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Recurrent Hepatocellular Carcinoma in an Adult With Alagille Syndrome Treated With Liver Resection Followed by Liver Transplantation: A Rare Case Report

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Abstract. Alagille syndrome (AGS) is a disorder that affects the liver, heart, kidneys, and skeleton. Development of hepatocellular carcinoma (HCC) is rare in AGS. A 41-y-old male with AGS presented with a 6×8-cm HCC and underwent transarterial chemoembolization (TACE) followed by right hepatic lobectomy. One year later, he developed HCC recurrence within Milan's criteria and received a deceased donor liver transplant. An interposition donor iliac artery graft from the supraceliac aorta to the donor hepatic artery was needed due to celiac axis occlusion noted on TACE. He subsequently underwent a Roux-en-Y hepaticojejunostomy for a bile leak. Surveillance imaging for HCC revealed a 3-cm pseudoaneurysm of his aortoiliac vascular anastomosis, 3 mo posttransplant. An infrarenal aortic jump graft to the donor hepatic artery and ligation of supraceliac aortic conduit was performed, followed by aortic stent-graft placement to occlude the pseudoaneurysm. He received a deceased donor kidney transplant 13 mo after the liver transplant. He remains HCC free with excellent liver and renal allograft function. Adults with AGS undergoing liver transplantation for HCC need special consideration due to related vascular, cardiac, and renal anomalies.

INTRODUCTION

Alagille syndrome (AGS) is an autosomal-dominant multisystem disorder that primarily affects the liver, heart, kidneys, and skeleton.[1] It is one of the most common inherited disorders to cause chronic liver disease in children secondary to intrahepatic bile duct paucity leading to chronic cholestasis. About 10%–50% of children develop cirrhosis,[2] development of hepatocellular carcinoma (HCC) is exceedingly rare, with <20 cases reported in the literature and only 7 of these were adults patients.[2] We present a rare case of a patient with AGS and HCC treated initially with liver resection followed by liver transplantation due to HCC recurrence.

CASE DESCRIPTION

The patient is a 41-y-old male with a history of AGS. At age of 38 y, he was diagnosed with a 6.7×8.2 cm mass involving the posterior segment of the right hepatic lobe (Figure 1). Percutaneous biopsy of the mass confirmed the diagnosis of HCC. He had child A liver cirrhosis with serum alpha-fetoprotein level of 3.7 ng/mL. The patient underwent transarterial chemoembolization (TACE), followed by uneventful right hepatic lobectomy. Of note, during the TACE procedure, it was established that his celiac axis was occluded, and access to the hepatic arterial system was achieved through the superior mesenteric artery via extensive pancreaticoduodenal collateralization through his gastroduodenal artery. One year later, he developed 2 new HCC lesions, 1 measuring 3.0×1.9 cm in the medial aspect of his left hepatic lobe and a second one measuring 1.4×1.3 cm in his residual right hepatic lobe (Figure 2). Both lesions were treated with percutaneous radiofrequency ablation. and the patient was referred for liver transplant evaluation giving he fit within Milan Criteria. Pretransplant evaluation did not reveal any major cardiovascular abnormalities (no pulmonary artery stenosis). Patient's workup was notable for a single horseshoe kidney, with a baseline serum creatinine of 1.6 mg/dL, GFR of 46.9 mL/min, and a calculated

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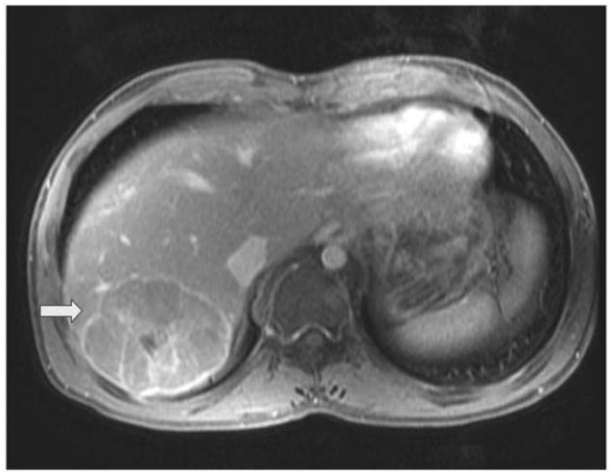

FIGURE 1. Cross-sectional abdominal MRI showing a 6.7 × 8.2 cm mass (arrow) in the posterior segment of the right hepatic lobe.

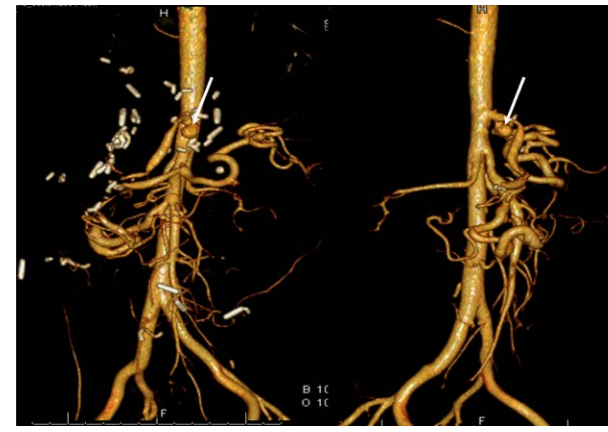

FIGURE 3. Computed tomography angiogram of the abdomen with 3-dimensional reconstruction showing a pseudoaneurysm (arrows) arising from the proximal segment of the supraceliac abdominal aorta to the donor hepatic artery bypass graft.

model of end-stage liver disease score of 11. Our center adheres to the Organ Procurement and Transplantation Network guidelines for liver and multiorgan allocation. Per these guidelines, he did not qualify for dual liver kidney listing and was listed solely for liver transplantation.[3,4]

Three months later (at the age of 42 y), he underwent a deceased donor liver transplantation from an 18-y-old brain-dead donor. An interposition donor iliac artery graft from the supraceliac aorta to the donor hepatic artery was needed due to known history of celiac axis occlusion. A choledocho-choledocho end-to-end biliary anastomosis was performed. The explanted native liver showed hepatic parenchyma with cholestatic changes and bile duct paucity, with underlying moderately differentiated HCC. The patient developed a bile leak on postoperative day 10 and underwent revision of his biliary anastomosis with conversion to a Roux-en-Y hepaticojejunostomy. He had an uneventful postoperative course with immunosuppression consisting of tacrolimus, mycophenolate mofetil, and tapering dose of prednisone. He was placed on aspirin 325 mg daily as per our protocol for liver transplant recipients.

Three months posttransplant, he underwent protocol HCC surveillance imaging and was found to have an incidental 3-cm diameter pseudoaneurysm close to his aortoiliac vascular anastomosis site (Figure 3). His allograft function was stable with serum bilirubin level of 0.1 mg/dL, serum alanine aminotransferase 6 U/L, serum aspartate aminotransferase 15 U/L, serum alkaline phosphatase 57 U/L, and INR of 1.2. Due to concerns for pseudoaneurysm rupture, he underwent an infrarenal aortic jump graft to the donor hepatic artery using donor external iliac artery. The old supraceliac aortic conduit was ligated intraoperatively. This was followed 12 d later by occlusion of the pseudoaneurysm by placement of a covered aortic stent graft (12 × 38 mm balloon-expandable covered stent, Atrium Medical) (Figure 4A) by interventional radiology. Subsequent imaging revealed that the stent graft head had slightly migrated caudally with partial occlusion of the superior mesenteric artery. For this reason, a new 6 × 18 mm balloon-expandable stent was placed over the proximal aspect of the superior mesenteric artery in an effort to buttress the stent graft (Figure 4B). After this complicated course, the patient developed acute-on-chronic kidney injury requiring hemodialysis. He successfully received a deceased donor kidney transplant 13 mo after his liver transplant. The patient remains HCC free with excellent liver and renal allograft function, 15, 27, and 35 mo after liver resection, liver transplant, and renal transplant, respectively.

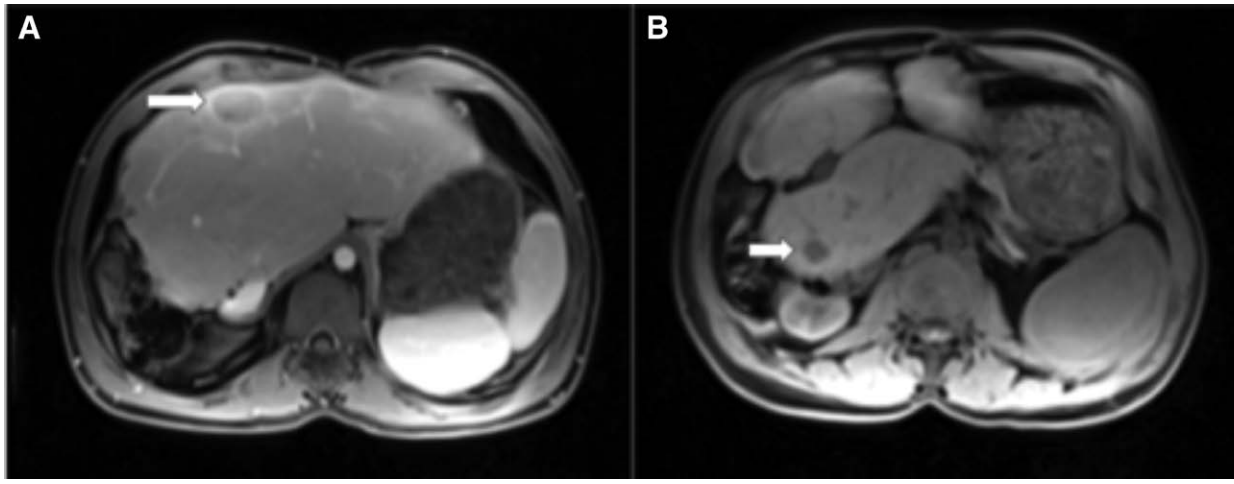

FIGURE 2. Cross-sectional abdominal MRI showing: (A) 3.0 × 1.9 cm hepatocellular carcinoma (arrow) in the medial left hepatic lobe and (B) 1.4 × 1.3 cm hepatocellular carcinoma (arrow) in the left hepatic lobe.

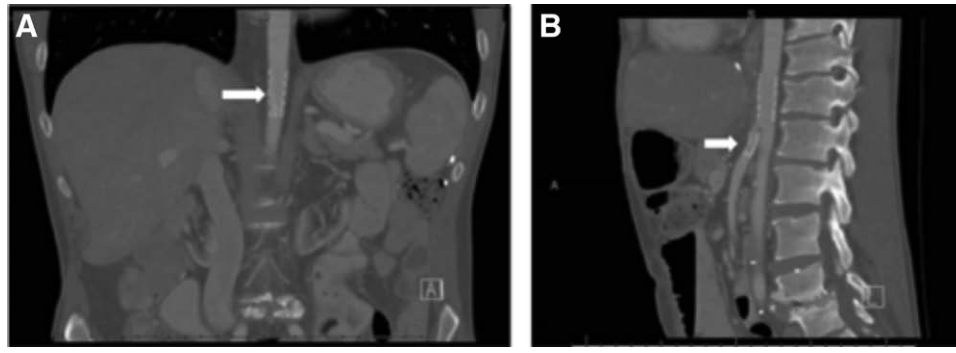

FIGURE 4. Computed tomography of the abdomen showing: (A) covered aortic stent stent (arrow) occluding the pseudoaneurysm and (B) covered stent (arrow) within the proximal superior mesenteric artery.

DISCUSSION

We present a very rare case report of an adult with AGS who developed recurrent HCC initially managed with liver resection followed by liver transplantation.

Development of HCC is exceedingly rare in adults with AGS, and only 7 cases have been reported in the literature.[2] First described in 1969, AGS is estimated to affect 1:30 000–50 000 live births.[5] Its pathogenesis is related to mutations in JAG1 or NOTCH2 genes[1] that are expressed in fetal liver, lungs, brain, and kidneys, as well as adult heart, lung, skeletal muscle, and kidneys. AGS is most commonly associated with paucity of intrahepatic bile ducts that may lead to chronic cholestasis, as well as cardiac (pulmonary stenosis), ocular, and skeletal abnormalities (characteristic facial features). It is almost exclusively diagnosed in children with either cardiac or hepatic manifestations. Portal hypertension and cirrhosis develop in 10%–50% of patients who present with liver disease in infancy.[2] Treatment of AGS is guided by the distribution and severity of the clinical symptoms. Liver transplantation is required in 21%–50% of the pediatric patients who develop hepatic cirrhosis, usually before the age of 5 y.[2] Only 10% of patients undergo first transplant above the age of 18 y.[6] The reported rate of 5-y graft survival for pediatric and adult liver transplant in this specific patient population are 76.1% and 79.5%, respectively.[6]

Vascular complications associated with liver transplantation occur in 6%–10% of cases. Our patient developed a pseudoaneurysm at the site of anastomosis of the iliac artery interposition graft to his supraceliac aorta. In liver transplant recipients, hepatic artery pseudoaneurysm has a reported incidence of 1%–2% with a mortality of up to 69%.[7] Risk factors for pseudoaneurysm formation after liver transplantation include infection, bile leak, and Roux-en-Y hepaticojejunostomy. Our patient developed a bile leak most likely due to inadequate vacularity to the recipient bile duct secondary to the presence of celiac artery stenosis. AGS patients have a predisposition to have or develop vascular anomalies. Experience in the pediatric population reveals that 21% of children with AGS have a vascular complication in the first 30 d after transplantation.[8] In addition, the use of anastomotic interposition grafts has been reported in up to 20% of these patients.[8] We, therefore, recommend that the biliary reconstruction be performed primarily using a Roux limb if there are any preoperative anomalies in the hepatic arterial vasculature.

The complex postoperative course along with calcineurin inhibitors likely worsened the patient's chronic renal insufficiency after liver transplantation. He subsequently underwent a successful kidney transplantation. The spectrum of renal manifestations in AGS is broad and includes structural disorders of the renal system (solitary kidney, ectopic kidney, horseshoe kidney, multicystic kidney),[9] abnormalities of the renal vasculature and intrinsic renal disorders. Progressive renal dysfunction after pediatric liver transplantation in AGS has been noted to occur in up to 22%.[8] We, therefore, recommend the use of renal sparing regimens for immunosuppression postliver transplantation in patients with AGS.

To our knowledge, this is the first reported case of recurrent HCC in an adult with AGS who was treated with liver resection followed by liver transplantation. Adults with AGS are prone to vascular, biliary as well as renal complications postliver tranplantation. Multidisciplinary planning in the pretransplant and posttransplant period is paramount for successful outcomes in this rare subgroup of patients undergoing liver transplantation.

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