Vascular lakes after doxorubicin drug-eluting bead chemoembolization with histologic analysis

Justin D. Sacks, MD^a , Evans Heithaus, MD^b , Alexia Ghazi, DO^c, and Marco Cura, MD^b

^aDepartment of Radiology, University of Texas Health Science Center at Tyler, Tyler, Texas; ^bDepartment of Radiology, Baylor University Medical Center, Dallas, Texas; ^cDepartment of Pathology, Baylor University Medical Center, Dallas, Texas

ABSTRACT

This brief case presentation addresses an imaging phenomenon sometimes seen during chemoembolization, referred to the literature as vascular lakes or vascular lakes phenomenon. Other papers have discussed the clinical significance of this imaging pattern. We present a case of vascular lakes seen at the time of chemoembolization, with associated histologic findings after liver explantation. To the authors' knowledge, this case represents the first histological correlative analysis of this imaging pattern.

KEYWORDS Chemoembolization; DEB-TACE; histology; vascular lakes

Doxorubicin drug-eluting bead transarterial chemoembolization (DEB-TACE) is an accepted locoregional treatment for hepatocellular carcinoma (HCC).¹ During hepatic angiograms after DEB-TACE at Baylor University Medical Center, we have observed pooling of contrast in the tumor bed, or vascular lakes, in 13% of cases.² We define *vascular lakes* as focal or multifocal irregular delineated areas of contrast pooling in the tumor bed, not present on pretreatment angiography, that increase in size on delayed images. One of these cases subsequently qualified for liver transplant, and histologic evaluation of the explanted liver was performed. Institutional review board approval was obtained.

CASE DESCRIPTION

A 70-year-old woman with Child-Pugh A cryptogenic cirrhosis, a Model for End-Stage Liver Disease score of 7, and an Eastern Cooperative Oncology Group performance status of 0 was found to have a 5-cm segment 7/8 lesion compatible with HCC by magnetic resonance imaging (MRI) characteristics. Tumor board consensus of this non-surgical lesion was to treat with DEB-TACE. The procedure was performed with moderate sedation and local analgesia. Common femoral artery access was obtained and diagnostic celiac and superior mesenteric angiograms were performed. Superselective catheterization and angiography of

the subsegmental arteries supplying the segment 7/8 tumor with a microcatheter (2.4-F Progreat, Terumo Europe, Leuven, Belgium) showed tumor enhancement (*Figure 1a*). One vial of 70- to 150- μ m-diameter beads followed by one vial of 100- to 300- μ m-diameter LC beads (Biocompatibles PLC, Farnham, UK), each previously loaded with 75 mg of doxorubicin following manufacturer recommendations, was administered via the microcatheter in a sequential fashion. One hundred percent of each vial was infused.

Partial response by modified Response Evaluation Criteria in Solid Tumors was seen on a follow-up MRI performed 44 days later. A second session of DEB-TACE 52 days after the first session was performed in a similar fashion, also using 100% of the same embolics. At the end of the second session, postembolization completion angiogram showed pooling of contrast within the tumor bed, not seen on any previous angiogram (*Figure 1b*). MRI after the second treatment showed complete response by modified Response Evaluation Criteria in Solid Tumors (*Figure 1c*). The tumor size decreased, measuring 3.8 cm at the time of liver transplantation 297 days later.

Histologic analysis of the treated tumor revealed 100% tumor necrosis. More than 40 beads were seen on average per high-power field (hpf) within the necrotic tumor (*Figure 1d*). On average, 4.4 beads per hpf were seen in adjacent extratumoral liver tissue, resulting in an intratumoral: extratumoral bead ratio of 9.1.

Corresponding author: Justin D. Sacks, MD, Department of Radiology, University of Texas Health Science Center at Tyler, 11937 US Highway 271, Tyler, TX 75708-3154 (e-mail: jsacksmd@gmail.com)

Color versions of one or more of the figures in this article can be found online at www.tandfonline.com/UBMC.

Received June 12, 2018; Revised July 8, 2018; Accepted July 9, 2018.

Figure 1. (a) Preembolization angiogram shows tumor enhancement in the right hepatic dome. (b) Postembolization intratumoral puddling of contrast along the periphery (white arrow). (c) MRI of the segment 7/8 tumor after the second treatment shows complete response without residual tumor. (d) Single slide of the tumor from the explanted liver shows high bead concentration within the tumor bed with surrounding necrotic tumor tissue.

DISCUSSION

A similar histologic evaluation was performed on 18 other explanted livers following DEB-TACE.³ On average, intratumoral bead concentration across all livers explanted after DEB-TACE in that study was 10.2 per hpf (range 0–40, standard deviation 9.5), and average extratumoral bead concentration was 3.7 per hpf (range 0–11.2, standard deviation 2.7), with an average intratumoral: extratumoral bead ratio of 3.2. In comparison, our case study with vascular lakes had a high intratumoral bead concentration, more than three standard deviations above the mean.

To our knowledge, this represents the first histologic evaluation of a lesion that demonstrates vascular lakes. Cavalcante et al reported higher response rates in lesions with this imaging pattern.⁴ Potential mechanisms include venous outflow obstruction as a result of high intratumoral bead concentration compared to other treated hepatomas without this imaging pattern. Alternatively, vascular puddling due to defective tumor vascular architecture and enhanced vascular permeability could result in contrast leakage into the interstitium. The histologic evaluation for this case supports the possibility that this imaging pattern, and

the previously reported higher response rates seen with vascular lakes, could be related to high intratumoral bead concentrations.

ORCID

Justin D. Sacks <http://orcid.org/0000-0003-1218-6079>
 Evans Heithaus <http://orcid.org/0000-0001-7949-0150>

1. Lammer J, Malagari K, Vogl T, et al; PRECISION V Investigators. Prospective randomized study of doxorubicin-eluting-bead embolization in the treatment of hepatocellular carcinoma: results of the PRECISION V study. *Cardiovasc Intervent Radiol*. 2010;33(1):41–52. doi:10.1007/s00270-009-9711-7.
2. Cura M, Mohammed F, Meler JD, Rees CR, Diamond N. Vascular lakes after doxorubicin drug eluting beads chemoembolization. *J Vasc Interv Radiol*. 2013;24(4):S108. doi:10.1016/j.jvir.2013.01.265.
3. Heithaus R, Cura M, Waller A, Hise J, Daoud Y, Lee M. Tumor necrosis after selective transarterial chemoembolization for hepatocellular carcinoma, the role of bead concentration. *J Vasc Interv Radiol*. 2017;28(2):S124. doi:10.1016/j.jvir.2016.12.899.
4. Cavalcante RN, Nasser F, Motta-Leal-Filho JM, et al. Occurrence of vascular lake phenomenon as a predictor of improved tumor response in HCC patients that underwent DEB-TACE. *Cardiovasc Intervent Radiol*. 2017;40(7):1044–1051. doi:10.1007/s00270-017-1678-1.