TriNav® INFUSION SYSTEM

Pressure-Enabled Conventional TACE for Hepatocellular Carcinoma: A Case Presentation

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OVERVIEW

A patient diagnosed with hepatocellular carcinoma (HCC) was previously treated at an outside clinic with conventional transarterial chemoembolization (cTACE) delivered via a standard microcatheter. Follow-up imaging showed poor intratumoral concentration of therapeutic, and residual viable tumor 2 months post-treatment. After referral to our clinic, subsequent cTACE delivered via the TriNav Infusion System achieved excellent intratumoral delivery and a complete response of the target tumors at the 6-month follow-up. This case demonstrates how cTACE administered via Pressure-Enabled Drug Delivery™ (PEDD) may provide a means to improve therapeutic delivery and to improve response rates.

PATIENT HISTORY

A 60-year-old male with alcoholic cirrhosis was referred to our center for liver transplant evaluation 11 months after being diagnosed with HCC. At the time of diagnosis, the patient had a MELD score of 22, and the HCC measured up to 3.7cm. He had previous TIPS placement for ascites and variceal bleeding 3 years prior. He initially did not receive locoregional or systemic therapy to treat the cancer, and the tumor grew to 4.3cm before treatment with cTACE at an outside institution 9 months after initial diagnosis. Cone beam CT at the completion of initial cTACE showed similar concentration of chemotherapy material within the target tumor to that of surrounding liver parenchyma.

On presentation to our center, the patient had repeat multiphase CT scans. There were persistent findings of cirrhosis and portal hypertension with TIPS in place. Of note, there was arterialization of the hepatic parenchyma. There was evidence of prior TACE, but extensive enhancement of the dominant HCC in segment 8, which measured up to 4.7cm in diameter, indicating persistent viable tumor. A small satellite nodule was also evident. There was poor staining of the target lesions by lipiodol from prior treatment **(Figure 1)**. The patient was Child-Pugh B and ECOG 0. He was not a candidate for radioembolization due to poor functional hepatic reserve. Total bilirubin was 6.5 mg/dL with no evidence for mechanical biliary obstruction.

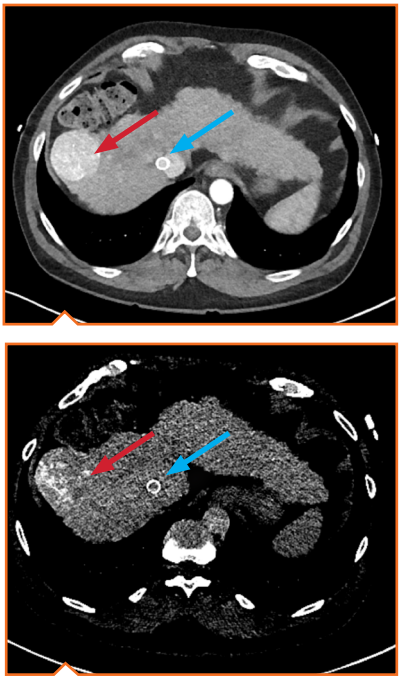

Figure 1: Arterial post cTACE via standard microcatheter (top); Delayed post cTACE via standard microcatheter (bottom). Red arrows indicate tumor. Blue arrows indicate TIPS shunt.

TREATMENT

Given absence of response from cTACE 2 months prior, we opted to treat with PEDD-cTACE using the TriNav Infusion System. The TriNav was successfully navigated into the segment 8 branch, a 2:1 emulsion of lipiodol:doxorubicin (50mg in 5mL Isovue-300) was administered, and there was excellent staining of the target mass (Figure 2). Additional embolization was performed with 100-300um spherical microspheres to near stasis. The rate of local recurrence has been shown to be significantly lower when a greater degree of portal vein visualization is demonstrated during TACE[1], and it should be noted that in this case portal vein staining was not observed post-treatment.

Following treatment of the segment 8 hepatic arterial branch, an additional feeding vessel was identified from segment 7, and bland embolization was performed with lipiodol and 100-300um spherical microspheres via the TriNav Infusion System.

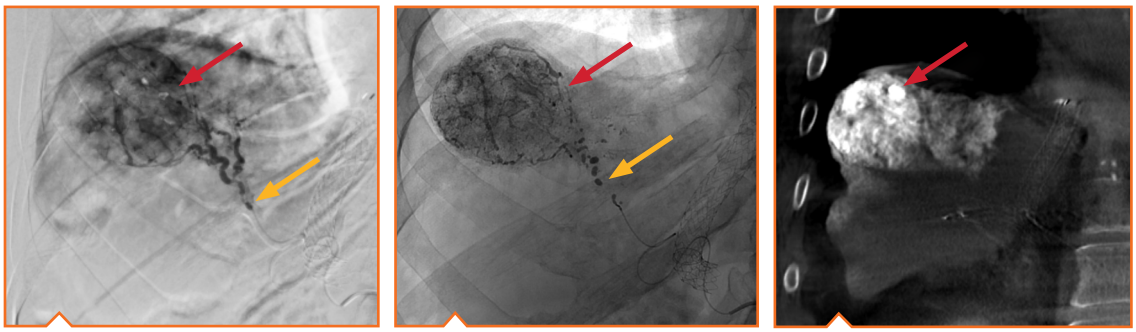

Figure 2: Pre PEDD-cTACE angiography (left); progress (center); completion CBCT (right). Red arrows indicate tumor. Yellow arrows indicate target vessel.

TREATMENT (Continued)

The patient returned 3 months following for treatment of an additional smaller segment 5 lesion that was not treated initially due to poor hepatic functional reserve. At the time of the segment 5 lesion treatment, angiographic evaluation was performed and demonstrated no evidence of flow to the target segment 8 tumor or satellite tumor.

Follow-up multiphase MRI of the abdomen performed 6 months post-treatment also demonstrated complete response of the segment 5 and segment 8 target lesions in addition to the satellite. There was no evidence of viable tumor in the liver **(Figure 3)**. The patient is now resuming workup for liver transplantation.

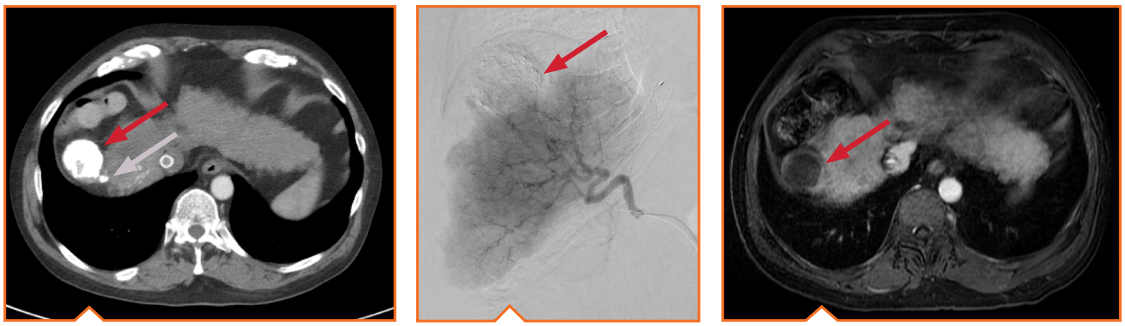

Figure 3: CT showing dense staining of target and satellite (left); Follow-up angiography (center); T1 post arterial MRI showing no residual enhancement (right). Red arrows indicate tumor. Lilac arrow indicates satellite tumor.

DISCUSSION

The liver has a dual blood supply, receiving blood from the portal vein and the hepatic artery.[2] In the noncirrhotic liver, approximately 70%-80% of blood is derived from the portal vein, with the remaining 20%-30% supplied by the hepatic artery. Hepatocarcinogenesis leads HCC to be supplied almost entirely by neovascular arteries.[3] The differential in blood supply between arterially supplied tumor and portal supplied liver parenchyma is used to improve delivery of locoregional therapies.

Patients with cirrhosis have increased arterial perfusion of the liver compared to noncirrhotics.[4] This effect is further potentiated by TIPS placement.[5] Increased arterial perfusion of the hepatic parenchyma makes the tumor-to-parenchymal ratio less favorable when performing transarterial locoregional therapy. In addition, rapid cellular proliferation in the center of a tumor can increase interstitial pressure, leading to compression closure of capillaries.[6] This patient had poor tumoral concentration of chemotherapy following cTACE delivered via a standard microcatheter.

Balloon occlusion catheters have been used to improve dose delivery for TACE with drug-eluting microspheres, and recent literature has shown promising results with balloon occluded TACE.[7-9] Whereas balloon devices eliminate physiologic flow when deployed,[10] PEDD provides a means to overcome intratumoral pressure[11] to improve drug delivery while maintaining antegrade flow.[12] Unlike balloons, PEDD devices such as the TriNav Infusion System can leverage natural blood flow and pressure during infusion to increase therapeutic uptake in target tissues.[12,15] PEDD has been shown to improve tumor to background concentration of CAR-T,[13] MAA,[14] and DEM-TACE.[15]

In this case, TriNav provided the means to achieve excellent intra-tumoral delivery and a complete response of the target tumor and satellite lesion after failed cTACE with a standard microcatheter. PEDD-cTACE may provide a means to improve tumor deposition of chemotherapy and improve response rates, particularly in patients with arterialization of the hepatic parenchyma and relatively decreased flow to the tumor tissue.

CONCLUSION

In this HCC case that was refractory to cTACE administered at an outside clinic via a standard microcatheter, cTACE administered via PEDD showed complete response at the 6-month follow-up. This case demonstrates how PEDD-cTACE may improve tumor deposition of chemotherapy and response rates.

ABOUT THE AUTHOR

Dr. Jonathan Lindquist is a specialist in vascular and interventional radiology at the University of Colorado. Dr. Lindquist serves as the Director of Interventional Oncology, Medical Director for Interventional Radiology, and Director of IR Quality and Patient Safety at the University of Colorado Hospital. His areas of clinical expertise and his research interests include liver cancer, interventional oncology, and venous thromboembolism.

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