ACG CASE REPORTS JOURNAL

CASE REPORT | LIVER

More Than a Rash: Recurrent Hepatocellular Carcinoma After Liver Transplantation

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ABSTRACT

Recurrent hepatocellular carcinoma (HCC) after liver transplant is uncommon in patients who have favorable pretransplant characteristics. We present a 56-year-old man with a history of liver transplant 8 weeks prior for hepatitis C cirrhosis and HCC who presented for shortness of breath. He was found to have a microangiopathic hemolytic anemia and an erythematous, nodular skin rash on his left lower abdomen. Biopsy of the skin rash would demonstrate metastatic HCC, determined to be the cause of hemolysis as well. Recurrent malignancy should be considered in patients with a history of HCC who present with new, unexplained skin nodules.

INTRODUCTION

Hepatocellular carcinoma (HCC) is the fifth most common cancer in the world, with metastatic sites including the lung, lymph nodes, and bones. Although rare, 0.5% to 3.5% of metastasis occurs to the skin.[1] These skin lesions are often found on the scalp, chest, and shoulders, appearing as a cluster of nodules 1 to 2.5 cm in diameter that are erythematous, firm, painless, and nonulcerative.[2,3]

CASE REPORT

A 56-year-old white man who had undergone liver transplantation for hepatitis C cirrhosis complicated by HCC 8 weeks previously presented with microangiopathic hemolytic anemia and severe thrombocytopenia. He had been diagnosed with HCC 4 months before his liver transplant, with computed tomography demonstrating 5.1-cm and 1.3-cm liver lesions. Hepatic decompensation precluded neoadjuvant therapy before his liver transplantation. At the time of liver transplant surgery, his explanted liver histology demonstrated poorly differentiated HCC with widespread vascular invasion (MpT3NxMx). After transplant, he was maintained on an immunosupressive regimen of tacrolimus, mycophenolate mofetil, and prednisone.

At the time of the presentation to the hospital, the patient complained of shortness of breath and fatigue with increasing pallor. His only other complaint was a new rash that appeared on his lower abdomen that appeared about 5 weeks after transplant. The rash was neither painful nor pruritic and came on very slowly. The rash consisted of several firm, nonblanching, erythematous papules and nodules in a band-like distribution in the left lower quadrant of his abdomen and crossed the midline (Figure 1).

Laboratory test results demonstrated pancytopenia with hemoglobin 4.9 g/L, elevated reticulocyte count 22.98%, lactate dehydrogenase 1,163 u/L, total bilirubin 4 mg/dL, and direct bilirubin 1 mg/dL. Haptoglobin was low, and peripheral smear showed schistocytes, all consistent with a hemolytic anemia. Skin biopsy and pathology revealed metastatic, poorly differentiated HCC to the dermis. Later imaging of his chest would demonstrate a speculated irregular right middle lobe airspace opacity, presumed to be HCC,

ACG Case Rep J 2019;6:1–3. doi:10.14309/crj.0000000000000107. Published online: July 10, 2019

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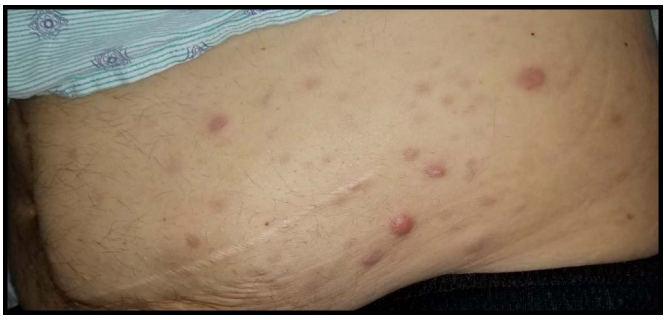

Figure 1. Firm, nonblanching, erythematous papules and nodules in a band-like distribution in the left lower quadrant of his abdomen and crossed the midline.

given the skin biopsy results (Figure 2). Abdominal computed tomography did not reveal evidence of recurrence of HCC. His alpha-fetoprotein remained normal as before at 4.6 ng/mL.

With the lack of response to withdrawal of calcineurin inhibitor therapy, our patient's hemolytic anemia was deemed likely due to the recurrent malignancy. He was restarted on low-dose cyclosporine and palliative chemotherapy with sorafenib 400 mg twice daily. To facilitate outpatient blood transfusions, a port was placed for vascular access. He was then discharged to home.

DISCUSSION

HCC incidence is increasing worldwide and arises from underlying chronic liver diseases such as hepatitis B or hepatitis C viruses. Common sites for HCC metastases include the lung, lymph nodes, and bones. Cutaneous manifestation of HCC occurs very rarely.[4]

There are few case reports of skin metastases from HCC. Previous case reports have described rapidly growing highly vascular lesions on the nostril, upper and lower eyelids, and abdominal cavity.[5] Some lesions can resemble pyogenic granulomas, and other lesions are localized firm nodules.[2] Other skin manifestations of HCC include paraneoplastic phenomena, such as Gottron papules or a heliotrope rash seen in skin manifestations of dermatomyositis.[6]

Our patient presented with firm, erythematous nodules on his abdominal wall, which then required biopsy to confirm metastatic HCC. Despite its rarity, cutaneous manifestations may be the first presentation of HCC, and clinicians should be mindful of this diagnosis. Unfortunately, recurrence of HCC in our patient was also associated with a transfusion-dependent hemolytic anemia, which may prove to be more life limiting than the malignancy itself. At the time of submission, the patient has done well requiring only 2 transfusions weekly.

Although this patient is outside of the Milan criteria, he had a 1-year HCC recurrence rate of 10%–12% based on the risk estimation of tumor recurrence after transplant score of his tumor profile (alpha-fetoprotein <20 ng/mL, largest tumor size 5–10 cm, and presence of lymphovascular invasion).[7] Interventional procedures such as transarterial chemoembolization have previously been speculated to cause tissue necrosis and potentially seed metastasis.[8] Although reported in few case reports, transarterial chemoembolization has not been consistently associated with metastatic spread of HCC.[9,10] There is, however,

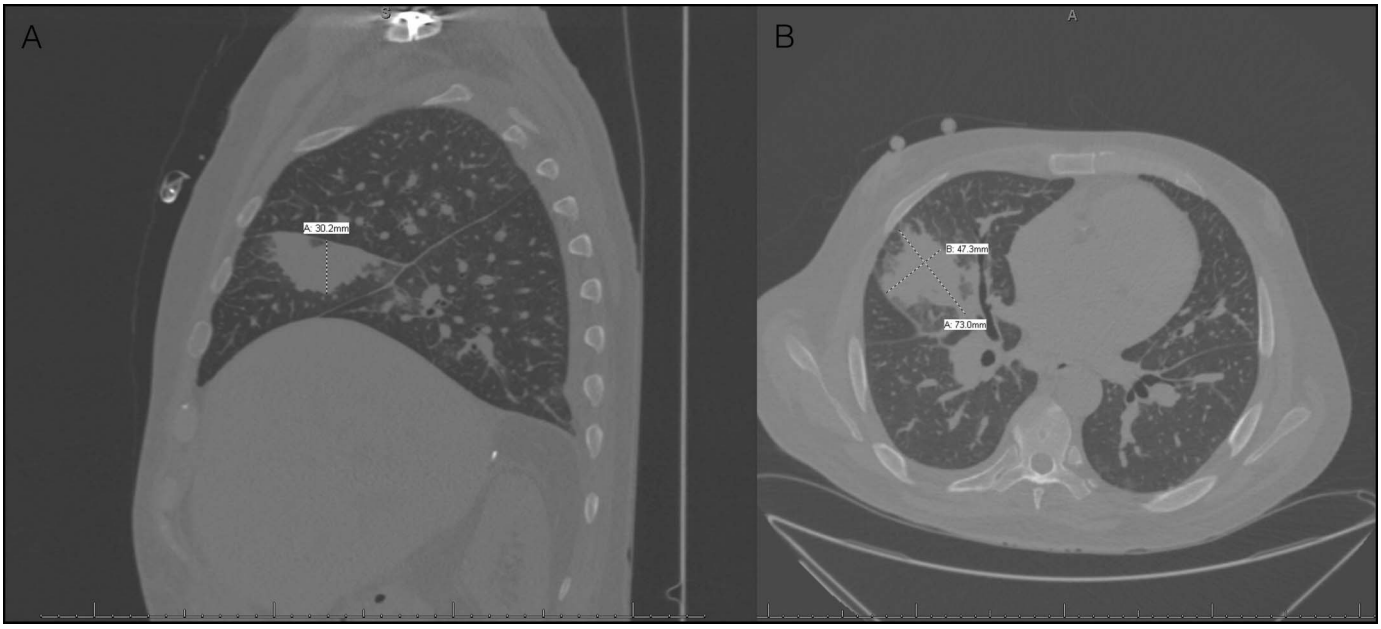

Figure 2. (A and B) Chest computed tomography revealed interval development of a spiculated, irregular right middle lobe airspace opacity measuring 7.3 × 4.7 × 3.0 cm.

a risk of seeding the tumor after a liver biopsy or transcutaneous ethanol ablation.[11–13]

Although this patient did not have any interventional procedures performed before transplant, he did have a moderate risk of recurrence based on his tumor characteristics. The etiology of such recurrence is unknown, but most likely related to microscopic extrahepatic metastasis, which can flourish under the immunosuppression used posttransplant.[14,15] Thus, attempts were made to mitigate the risk of recurrence by early steroid withdrawal and minimization of his tacrolimus dosing. His case report illustrates an uncommon cutaneous manifestation of metastatic HCC. Malignancy should be considered in patients with a history of HCC who present with new, unexplained skin nodules.

DISCLOSURES

Author contributions: S. Moraveji and MR Pedersen wrote the manuscript. S. Chandramouli and TA Kerr edited the manuscript. LM Grant wrote and edited the manuscript. S. Moraveji is the article guarantor.

Financial support: None to report.

Informed consent was obtained for this case report.

Received November 30, 2018; Accepted March 27, 2019

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