De Novo Hepatocellular Carcinoma in Primary Sclerosing Cholangitis Post-Liver Transplant: The Case for Surveillance

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ABSTRACT

Introduction: While recurrent primary sclerosing cholangitis and de novo malignancies such as skin cancer are common after liver transplantation, de novo hepatocellular carcinoma (HCC) after liver transplantation for primary sclerosing cholangitis is exceedingly rare.

Case Presentation: A 72-year-old man with ulcerative colitis underwent liver transplantation for primary sclerosing cholangitis. Thirty years later, abdominal imaging incidentally revealed cirrhotic liver morphology with a new, bulky, and locally invasive hepatic mass. Biopsy confirmed stage IIIA hepatocellular carcinoma, which was treated successfully with Y-90 radioembolization segmentectomy.

Discussion: Immunosuppression-related malignancies are prevalent in long-term liver transplant survivors, and HCC recurrence can occur in patients transplanted for HCC. However, de novo HCC is rare in liver transplant recipients with primary sclerosing cholangitis and has primarily been reported in patients with viral hepatitis.

Conclusions: Vigilant screening for allograft fibrosis, cirrhosis, and malignancy using emerging modalities in long-time liver transplant survivors warrants consideration.

INTRODUCTION

Malignancy beyond 1 year post-liver transplant occurs at rates approximately twice those in the general population, driven by prolonged immunosuppression, recurrent or de novo liver diseases, and lifestyle factors such as tobacco or alcohol use.[1] Up to 20% of patients transplanted for hepatocellular carcinoma (HCC) develop recurrence,[2] while among patients transplanted for primary sclerosing cholangitis (PSC), the 10-year cumulative risk of malignancy is 21%, primarily due to colorectal cancer or cholangiocarcinoma.[3] The prevalence of de novo HCC after liver transplantation in patients with PSC is rare but has been observed in patients with viral hepatitis, metabolic liver disease with advanced fibrosis/cirrhosis, older donor age, male sex, and exposure to environmental carcinogens.[4,5] However, de novo HCC after liver transplantation in patients with PSC is rare, with only a few reported cases occurring in patients with recurrent liver disease (including 1 case without fibrosis) or secondary causes such as hepatitis C infection.[6,7]

CASE PRESENTATION

We present the case of a 72-year-old man with ulcerative colitis who received an orthotopic liver transplantation in 1994 for PSC and cirrhosis. Following transplantation, he maintained excellent allograft function on immunosuppression with prednisone, tacrolimus, and mycophenolate. His course was complicated by mucinous adenocarcinoma of the colon, treated with curative total colectomy and ileal pouch creation in 1998; elevated alkaline phosphatase in 2014, for which magnetic resonance cholangiopancreatography (MRCP) findings were unrevealing; and Crohn's disease of the ileal pouch, controlled with vedolizumab since 2021. Computed tomography (CT) of the abdomen in 2021 incidentally revealed hepatic fissural prominence and undulation of the liver surface without a focal lesion. He continued routine follow-up in hepatology and inflammatory bowel disease clinics.

In May 2024, nearly 29 years posttransplant, he was hospitalized for viral pneumonia. Laboratory testing showed mild anemia (hemoglobin 12.5 g/dL), thrombocytopenia (platelet count,

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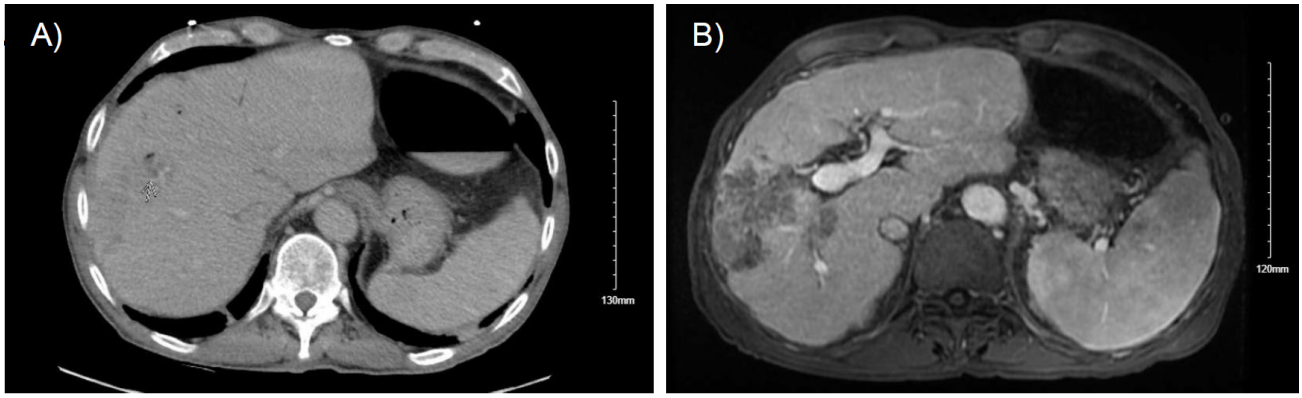
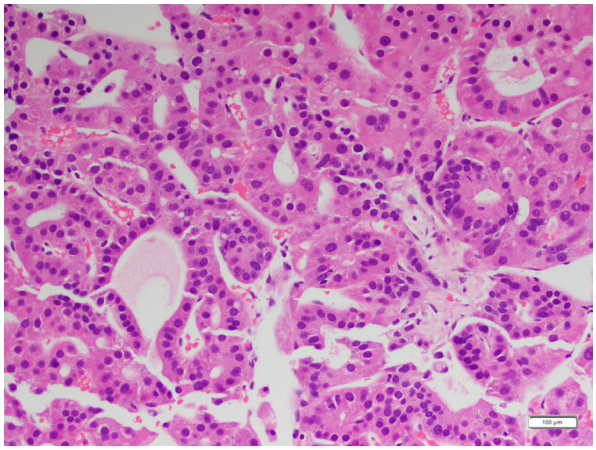
Figure 1. Computed Tomography and Magnetic Resonance Imaging of the Abdomen



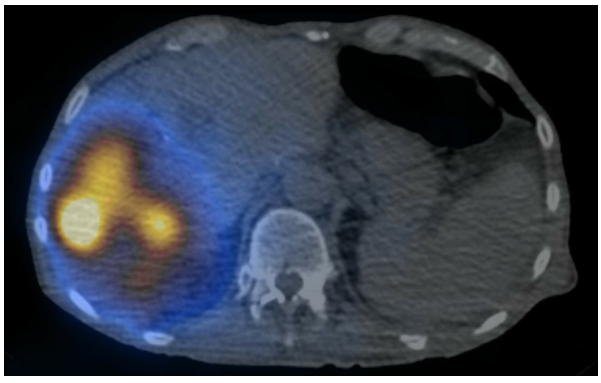
A) CT indicates a new portal venous thrombus. Low attenuation of the liver seen peripheral to the thrombus is concerning for underlying mass.
B) MRI indicates a 7.3 x 5.5-cm infiltrative mass in the right hepatic lobe with multiple satellite lesions.

Figure 2. H&E Stain of Liver Mass Showing Moderately Differentiated Hepatocellular Carcinoma With Predominant Pseudoacinar Pattern



Abbreviation: H&E, hematoxylin and eosin.

Figure 3. Liver Biopsy Specimen Showing Moderately Differentiated Hepatocellular Carcinoma



131 × 10^3/μL), elevated alkaline phosphatase (166 U/L), and stable liver function test results. Viral polymerase chain reaction testing was negative, and no significant alcohol use was identified. CT of the abdomen revealed cirrhotic liver morphology and a lesion concerning for a hepatic mass. Magnetic resonance imaging (MRI) confirmed a 7.3 x 5.5-cm infiltrative mass in the right hepatic lobe with associated portal vein thrombus (Figure 1). Biopsy pathology (Figure 2) confirmed moderately differentiated HCC with a pseudoacinar pattern, and immunohistochemical staining corroborated HCC rather than metastatic colorectal cancer or cholangiocarcinoma.

Because safe resection was not feasible, a multidisciplinary tumor board recommended yttrium-90 (Y-90) transarterial radioembolization segmentectomy (Figure 3), which he tolerated well. Follow-up MRI demonstrated stable posttreatment changes 11 months after diagnosis. Adjunctive chemotherapy remains under consideration.

DISCUSSION

This case presents a rare instance of de novo HCC nearly 30 years after liver transplantation for PSC. Although de novo HCC after liver transplantation for PSC is rare, our patient highlights its potential emergence in the setting of subclinical recurrent PSC. Cholangiocarcinoma and metastatic colorectal cancer were more likely diagnostic considerations given his history of PSC and colorectal cancer. Accurate diagnosis required high-quality MRI and image-guided biopsy with pathologic evaluation..

Survival beyond 20 years after liver transplantation is increasingly common. Patients undergoing liver transplant for PSC have reported life expectancies of 9 to 20 years,[3] with >69% surviving beyond 10 years.[8] As patients with PSC have longer survival than non-PSC liver transplant recipients,[9] This extended survival underscores the need for proactive screening for posttransplant

liver disease, risk factor mitigation, and enhanced malignancy surveillance in this subpopulation.

Recurrent and de novo liver disease after liver transplantation are common and warrant close evaluation. Clinically significant PSC recurrence after liver transplantation ranges from 18% to 37%, with risk factors including concurrent inflammatory bowel disease, acute cellular rejection, male recipients, intact colon prior to liver transplant, cholangiocarcinoma prior to liver transplant, or cytomegalovirus,[8] several of which were present in our patient. MRI/MRCP findings in 2014 showed no evidence of recurrent PSC. Because subtle signs of liver disease were present on imaging in 2021, subclinical recurrence of PSC after 2014 is likely. Similarly, de novo metabolic dysfunction-associated liver disease has been shown to affect >70% of patients 5 years after liver transplantation, with risk factors including metabolic syndrome, calcineurin inhibitor or corticosteroid use, alcohol use, and genetic factors.[10] Given the high prevalence of recurrent and de novo liver diseases after liver transplantation, screening for and diagnosing progression to advanced fibrosis or cirrhosis is crucial.

Currently, no routine screening exists for hepatic malignancy after liver transplantation unless cirrhosis is identified. The most recent International Liver Transplantation Society/Spanish Society of Liver Transplantation consensus conference and the American Association for the Study of Liver Diseases guidelines recommend individualized malignancy screening based on viral infection status, burden of immunosuppression, and estimated cancer risk (eg, abdominal imaging every 6 to 12 months for HCC screening in patients who develop allograft cirrhosis).[11,12] Increasing uptake of newer screening modalities such as elastography[13] may allow earlier identification of posttransplant liver disease and guide targeted HCC screening in higher-risk patients. Screening protocols using biannual imaging (abdominal CT, MRI, or bone scan with nuclear tracing) for transplant recipients have demonstrated improved survival.[14,15] Thus, among long-term transplant recipients, elastography or even routine CT or MRI every 3 to 5 years after transplantation may improve detection of liver disease, fibrosis, and malignancy; however, formal cost-effectiveness and benefit analysis are needed.

The occurrence of HCC 30 years after liver transplantation for PSC highlights the potential for asymptomatic allograft liver disease, particularly allograft fibrosis or cirrhosis. Given the increasing longevity of liver transplant recipients, there is a growing need to maintain a high index of suspicion for recurrent or de novo liver disease and malignancy. Although current guidelines recommend individualized approaches to malignancy screening after transplantation, emerging literature suggests a potential benefit from more proactive screening strategies, including elastography.

CONCLUSIONS

Our patient's asymptomatic recurrent PSC and de novo HCC detected decades after liver transplantation underscore the need for proactive screening for late-onset disease, allograft fibrosis, and malignancy in long-term transplant survivors. Because his HCC was identified incidentally at a relatively early stage, allowing treatment with Y-90 radioembolization, this case suggests that routine screening for recurrent liver disease, fibrosis, and malignancy in long term liver transplant survivors may be beneficial.

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