

Rare pulmonary infarction after superior epigastric artery chemoembolization of unresectable hepatocellular carcinoma

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Nontarget organ complications are a rare, yet serious side effect of transarterial chemoembolization (TACE) procedures. We describe a case of a patient with unresectable hepatocellular carcinoma who subsequently developed right-lower-lobar pulmonary infarction approximately three weeks after receiving TACE, owing to an abnormal vascular connection between the superior epigastric artery and the distal right pulmonary artery. Our case stresses the importance of pre-operative planning and imaging to familiarize oneself with variations in vascular anatomy and to recognize symptoms associated with even the rarest complication associated with TACE procedures, so as to initiate treatment and improve patient outcome.

Introduction

Primary hepatocellular carcinoma (HCC) is usually fatal; fewer than 5% of patients survive 5 years after diagnosis. The median survival is 4-6 months for patients with unresectable tumors (1). For the past 15 years, TACE has served as a palliative option to extend the overall survival rate by 66%, 47%, and 36.4% at 1, 2, and 3 years, respectively (2). TACE targets unresectable HCCs by delivering chemotherapeutic and embolic agents into the tumor to induce ischemia and necrosis. HCC chemoembolization is based on the fact that the normal liver parenchyma receives a dual blood supply from the hepatic artery and the portal vein, whereas HCCs are supplied exclusively by the hepatic artery (2). However, depending on the location (in conjunc-

tion with various other unknown factors), HCCs may occasionally recruit and receive extrahepatic arterial supply. This makes pre-operative image planning an even more crucial step in achieving optimal results and favorable patient outcome. In some instances, these vessels themselves can extend to supply neighboring tissue or organs that are in close proximity, due either to exophytic tumor growth or extracapsular HCC infiltration to adjacent structures in close, direct contact with the liver. Nakai et al. have noted that, regardless of tumor size, when HCCs are located in the ventral hepatic area directly beneath the diaphragm, the internal mammary artery can serve as a feeding vessel with hepatic artery occlusion caused by repeated TACE (3).

Case report

A 76-year-old man with a past medical history significant for longstanding hypertension, cirrhosis, and HCC presented to physicians in 2005 for placement of a peritoneal catheter for dialysis. Subsequently, he developed diffuse abdominal pain. A CT scan incidentally revealed a large, confluent mass located in the left lobe of the liver measuring 8.4 cm x 12.9 cm, with heterogeneous attenuation and hypodense areas (Fig. 1). Because of the nonconfirmatory imaging and borderline alpha-fetoprotein and transaminase levels, a biopsy was initiated, which later confirmed the mass to be consistent with HCC. The patient was not a candidate for surgical resection because of an already

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Figure 1. 76-year-old male with rare pulmonary infarction. Repeat CT scan of liver shows hyperenhanced mass (arrow) located in upper left lobe near the dome of the liver.

compromised cirrhotic liver. Instead, the patient underwent chemoembolization and radiofrequency ablation, and the HCC initially responded to the treatments. However, despite two aggressive TACE sessions, the mass continued to grow in size.

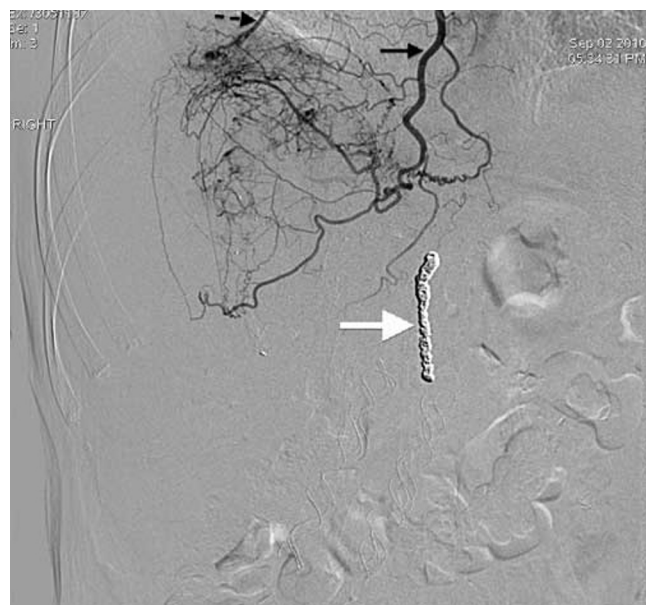


Figure 2. 76-year-old male with rare pulmonary infarction. Hepatic angiogram reveals hypervascularity of the HCC and extrahepatic collateral feeder vessel (superior epigastric artery, black arrow) supplying hepatic mass. Angiogram also reveals contrast filling in distal portion of pulmonary artery post-embolization (dotted black arrow). GDA coils are also seen from prior TACE operations (white arrow).

Given the frequent attempts at embolization procedures, and the hyperenhancement of the tumor and its peripheral location, we suspected there might be an extrahepatic vascular component supplying the HCC. Following an angiogram, the right internal mammary artery and superior epigastric artery were selectively catheterized via the right brachial artery approach (owing to the threat of clot embolization from pre-existing iliofemoral occlusive disease). Presurgical imaging did not show vascular connections from the superior epigastric artery to the right pulmonary artery.

Arteriography after catheterization demonstrated a visible reflux of contrast material into the distal portion of the right-lower-lobe pulmonary artery, which could be attributed to the rerouting of blood flow to accentuate the vascular connection that was difficult to detect in the pre-operative arteriogram. Arteriography also showed GDA coils deployed, most likely during previous TACE attempts to block off the gastro-omental artery feeding the HCC. However, it is difficult to know for sure because the patient received care at another facility before coming to our department (Fig. 2). Chemoembolization of the HCC via the right-superior epigastric artery was performed using QuadraSphere (Biosphere Medical, South Jordan, Utah)

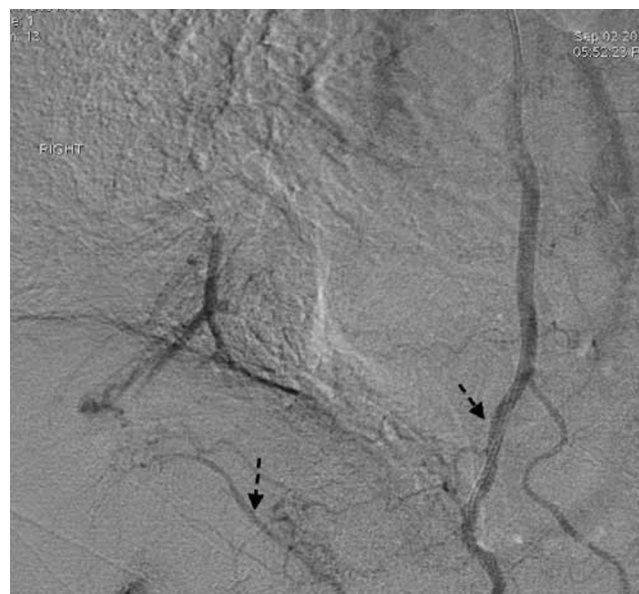


Figure 3. 76-year-old male with rare pulmonary infarction. Following embolic injection of microspheres, hepatic angiogram shows diminished antegrade flow and reduced vascular filling (dotted arrows).

embolic material mixed with doxorubicin, cisplatin, and mitomycin C. One-half of a vial of 100-300 micron Embospheres (South Jordan, Utah) was injected until stasis to antegrade blood flow, and devascularization of the hepatic tumor was achieved (Fig. 3). The patient tolerated the procedure well, was admitted for overnight observation, and

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was discharged the next day as per standard hospital protocol.

Approximately three weeks following the TACE procedure, the patient presented to the emergency department complaining of low-grade fever, yellowish-productive spu-



Figure 4. 76-year-old male with rare pulmonary infarction. Chest X-ray image shows right lower lobar consolidation with hypervascular lung markings. The opaque mass (blue arrow) is clearly visible, with the distribution consistent with the lower lung zone.



Figure 5. 76-year-old male with rare pulmonary infarction. Supplemental axial CT scan shows wedge-shaped infarct (arrow) that developed post-TACE. The distribution spans to the rib wall and pleura.

tum, coughing, chest discomfort, tachypnea, and generalized pain. Laboratory results revealed a normal white-blood-cell count of 5.5 cells/mL, hemoglobin of 9.8 g/dL, platelet count of 137,000, and glucose of 198 mg/dL. Chest X-ray revealed a round, opaque mass located in the right-lower-lung zone (Fig. 4). The patient was admitted to the hospital and immediately started on intravenous antibiotics. A chest CT scan confirmed the same findings as the chest X-ray, revealing a wedge-shaped hyperdense mass in the right-lower lobe that was consistent with pulmonary infarction (Fig. 5). Pulmonary embolism was ruled out as the cause of the infarction. The remainder of the hospital stay was uneventful. The patient responded well to the intravenous antibiotics and was discharged several days later in stable condition. A chest CT scan was repeated three months later, which showed a substantial resolution of the lobar infarct (Fig. 6).

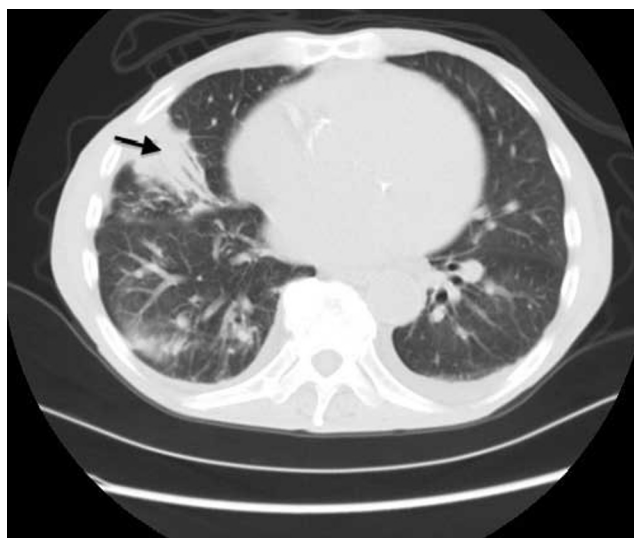


Figure 6. 76-year-old male with rare pulmonary infarction. Following treatment, CT scan 3 months later shows significant resolution of infarcted lung tissue (arrow).

Discussion

The superior epigastric artery originates from the internal mammary artery, at the level of the sixth intercostal space. This artery gives off some branches to the diaphragm; they extend into the falciform ligament of the liver and anastomose with the hepatic artery. Attempts to selectively catheterize and embolize extrahepatic collateral feeding vessels supplying HCCs remain a constant challenge for clinicians. According to Cheng et al., the most common extrahepatic collateral arterial supply of HCC involves the inferior phrenic artery and the omental arteries that arise from the gastroduodenal artery and, in some cases, the splenic artery. However, considering the close proximity of the liver and the diaphragm and the broad contact between them, it may be expected that diaphrag-

matic blood supplies, including the internal mammary and intercostal arteries, are also key sources of collateral circulation as well (4). It is important to recognize that not all such vessels can be safely treated without risk to other important organs.

It is unclear whether this patient had a congenital explanation for this abnormal vascular connection between the superior epigastric artery and the right-pulmonary artery, or whether this anatomy could be explained away by vascular endothelial growth factors coaxed by the tumor. Nevertheless, these variations underscore the need for thorough visceral arteriography before initial chemoembolization to reduce the chances of nontarget embolization. It was also inferred that the patient's symptoms could be explained by rogue embolization (which is defined by embolic material unintentionally inhibiting blood supply to nontarget organs), considering that the patient had no history of pulmonary disease or prior chest X-rays displaying the consolidation that was revealed at admission. Pre-operative imaging did not show vascular connections from the superior epigastric artery to the right pulmonary artery. Imaging after arteriography demonstrated a visible reflux of contrast material into the distal portion of the right-lower-lobe pulmonary artery, which could be attributed to the re-routing of blood flow to accentuate the vascular connection that was difficult to detect during the pre-operative arteriogram.

Some would speculate that symptoms directly related to intraprocedural reflux of embolic material into the pulmonary artery would present rapidly, within a couple of days after the procedure had been done. However, one possible explanation for this patient's delayed presentation might be that the pulmonary infarct was masked by the patient's post-procedural pain medication, and the onset of bacterial pneumonia added further insult, causing a breakthrough of symptoms three months later.

This case report stresses some key points. First, thorough pre-operative imaging to detect any anatomic variations of parasitized tumor vessels is vital to assess the amount of risk for nontarget organ involvement. Although arteriographic studies are arguably suggestive at best, they can offer detailed imaging information that the interventionalist must carefully evaluate. Second, what is considered acceptable risk when it comes to patient's current disease status vs. the likelihood of inadvertent nontarget organ damage has still yet to be defined. In cases where nontarget organ vascular supply is confirmed through imaging, perhaps the inclusion criteria of super-selective catheterization of these vessels (to avoid collateral organ damage) needs to be assessed. Of course, these options must be carefully weighed against the possible risk of vessel spasm or rupture. Super-selective catheterization is also limited by the diameter and tortuosity of the involved vessel that allows a catheter to be placed (5). It is important for clinicians to keep in mind that, although pulmonary involvement is rare, complications associated with TACE should be recognized and addressed swiftly, to ensure patient safety and decrease hospitalization.

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