper hepatic artery, we elected to inject contrast and pull back to find the origin. However, after removing the wire, no blood return was noted. The catheter was retracted with gentle aspiration until blood return was achieved. Contrast injection revealed extensive dissection of the common hepatic artery with extension into the origin of the left lateral segmental artery, GDA, and the origin of the right hepatic artery (Fig. 2C). Rather than attempt further manipulation, the procedure was terminated to avoid worsening the dissection. After discussing the outcome with the patient, he wanted to

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Figure 1 Preprocedure positron emission tomography-computed tomography scans demonstrate multiple hypermetabolic foci in the left lobe of the liver.

reattempt treatment after allowing the dissection to remodel over several weeks. We were hesitant to fully anticoagulate the patient while he was on bevacizumab and prescribed clopidogrel (Plavix[®], Bristol-Myers Squibb/Sanofi, Bridgewater, NJ) instead.

Four weeks later, the patient returned for a repeat mapping arteriogram. His liver functions remained normal with a bilirubin less than 1 mg/dL. The SMA injection demonstrated retrograde supply to the hepatic arteries, a finding not present on the initial study (Fig. 3A). The celiac injection revealed a sizable pseudoaneurysm extending from the common hepatic artery at the likely entry site of the dissection (Fig. 3B-C). The hepatic artery branches were diminutive and the lateral segmental branch remained occluded.

Several options were considered at this point, including stent graft placement across the pseudoaneurysm or bare metal stent placement with coil embolization via the interstices into the pseudoaneurysm. However, given the small residual diameter of the common hepatic artery, we were concerned that any device would further stress the abnormal vessel and potentially lead to catastrophic rupture. We elected to coil embolize the common hepatic artery in light of the

already existing collateral flow via the SMA. A microcatheter was carefully advanced into the common hepatic artery distal to the pseudoaneurysm and coils deployed distal to proximal until exclusion was achieved (Fig. 3D). The patient was observed for several hours and discharged home. Follow-up laboratories demonstrated no change in his liver functions over several weeks. He was then placed on salvage chemotherapy by his oncologist.

DISCUSSION

Perioperative complications in patients on bevacizumab are an area of concern in patients undergoing colonic, hepatic, pancreatic, and breast resection.¹⁻⁶ Bevacizumab is a monoclonal antibody against vascular endothelial growth factor (VEGF) that is commonly used with oxaliplatin-based chemotherapy regimens, either in the neoadjuvant or adjuvant settings. Given this agent's initial U.S. Food and Drug Administration approval for treatment of colorectal carcinoma, outcomes and toxicities in relatively more patients with this disease have been reported compared with other neoplasms. Prospective randomized data regarding perioperative

Figure 2 (A) Superior mesenteric artery injection at mapping arteriography. No hepatic supply is present. (B) Initial celiac injection at mapping angiography. (C) Injection after dissection demonstrates absence of the gastroduodenal artery, truncation of the left lateral segmental artery, and a linear defect spiraling from the common hepatic artery to the right hepatic artery.

complications does not exist in any organ system although trials are in discussion.⁴

In 2005, Scappaticci, et al published a review focused on wound healing outcomes from two previously randomized trials where bevacizumab was studied versus placebo against either fluorouracil/leucovorin or irinotecan/fluorouracil/leucovorin.^{5,7,8} Patients undergoing surgery 28–60 days prior to receiving therapy had no increased risk of complications on bevacizumab. Patients undergoing surgery after initiating treatment had a higher rate of wound infections compared with controls (13% vs 3.4%).

A recent retrospective review has generated much discussion. Kesmodel reported 2 groups of patients who received chemotherapy with or without bevacizumab prior to resection of liver metastases.³ The study group consisted of 81 patients who received chemotherapy plus bevacizumab versus a control group of 44 patients who received chemotherapy alone. Postoperative complications developed in 49% of the study patients and 43% of the controls with a minimum and median time to surgery following treatment of 31 and 58 days. The authors concluded that bevacizumab administration did not raise perioperative risk with an appropriate delay from drugs

to surgery. This conclusion was challenged because as compared with controls, the bevacizumab group had a higher requirement of vacuum-assisted closure dressings, a higher rate of wound dehiscence that required operative management, and a 9% rate of other infectious complications (vs 2% for the controls) including all abdominal collections in the series and a patient who died of sepsis.²

Cheon et al recently completed a review on the outcomes in patients with colorectal and pancreatic cancer who received preoperative bevacizumab.⁶ In colorectal surgery patients, postoperative complication rates on treatment have ranged from 1.3% to 22%. Their critical review found that although the number of complications related to bevacizumab was higher in some studies, the majority of complications were minor. They also described a trend to fewer postoperative complications in patients who were more than 60 days from therapy (1.8% vs 6.5% in patients less than 60 days from treatment). The absolute increase in risk of invasive procedures remains unknown as does the best way to limit complication rates in patients on therapy. However, the risk of complications following surgery appears to be elevated in patients on bevacizumab.

Figure 3 (A) Superior mesenteric artery injection at follow-up angiography. There is new demonstration of retrograde flow to the hepatic arteries. (B) Celiac digital subtraction angiography demonstrates a pseudoaneurysm of the common hepatic artery. (C) Close up of the pseudoaneurysm reveals the narrowed arterial lumen with a jet of contrast into the surrounding defect. (D) Final angiography after embolization of the common hepatic artery.

Even less is known about outcomes in patients treated in interventional radiology. Erinjeri et al reviewed their experience with 1108 port placements in patients receiving bevacizumab.⁹ They found a statistically significantly higher rate of wound dehiscence when bevacizumab was given less than 2 weeks prior to port placement. As most interventional radiology procedures are minimally invasive, the 6-week delay from treatment that some authors recommend for surgery is likely excessive.³ Our patient was 2 weeks from therapy and his dissection evolved into a sizable pseudoaneurysm. Hepatic artery dissection typically occurs in less than 1% of arterial directed therapy cases.¹⁰ Although this finding may not have been directly related to his bevacizumab, similar outcomes following hepatic artery dissection are rarely reported.¹¹ As bevacizumab is a radiation sensitizer, it is tempting to treat patients with Y90 microspheres while on therapy.⁶ However, treating interventional radiologists need to be aware that risks may be increased in this setting and proceed with caution.

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