Transarterial Chemoembolization Complicated by Deteriorating Hepatic Function

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ABSTRACT

Worsening hepatic function is a well-known potential complication of chemoembolization and occurs in up to 58% of patients undergoing chemoembolization. Although liver function returns to baseline levels within 3–4 weeks in the majority of patients, fulminant liver failure and death occur with a reported frequency of ~2–10%. Poor performance status, portal vein obstruction, biliary obstruction, extensive tumor burden, and Child-Pugh status B or C are among factors predisposing to an increased risk of transient or fulminant hepatic failure, with Child-Pugh status being the most accurate. Unless the patient is a candidate for liver transplantation, treatment for hepatic failure is limited to supportive measures.

KEYWORDS: Chemoembolization, liver failure, complications

CASE REPORT

The patient is a 72-year-old man with metastatic colorectal cancer who presented for transarterial chemoembolization for hepatic metastatic disease, which had progressed following intravenous chemotherapy with oxaliplatin, capecitabine, cetuximab, and irinotecan. He had undergone previous Y-90 radioembolization for metastatic disease in the right hepatic lobe and 2 prior chemoembolization procedures for metastatic disease in the left hepatic lobe (Fig. 1). Progressive metastatic disease excluded consideration for metastasectomy. Baseline AST and ALT were 50 units/L (normal 0–40 units/L) and 61 units/L (normal 0–48 units/L), respectively. Baseline albumin was 2.1 g/dL (normal 3.5–5.0 g/dL) and baseline total bilirubin was 1.1 mg/dL (normal 0–1.3

mg/dL). Although not technically cirrhotic, the Child-Pugh score based on laboratory values was 7 on the day of the procedure (Child-Pugh class B).

Prior to chemoembolization, right common femoral access was obtained with a 5.5 French sheath. A Simmons I catheter (Cook, Bloomington, IN) was used to engage the superior mesenteric artery and superior mesenteric arteriography was performed, which demonstrated patency of the portal vein. The right hepatic artery, which was replaced to the superior mesenteric artery, was selected by coaxially advancing a Renegade[®] high-flow microcatheter (Boston Scientific, Natick, MA) and a Glidewire GT guidewire (Terumo, Somerset, NJ). Right hepatic arteriography was performed, and the microcatheter and guidewire were advanced in the

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Figure 1 Axial computed tomography image with oral and intravenous contrast demonstrates a peripherally enhancing metastatic lesion in the right hepatic lobe (thick white arrow). Ethiodol contrast material is also seen in a metastatic lesion in the left hepatic lobe from prior chemoembolization (thin white arrow).

right hepatic artery beyond the origin of the cystic artery (Fig. 2).

Selective right hepatic artery chemoembolization was performed to a substasis endpoint. The entire 20 cc aliquot of ethiodized oil (Ethiodol[®]; Savage Laboratories, Melville, NY) /triple chemotherapy (1:1) was injected (100 mg of cisplatin, 30 mg of doxorubicin, and 30 mg of mitomycin C [Bedford Laboratories, Bedford, OH]), followed by a vial of 500–700 micron-sized trisacryl gelatin microspheres (Embosphere[®]; Biosphere Medical, Rockland, MA). Completion right hepatic arteriography (Fig. 3) showed reduced perfusion to the tumor, with persistent antegrade blood flow in the hepatic artery distal to the catheter tip. Vascular access was removed and hemostasis achieved with manual compression.

The patient was admitted to the hospital for routine postprocedural care. Routine postprocedural noncontrast CT (Fig. 4), obtained 1 hour after chemoembolization, demonstrated appropriate Ethiodol[®] staining within the tumor, without nontarget embolization. Bilirubin elevated from 1.1 mg/dL to 2.1 mg/dL the day after the procedure, and AST and ALT elevated to 118 units/L and 187 units/L, respectively. The patient developed abdominal pain, fatigue, nausea, and weakness 2 days after the procedure, which symptomatically improved with supportive therapy 2 days after the procedure. Hepatic function progressively worsened, with bilirubin peaking at 18.6 mg/dL 1 week after the procedure, and AST and ALT peaking at 484 units/L and 1129 units/L, respectively. Liver ultrasound obtained 5 days after chemoembolization demonstrated no evidence of biliary obstruction. The

hepatology service was consulted and recommended continued supportive measures. He became progressively encephalopathic 12 days after the procedure and passed away in palliative care 13 days after the procedure.

DISCUSSION

Approximately 50–60% of patients diagnosed with colorectal cancer will develop liver metastases. Only 20–25% of these patients will meet criteria for resection, which offers 5-year survival rates ranging from 37–58%. Hepatic failure from disease progression is the most common cause of death in patients whose metastatic disease progresses with standard-of-care intravenous chemotherapy, which occurs in 60% of patients with hepatic metastases.^{1,2}

Locoregional therapies, including transarterial chemoembolization, have demonstrated improved local control of and survival rates for colorectal metastases.¹ These therapies are predicated on the fact that both primary and metastatic liver tumors are primarily supplied by the hepatic artery; hepatocytes receive the majority of their blood flow from the portal vein. Several benefits are derived from the combined effects of concentrated chemotherapy infusion and hepatic artery embolization beyond minimizing systemic toxicity. The stasis following embolization results in local chemotherapy concentrations that are 10–25 times higher than with intraarterial chemotherapy infusion with embolization. This combined approach also results in tumor ischemia and hypoxia at the time of chemotherapy infusion.³

Absolute contraindications to chemoembolization include severe systemic infection and Child-Pugh class C liver disease. There are myriad relative contraindications, including poor performance status, encephalopathy, uncorrectable coagulopathy, intractable arteriovenous shunting, renal failure, and the presence of extrahepatic metastases. As liver is a frequent cause of morbidity and mortality with hepatic metastases, chemoembolization can be performed in properly selected patients with extrahepatic metastases. Biliary obstruction is a relative contraindication due to the increased risk of biliary necrosis with hepatic artery embolization. Portal vein thrombosis is also a relative contraindication to chemoembolization, although the procedure may still be performed if there is adequate collateral hepatopetal flow.^{1,3–5}

Even in properly selected patients, hepatic failure is a well-known potential complication of chemoembolization. Published criteria include postprocedural encephalopathy, increasing bilirubin, increasing prothrombin time, increasing ascites, and deterioration of Child-Pugh status.^{6,7} The true incidence of liver failure following chemoembolization is difficult to ascertain because of

Figure 2 Right hepatic arteriography prior to chemoembolization demonstrates the Renegade[®] high flow microcatheter tip distal to the origin of the cystic artery arising from the right hepatic artery (white arrow).

varying definitions used, although it occurs with a median incidence of 7.5% and a broad range of 0–48%,⁶ with liver function returning to baseline levels within 3–4 weeks in a majority of patients. Fulminant liver failure and death occur with a reported frequency of ~2–10%.⁸

Poor performance status, portal vein obstruction, biliary obstruction, extensive tumor burden and Child-Pugh status B or C are among factors predisposing to an increased risk of transient or fulminant hepatic

failure, with Child-Pugh status being the most accurate.^{4,8–10} Some authors propose a Child-Pugh score of at least 9 a contraindication¹¹ to chemoembolization due to an increased risk of precipitating fulminant hepatic failure despite the fact that this is still Child-Pugh class B.

The mechanism of hepatic failure following chemoembolization is not precisely known, but is believed to be induced by cytolysis and treatment-induced ischemic changes to nontumoral hepatic cells.^{6,8,12} The

Figure 3 Completion right hepatic arteriography following chemoembolization and injection of 1 vial of 500–700 micron Embospheres[®] demonstrates Ethiodol[®] staining within the large right lobe tumor (white arrows) that is increased in degree compared with the remaining right lobe. Chemoembolization was performed until a substasis endpoint as evidenced by persistent antegrade filling of all of the right lobe hepatic arteries.

Figure 4 Axial noncontrast computed tomography following chemoembolization demonstrates Ethiodol contrast material within the right hepatic lobe (thick white arrow). Ethiodol[®] contrast material is again seen in a metastatic lesion in the left hepatic lobe from prior chemoembolization (thin white arrow).

etiology of hepatic failure in this case is uncertain, as completion arteriography showed continued antegrade blood flow into the right hepatic lobe and patency of the portal vein. Treatment for hepatic failure is limited to supportive measures.

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