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CASE REPORT | LIVER

Hepatocellular Carcinoma in a Patient With Hepatic Steatosis

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ABSTRACT

Hepatocellular carcinoma (HCC) has historically developed in the setting of known risk factors—chronic liver disease from viral hepatitis and cirrhosis. In the absence of a risk factor, the development of HCC was rare. However, the increasing prevalence of nonalcoholic liver disease and nonalcoholic steatohepatitis, the paradigm is shifting. Currently, no HCC screening guidelines exist for these patients. We report a 30-year-old man with a medical history of treated nonseminomatous germ cell testicular cancer who presented with asymptomatic transaminitis. Subsequent workup was notable for a 1.6-cm liver lesion. The patient underwent a left lobe wedge resection with pathology demonstrating a well-differentiated HCC in a background of hepatic steatosis.

INTRODUCTION

Hepatocellular carcinoma (HCC) is the most common primary liver malignancy.[1] Risk factors for HCC include viral hepatitis associated-chronic liver disease and cirrhosis of any etiology. The prevalence of nonalcoholic liver disease (NAFLD) and non-alcoholic steatohepatitis (NASH) is increasing, perhaps due to the limited data of appropriate screening guidelines for this patient population before the development of cirrhosis.[2] Early diagnosis is a key predictive factor in the treatment success of HCC.[1] We report a patient with a medical history of treated nonseminomatous germ cell (NSGC) testicular cancer with de novo development of HCC.

CASE REPORT

A 30-year-old man presented with transaminitis; his history was significant for remote stage IIIC NSGC cancer after right orchiectomy and chemotherapy in remission, and imaging was suggestive of hepatic steatosis, presented with transaminitis. The testicular tumor was 5.6 cm, staged pT2 with mixed components (α-fetoprotein [AFP] was <3 ng/mL and human chorionic gonadotropin was negative). Staging workup at the time of diagnosis revealed aspartate aminotransferase (AST) of 49 U/L and alanine aminotransferase (ALT) of 59 U/L. Computed tomography (CT) displayed metastatic disease with 3 hypoattenuating hepatic lesions, the largest being 3.0 × 2.9 cm. The primary tumor was treated with radical right orchiectomy and adjuvant chemotherapy. He tolerated this well with complete response to treatment. Follow-up imaging was negative for persistent disease. Over the subsequent 8 years, the liver enzymes, AST and ALT fluctuated from normal to a peak value of 69 and 74 U/L, respectively.

Five years after completing therapy, during scheduled surveillance, he developed further elevation of AST and ALT to 53 and 130 U/L, respectively. The patient denied heavy alcohol abuse or new medications. His family history was notable for unspecified liver cancer in paternal grandfather. On examination, the patient appeared well with normal vitals, no jaundice, and body mass index of 35 kg/m^2. Alkaline phosphatase, total bilirubin, and international normalized ratio were within the normal limits. His workup for viral and autoimmune hepatitis, primary biliary cholangitis, Wilson's disease, hemochromatosis, and α-1 antitrypsin disease was negative. AFP and hemoglobin A1C were normal. Complete blood count was unremarkable. Contrast-enhanced CT showed a focal 22.5 mm area of hypoattenuation in the left hepatic lobe (Figure 1). Magnetic resonance imaging (MRI) demonstrated a 17 mm hypoattenuation in the left lobe with arterial enhancement (Figure 2). Endoscopic ultrasound-guided fine-needle biopsy was

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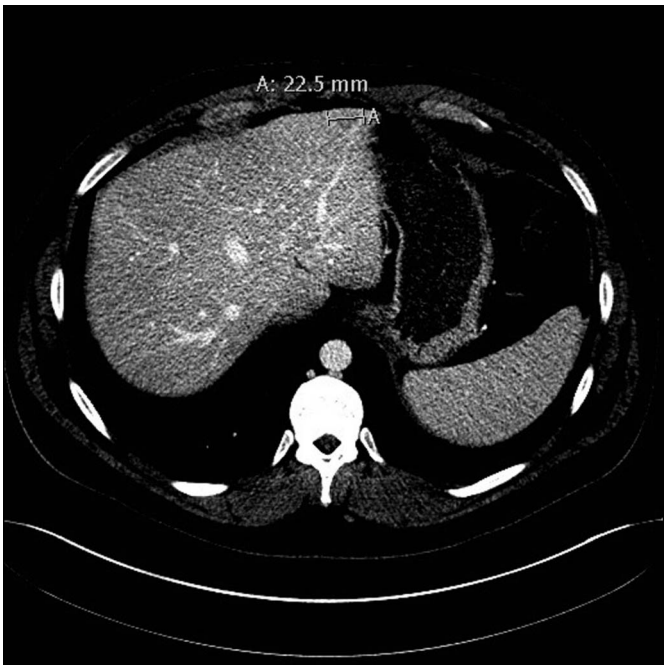

Figure 1. Abdominal and pelvic computed tomography with contrast shows a focal 22.5 mm area of hypoattenuation in the left hepatic lobe.

performed, and the results were primary hepatic neoplasm vs adenoma. Given the broad differential, a multidisciplinary tumor board recommended hepatic resection. Laparoscopic left lobe wedge resection revealed a well-differentiated HCC (T1b) and background liver steatosis. Staging was negative for metastasis. Since the resection, the patient has been well, although liver enzymes remain slightly elevated at 43 U/L and 77 U/L, for AST and ALT respectively.

DISCUSSION

HCC is the most common primary liver malignancy with over 500,000 cases diagnosed annually.[2,3] Historically, in the absence of risk factors the development of HCC was rare, but with the increase in the prevalence of NAFLD and NASH, the paradigm is shifting. HCC has been recently reported in patients with NAFLD and NASH without evidence of underlying cirrhosis. A large cohort study found an unadjusted odds ratio of 5.0 (95% confidence interval, 3.1–7.8) with patients with both HCC and NAFLD without cirrhosis when compared with patients with hepatitis C virus-related HCC without cirrhosis.[4] Another recent study of patients with NAFLD found approximately 20% had HCC in the absence of cirrhosis. Interestingly, they found the overall risk for patients with NAFLD without cirrhosis to be too low to recommend HCC screening programs.[5]

There are several noninvasive scoring systems validated to predict advanced fibrosis and cirrhosis in patients with NAFLD, including the NAFLD fibrosis score and Fibrosis-4 (FIB-4) index, which include factors such as glucose, age, AST/ALT, platelet count, body mass index, and albumin. This patient's scores were as follows: NAFLD fibrosis score −1.25 indicating indeterminate risk and a FIB-4 index of 1.16 indicating F0-F1.[6–8] As evidenced by our patient, regardless of the presence or absence of advanced fibrosis, the index of suspicion for HCC should remain high.

Typically, the initial diagnostic approach for suspected HCC is abdominal imaging with quadruple-phase CT or MRI. In patients with known HCC risk factors, culprit lesions normally enhance and appear hyperintense on arterial phase with the hallmark development of neovascularity and washout of contrast in the portal venous phase. The appearance of HCC on T2-weighted images is more variable, with the lesion typically appearing isointense to background liver tissue. HCC diagnosis with MRI has a per-lesion sensitivity of 72% and specificity of 87%.[9,10] Our patient had a typical arterial enhancement, but notably had a marked degree of T2 hyperintensity. When a suspicious lesion is found in patients without underlying cirrhosis, a liver biopsy should be performed.[11] Liver biopsy is often performed with both FNA and core techniques because this provides greater accuracy than either alone, with a sensitivity and specificity of 96% and 95%, respectively.[12] The American Association for the Study of Liver Diseases (AASLD) recommends the use of the Barcelona-Clinic Liver Cancer classification over the tumor-node-metastasis classification for staging purposes because the former takes into account the severity of liver dysfunction and can better guide treatment decisions.[13,14] Treatments available include lesion resection, radiofrequency

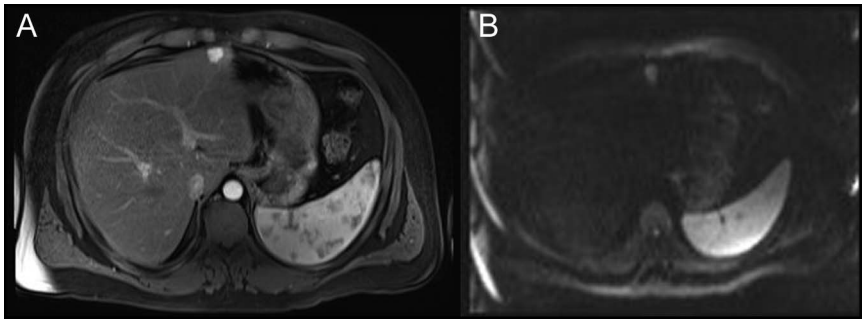

Figure 2. Abdominal magnetic resonance imaging showing (A) a 17 mm lesion in the left anterior hepatic lobe in the arterial phase and (B) a hyperintense left lobe lesion in the T2 phase.

ablation, transarterial chemoembolization, and liver transplantation. Surgical resection, if technically feasible, is often the preferred treatment method because it is curative. Liver transplant is also considered curative but is a much larger undertaking.[15] There are currently no AASLD guidelines on the surveillance regimens for recurrent HCC after treatment with curative intent.[14] The current National Comprehensive Cancer Network guidelines based on expert opinion recommend imaging every 3–6 months for 2 years and then every 6–12 months thereafter.[16]

There are no documented cases of patients with a de novo HCC after an initial diagnosis of NSGC cancer. The only linkage between these 2 events involve the tumor marker AFP, which can be used to aid in the diagnosis of both. However, AFP should not be used as a single entity in HCC because it has a sensitivity of only 60%.[14] AFP in NSGC should be measured before orchiectomy for diagnostic and postoperative surveillance.[17] In conclusion, clinicians should have a high index of suspicion to assess for HCC in patients with hepatic steatosis, particularly those with a genetic predisposition to developing malignancy.

DISCLOSURES

Author contributions: J. Romano wrote the manuscript and is the article guarantor. E. Forster revised the manuscript for intellectual content.

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Informed consent was obtained for this case report.

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