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Focal Fat Masquerading as Malignancy in the Liver Graft of a Post-Transplant Patient

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Abstract

Background and Aims—Liver failure from non-alcoholic fatty liver disease (NAFLD) is an increasing indication for liver transplant and recurrence of fatty liver in transplanted grafts has been documented. Herein is described an atypical recurrence of steatosis as a de novo focal fatty lesion that mimicked a more ominous cancerous lesion. This presentation of recurrent NAFLD has not previously been described in the literature.

Methods—Chart review.

Results—Biopsy of an atypical lesion was found to be focal fat with surrounding steatohepatitis.

Conclusions—Non-alcoholic fatty liver disease may recur after liver transplant and manifest as a focal fatty lesion. It is important to catalogue the atypical presentations of the increasingly common NAFLD developing in transplanted livers.

Keywords

Liver transplant; NAFLD; NASH; Focal fat; Hepatocellular carcinoma

Introduction

End-stage liver disease from non-alcoholic steatohepatitis (NASH) is an increasing indication for liver transplantation as the prevalence of the metabolic syndrome increases

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worldwide. As physicians gain experience with the post-transplant course of these patients, the recurrence of hepatic steatosis in transplanted grafts can be anticipated and is frequently reported throughout the literature. Here we report a case of a patient transplanted for NASH-induced cirrhosis and subsequently found to have an atypical recurrence of steatosis that mimicked a mass lesion, concerning for hepatocellular carcinoma (HCC) or post-transplant lymphoproliferative disorder (PTLD).

Case Report

In 2010, a 57-year-old Caucasian male who received an orthotopic deceased donor liver transplant secondary to NASH cirrhosis in 2008 presented for his second annual exam. His medical history prior to transplant was notable for diabetes for 18 years and a BMI of 37.5. There was no history of alcohol use. His MELD score at the time of transplant was 16, ABO blood group B. He had no evidence of HCC on his pretransplant biopsy or imaging studies. The allograft had a normal gross appearance at the time of organ procurement and had 30% macrovesicular steatosis on both the immediate pre- and post-transplant biopsies. No hepatocellular carcinoma was seen on 5–8 mm full cross sections through the liver. The post-transplant course was complicated by an initial episode of acute rejection, an episode of CMV viremia, and stenting of a bile duct stricture 1 year after his transplant. An MRI performed 6 months after transplant and an abdominal ultrasound performed 1 year after transplant showed a heterogeneous liver, but no evidence of a focal mass. In 2010, a repeat ultrasound showed findings concerning for a new mass lesion within the right lobe of the liver along with steatosis. His liver function tests were notable for an elevated gamma-glutamyl transpeptidase of 870 U/l, from his baseline near 400 following transplant, and an elevated alkaline phosphatase of 289 U/l. His transaminases, bilirubin, and INR were within normal limits and had remained so following his initial episode of rejection and placement of a bile duct stent 1 year prior. His CEA was 3.3 ng/ml, CA 19-9 was 28 units/ml, AFP was 3.54 ng/ml, all within normal limits, and his EBV and CMV viral loads were undetectable. The immunosuppressive regimen at the time of follow-up included tacrolimus and mycophenolate mofetil. Prednisone had been tapered and discontinued. He had gained approximately 40 lbs since his transplant. We proceeded with an MRI/MRA of the abdomen that showed diffuse ill-defined confluent areas of signal abnormality involving the right hepatic lobe with a small degree of enhancement and some areas that demonstrated washout. There was also evidence of hepatic steatosis, with sparing of the left hepatic lobe (Fig. 1).

The dramatic appearance of these findings, and discordance with the ultrasound, caused the interpreting radiologist to request and perform ultrasound-guided biopsy. The biopsy of the area in question showed lobular macrove-sicular steatosis involving approximately 25% of the total liver tissue with features consistent with steatohepatitis (grade 1, stage 1–2 by Brunt classification). There was no evidence of acute cellular rejection, PTLD, or hepatocellular carcinoma in multiple biopsy cores (Fig. 2). This case was then reviewed again at our hepatobiliary radiology conference. Upon this retrospective review of the abdominal MRI, the concerning irregular mass-like areas in the right hepatic lobe had heterogeneous loss of signal on out-of phase images (Fig. 1). This was observed in conjunction with no increased enhancement of the abnormal hepatic tissue on early post-gadolinium images. Overall, these findings were considered consistent with heterogeneous, massive fatty infiltration of the liver and consistent with the pathologic interpretation of the liver biopsy. Repeat surveillance imaging 3 months later showed persistent extensive multi-focal fatty infiltration centered in the right hepatic lobe unchanged from the index MRI. The patient remains well and without symptoms.

Discussion

This is a unique case report demonstrating the post-transplant recurrence of NASH manifesting as a focal fat mass on MRI mimicking a more ominous cancerous lesion. This particular finding has not been previously reported in the liver transplant literature to our knowledge. There is a one case report of focal fat masquerading as hepatic metastases on positron emission tomography (PET)/CT imaging [1] and another where a *lack* of fat appeared as metastatic disease on PET imaging [2], but these reports are from native livers in patients with known breast and colorectal cancer, respectively, using an imaging modality not commonly used in the post-liver transplant setting.

The first reports of recurrent NASH following liver transplantation were published in the late 1990s [3]. Since then, the phenomenon of post-transplant NASH is common, if not expected in certain populations. The major risk factors for developing recurrent or de novo NASH include components of the metabolic syndrome [4, 5] and may be more prevalent in post-transplant patients due to the use of corticosteroids and calcineurin inhibitors [6]. Additional studies have also identified pre-transplant liver graft steatosis as a risk factor [7]. Our patient had many of these risk factors including a BMI of 40 with significant weight gain following transplant, difficult to control diabetes mellitus, and the current use of tacrolimus as well as the initial use of prednisone therapy following his transplant.

Given the increased recognition of disease recurrence and the risk factors involved, studies have now begun to focus on the implications of such findings. Initial case studies reported that steatosis can develop within 6 months of transplant and cirrhosis within 2 years in patients that had been transplanted for NASH [4, 8, 9]. A more recent retrospective review in 2009 concluded that although recurrent fatty liver disease was seen in up to 70% of their post-transplant population, only 25% had recurrent NASH, and none of these patients had graft failure requiring re-transplantation at 3 years. This study also found that in the patients with recurrent NASH over one-third had normal liver functions tests at the time of diagnosis [10]. Other studies have estimated up to 50% of patients have normal liver enzymes at the time of diagnosis [7]. In contrast, another extended study of patients transplanted for cryptogenic cirrhosis or NASH saw a 10% incidence of bridging fibrosis or cirrhosis at the 10-year time point mostly in patients who developed recurrent NASH. However, the recurrence of fatty liver disease in this patient population did not significantly affect survival compared to patients who had other indications for transplant in the control group. In fact, patients who were transplanted for NASH or cryptogenic cirrhosis were more likely to die of cardiovascular disease than recurrent liver disease [11]. Other studies have shown an increase in early mortality among patients transplanted for NASH with survival equilibrating with other indications for transplant at 3 years and beyond [12, 13] inferring that the reduced survival was a perioperative complication of cardiovascular disease rather than recurrent liver disease.

In a recent study, Dumortier et al. examined the development of de novo NASH in patients transplanted for other indications, mainly alcoholic and HCV-related cirrhosis. It was found that even in this patient population, excluding patients with recurrence of their primary disease, 31% of patients developed steatosis and 3.8% developed NASH [7]. Based on these, patients with significant risk factors for fatty liver disease pre-transplant can have these factors exacerbated after transplantation because of the required immunosuppressive regimens; therefore considerations need to be made in the management of these patients post-transplant.

As the transplant community continues to grapple with metabolic syndrome care, it is important to catalogue the atypical presentations of the increasingly common NAFLD

developing in transplanted livers. Detection of a new liver mass in a post-transplant patient should always raise concerns for malignancy or infection. However, it is important to remember that uneven or focal fatty infiltration is also possible, particularly in patients with risk factors for recurrent fatty liver disease. Awareness of this entity can prevent unnecessary and invasive testing.

Acknowledgments

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Abbreviations

NAFLD	Non-alcoholic fatty liver disease
NASH	Non-alcoholic steatohepatitis
HCC	Hepatocellular carcinoma
MRI	Magnetic resonance imaging

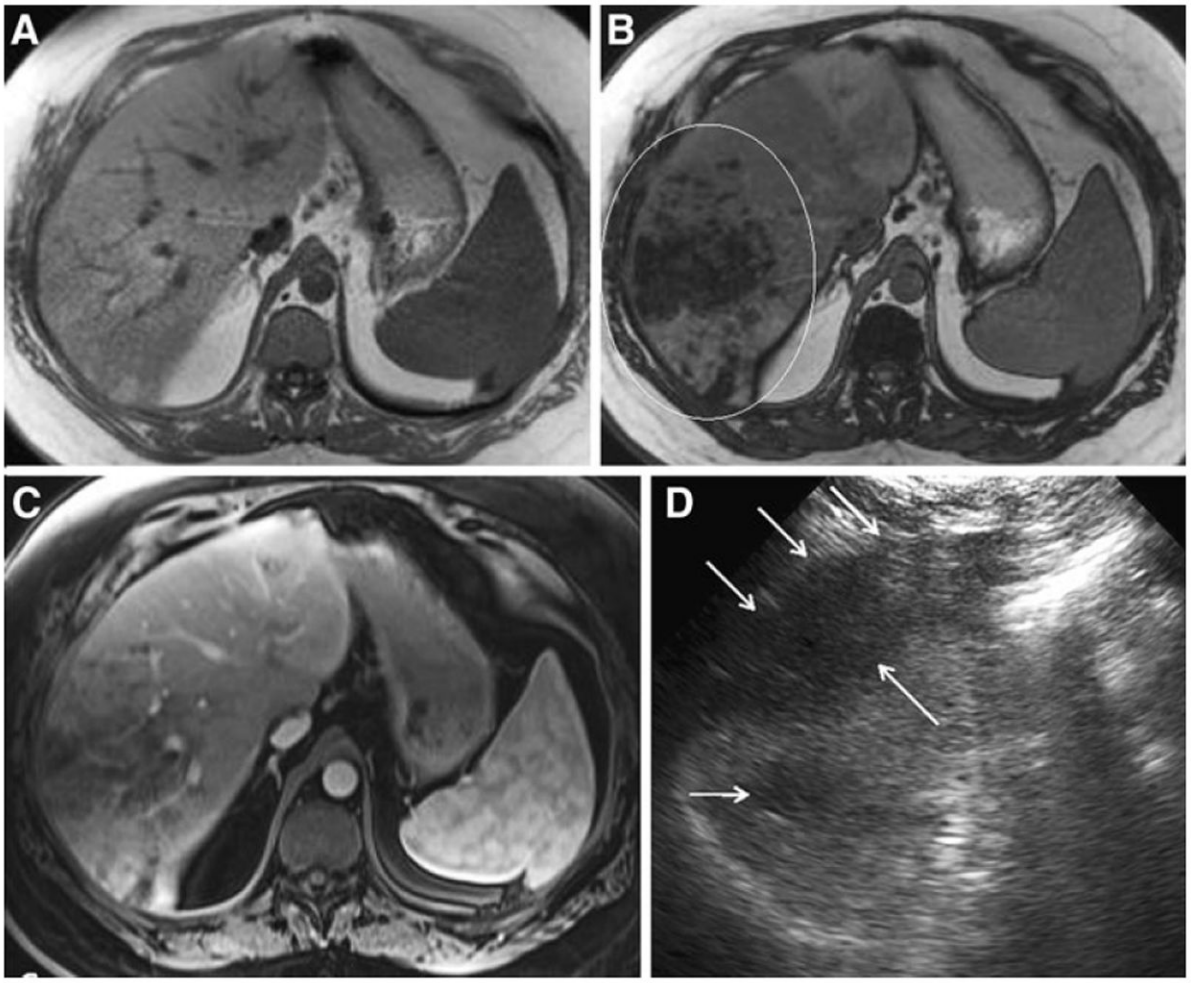

Fig. 1.

Transverse images of the abdominal MRI (**a, b, c**) and longitudinal image of liver ultrasound (**d**). There is no remarkable liver abnormality on the T1-weighted in-phase image (**a**). However, on the T1 out-of-phase image (**b**), there are areas with great loss of signal in the right hepatic lobe. This is observed in conjunction with no increased enhancement of the abnormal hepatic tissue on post-gadolinium image (**c**). These MR findings are consistent with heterogeneous, massive fatty infiltration of the liver. The heterogeneous fat infiltration mimicked an infiltrating lesion on ultrasound (*arrows* in **d**)

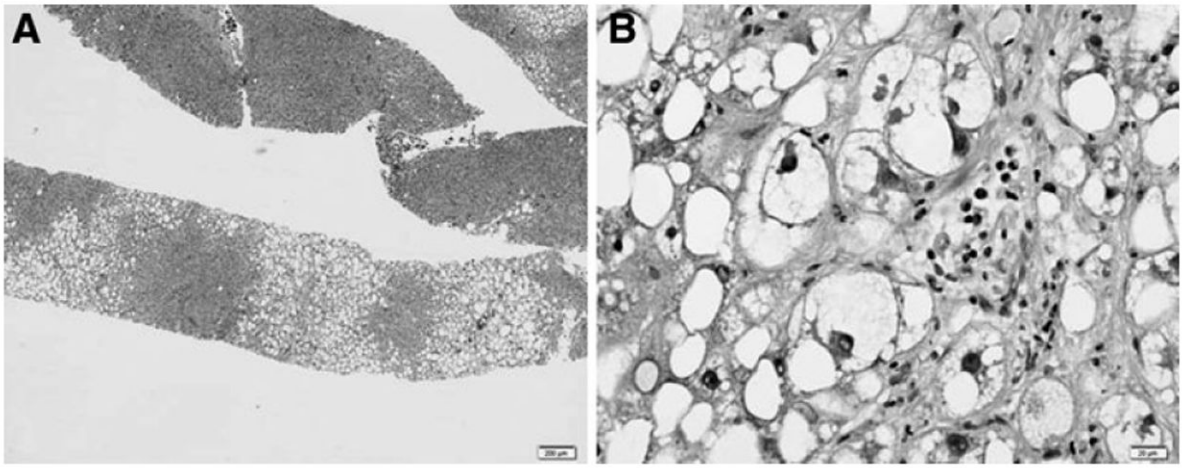

Fig. 2.
a Liver biopsy cores demonstrating areas of steatosis. No evidence of HCC or PTLD was found in multiple biopsy cores (40×). **b** Balloon cells and Mallory's hyaline (400×)