Pulmonary Complication following Drug-Eluting Bead Hepatic Chemoembolization

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A 70-year-old man with a history of essential hypertension presented to his gastroenterologist with a 6-month history of unintentional weight loss. After an unremarkable colonoscopy, a computed tomographic (CT) scan of the abdomen was performed demonstrating a 6.2-cm arterially enhancing hepatic mass with delayed washout and extension into the hepatic vein (►Fig. 1a, b). The patient was found to have no associated liver disease or serologic evidence of viral hepatitis. A biopsy of the mass was performed demonstrating poorly differentiated hepatocellular carcinoma (HCC), and the patient was referred to interventional radiology for locoregional therapy. Prior to liver-directed therapy, imaging demonstrated a small pleural effusion felt to be related to venous invasion and narrowing of inferior vena cava (IVC). The drug-eluting beads transarterial chemoembolization (DEB-TACE) was performed with 100- to 300- μ m drug-eluting beads loaded with 75 mg of doxorubicin (LC Beads, BTG, West Conshohocken, PA) followed by 300 to 500 μ m “bland” particle (Embosphere; Merit Medical, Salt Lake City, UT) embolization. An angiographic endpoint of 5-beat stasis was reported. No angiographic images were stored demonstrating arteriovenous shunting; however, in retrospect, shunting could have been suspected based on attenuation of caval blood surrounding the tumor on arterial phase imaging on both CT and angiography (►Fig. 1c, d). Approximately 48 hours after discharge, the patient presented to his primary care physician with fevers and mild dyspnea. This was attributed to an increased right pleural effusion following DEB-TACE, which was managed conservatively without thoracentesis. The patient’s oxygen saturation was incidentally noted to be decreased at 92%; however, patient was judged not to be symptomatic enough to require treatment and as such was discharged from medical care with instructions to follow up if symptoms worsened. The patient improved over the course of the next month, but follow-up imaging demonstrated a minimal response of the treated HCC. After discussion with the patient, repeat DEB-TACE was performed.

The interval between treatments was 5 weeks. The patient was again treated with 100 to 300 μ m DEB-TACE. Following the second treatment, the patient developed significant dyspnea. This was again presumed to be related to the right pleural effusion and postembolization symptoms; and thus, after an overnight admission following DEB-TACE the patient was discharged home with instructions to return if the symptoms did not improve or worsened. The patient re-presented to the emergency department 1 week later with significant hypoxia. A CT of the chest was performed to rule out pulmonary embolism. Although no pulmonary embolism was identified, imaging demonstrated diffuse patchy infiltrates and an enlarging right pleural effusion (►Fig. 1e, f), likely representing chemoembolization-induced pneumonitis. The patient was also found to be severely hypoxic with oxygen saturation of 82% on room air. He required hospitalization for 2 weeks with oxygen-dependent hypoxia and pneumonitis, which also required 1 month of home oxygen postdischarge. The dyspnea eventually resolved completely and home oxygen therapy was discontinued. Follow-up imaging again demonstrated stable disease by mRECIST criteria.

The patient was referred to the authors’ institution for additional liver-directed therapy. Given the history of severe complications from first set of interventions, the patient’s treatment plan incorporated staged embolization which was first performed with 700 to 1,100 μ m polyvinyl alcohol (PVA) particles followed by conventional TACE with 50 mg of doxorubicin in 5 mL of contrast emulsified with 10 mL of lipiodol (Guerbet, Paris, France). Following PVA embolization and prior to TACE, digital subtraction angiography was also performed to ensure that the bland particle size was large enough to occlude tumor vessels to preclude shunting. The intravascular component of the tumor was referred for treatment with stereotactic beam radiation therapy following TACE, as this component was felt to be untreatable with transarterial therapy without significant complication. The patient achieved a 1.5-year complete response following this sequence of therapy without development of secondary sites of disease or distant metastasis.

Fig. 1 (a, b) Hepatocellular carcinoma (HCC) on presentation with a large hepatic mass (*white arrows*) with clear venous invasion into the hepatic vein and extending into the right atrium (*black arrow*). Given the patient's lack of cirrhosis, this mass was biopsied revealing poorly differentiated HCC. (c) Careful examination of pretreatment CT demonstrates opacification of the cava surrounding the tumor during the arterial phase (*arrows*). (d) Initial DSA on TACE following complication demonstrating clear venous shunting concerning when treating with smaller particles. Direct AV shunting depicted by *arrow*. (e, f) PE protocol CT performed after second TACE demonstrates bilateral infiltration without HCC. This required a total of 6 weeks of oxygen therapy to resolve as well as an extended inpatient admission.

Discussion

Hepatic artery to hepatic vein shunting is widely recognized as a component of HCC.^{1,2} While hepatic artery to hepatic venous shunting is recognized as an important factor in both response and complications associated with Yttrium-90 (Y90) radioembolization, it is less well appreciated in the context of chemoembolization. This can be clinically important as in this case, with patients developing pneumonitis, and also can limit response since many particles may not be deposited in the tumor due to shunting. Shunting can be visible angiographically as in this patient (►Fig. 1d), but also can be identified as likely based on preprocedural CT enhancement of hepatic veins or the IVC as in this case on arterial phase CT or MRI (►Fig. 1b). Venous enhancement on arterial phase imaging has proven to be predictive of high shunt fraction for Y90 mapping;³ however, evaluation of shunting is not routinely performed on pre-TACE imaging. As in this case, when arteriovenous shunting is present bland particle embolization may be performed to decrease the degree of shunting. The size of particles used for this depends on the rapidity with which the shunting occurs,

with faster traversal of contrast into the venous system indicating larger vascular shunts.⁴ Preprocedural imaging can be evaluated for the presence of shunting given these findings. While inappropriate shunting of particles in TACE does not have the same degree of morbidity of Y90, lack of recognition of shunting can lead to poor response to TACE as well as increased complications. This sequence of events may, however, be preventable with timely recognition and appropriate management.

References

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