

## Case in Point

# Hepatocellular Carcinoma: To Biopsy or Not?

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Biopsy may provide definitive evidence of disease, but the benefits of avoiding unnecessary treatment must be weighed against the risk of possible complications.

**H**epatocellular carcinoma (HCC) accounts for 90% of all primary liver cancers and is the third leading cause of cancer-related mortality. Although HCC is often deadly, it is potentially curable if diagnosed at an early stage. Generally, needle biopsy of a suspicious liver lesion is not recommended, because it raises the risk of needle track seeding. It may be used, however, to guide management when imaging studies and tumor biomarker levels are equivocal. The following report describes a case of biopsy-related metastatic HCC, illustrating the potential risk involved in performing needle biopsy on liver lesions.

### INITIAL EXAMS

A 48-year-old white man was referred to the hepatitis C clinic at the Minneapolis VA Health Care System. His history indicated that he had hepatitis C virus (genotype 3a) with a viral load of 775,000 IU/mL and transaminase levels that were persistently elevated at 100 to 200 IU/mL documented for the past 12 months. A

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Figure 1. A triphasic contrast computed tomography scan shows a 3- x 2.5- x 3.5-cm liver mass, which was less enhanced than the surrounding parenchyma but with a rim that was enhanced in the arterial phase.

liver biopsy was part of the comprehensive evaluation for possible HCV treatment at the initial visit in the hepatitis clinic, and he was assigned a Metavir classification of grade 2 (indicating moderate inflammation), stage 4 (signifying advanced fibrosis or cirrhosis). The hepatologist recommended hepatitis C virus treatment, but it was not initiated because the patient was lost to follow-up.

When the patient returned to the clinic for care 18 months later, the HCV provider ordered an ultrasound for HCC screening which showed a 2.6- x 2.7-cm mass on the right lobe of the patient's liver. A triphasic contrast computed tomography (CT) scan confirmed the presence of a mass, but on the CT scan, it was accurately measured at 3 x 2.5 x 3.5 cm. The mass was less enhanced than

the surrounding parenchyma, and only its rim was enhanced in the arterial phase (Figure 1)—suggesting an equivocal finding as HCCs tend to be hypervascular, signified on CT by enhancement in the arterial phase and washout in the venous phase. The patient's alpha-fetoprotein (AFP) level was normal at 6.7 ng/mL, and a nuclear medicine liver blood pool study was negative for hemangioma. Ultrasound-guided needle biopsy of the lesion confirmed that the mass was a well-differentiated HCC.

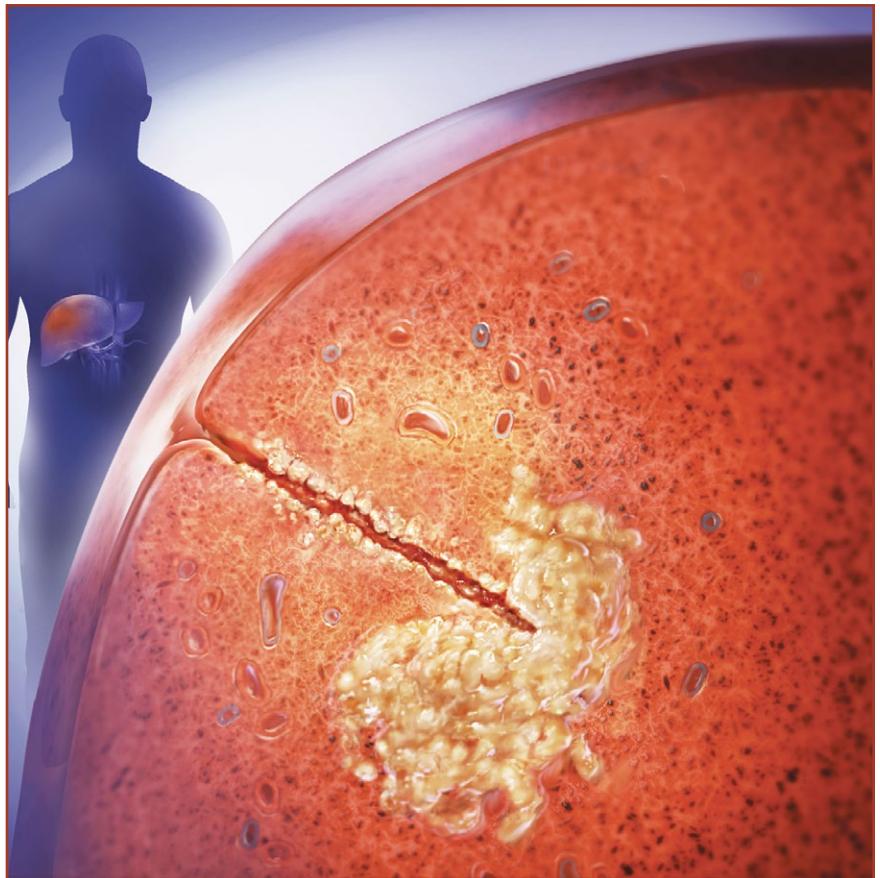
### TREATMENT COURSE

The patient was not a candidate for surgical resection, because he had advanced disease with significant portal hypertension. He could not be considered for transplantation, because he had an ongoing substance abuse disorder and little social support. He was offered treatment with radiofrequency ablation (RFA), but declined, and he was again lost to follow-up.

Upon his return several months later, a triphasic contrast CT scan of the liver showed 2 arterial enhancing lesions, with the dominant lesion being larger than 3 cm. The oncologist prescribed transarterial chemoembolization (TACE) using a combination of cisplatin, doxorubicin, and mitomycin.

Over the next 2 years, the patient had 3 treatments, and both lesions regressed somewhat. To monitor the patient's response to TACE, the oncologist ordered CT scans to be performed 6 weeks after the procedure and then at 3-month intervals.

A CT scan taken 39 months after the lesion was biopsied revealed a new enlarging mass within the right abdominal musculature (Figure 2). A biopsy of this lesion confirmed well-differentiated, intramuscular, metastatic HCC in the area of the previous biopsy's needle tract (Figure 3). Pallia-



tive radiation therapy for the abdominal wall metastasis was successfully performed and improved his pain related to this lesion. He developed metastatic disease to his lungs and ribs with subsequent hypercalcemia. Pamidronate infusion was prescribed. He also completed systemic chemotherapy with sorafenib for 4 months; however, therapy was stopped due to nonadherence with follow-up visits.

The patient returned to primary care for pain management and is doing reasonably well. He has survived 6 years and 6 months to date, which is far above the median survival for metastatic HCC.

### ABOUT THE CONDITION

Oncologists often consider pathologic tumor confirmation a prerequisite for HCC management, but when

the HCC is resectable or the patient is a potential candidate for liver transplantation, its necessity should be critically evaluated. Our case of intramuscular, metastatic HCC following a diagnostic biopsy of a liver lesion illustrates the associated risk. Tract seeding has been reported following biopsies of primary cancers of the lung, liver, pancreas, kidney, and colon.<sup>1-3</sup>

Anywhere from 1,000 to 10,000 tumor cells may be implanted within the needle tract following lesion biopsy.<sup>4</sup> Risk of needle tract seeding is about 1% to 3% following biopsy for HCC diagnosis<sup>3,5</sup> and as high as 4.4% and 1.4%, respectively, following RFA and percutaneous ethanol injection.<sup>1-3,5</sup> Several factors may play a role in raising the risk of needle tract seeding, including number of needle

## CASE IN POINT

passes required to procure adequate tissue, needle bore, tumor size, tumor differentiation, and the amount of time the needle is within the tissue.<sup>5-7</sup> Median time to needle tract metastasis has been reported to be as long as 17 months following lesion biopsy.<sup>5</sup>

According to the guidelines developed by the American Association for the Study of Liver Disease<sup>8</sup> and the European Association for the Study of the Liver,<sup>9</sup> it is unnecessary to obtain histologic confirmation of HCC in hepatic lesions larger than 2 cm that have a typical appearance (enhancement in the arterial phase and washout in the early or late venous phase) on contrast CT or magnetic resonance imaging (MRI), especially in patients with cirrhosis. In lesions less than 2 cm, 2 concordant imaging tests (CT and MRI) showing typical appearance are needed.<sup>8-11</sup>

The specificity of biopsy is nearly 100%, but its negative predictive value is low. Negative biopsy findings do not rule out HCC. When biopsies are negative and clinical findings are highly suggestive of HCC, clinicians should either perform a second biopsy or prescribe an enhanced surveillance protocol.<sup>8,9</sup>

Between 10% and 20% of HCCs have an atypical appearance on imaging.<sup>12</sup> Furthermore, though AFP has a high positive predictive value for HCC at levels greater than 200 ng/mL in patients with focal mass lesions, 20% to 50% of HCCs are not associated with an elevated AFP level. In our case, because AFP was normal and CT showed a 3-cm lesion without typical arterial enhancement, subsequent biopsy was necessary to confirm the diagnosis of HCC. In similar cases, MRI might be performed to reassess vascularity of the mass, but our patient's imbedded shrapnel precluded that possibility.

Current guidelines for diagnosis

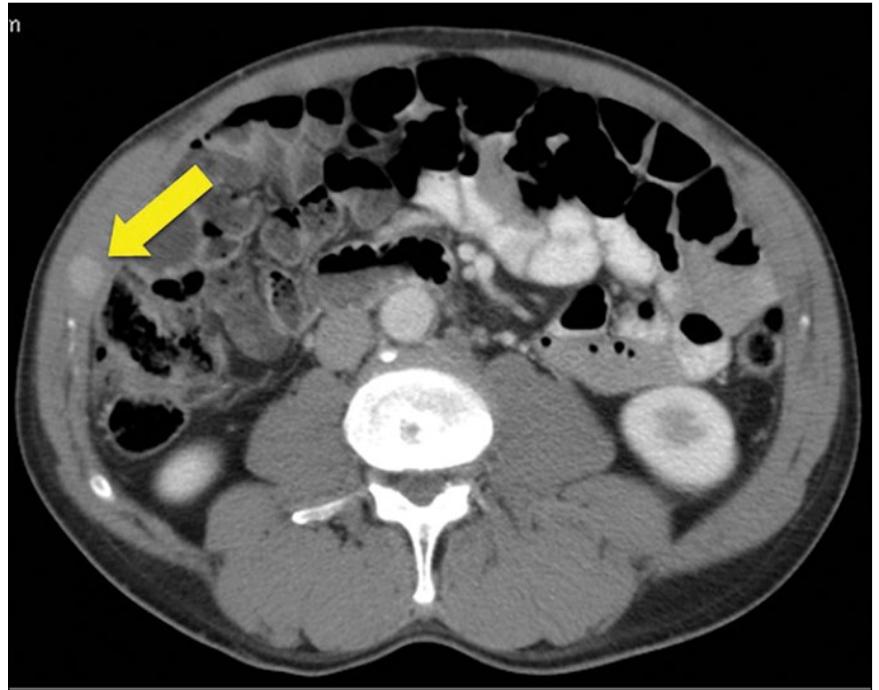


Figure 2. A computed tomography scan taken 39 months after the lesion was biopsied reveals a new enlarging mass within the right abdominal musculature.

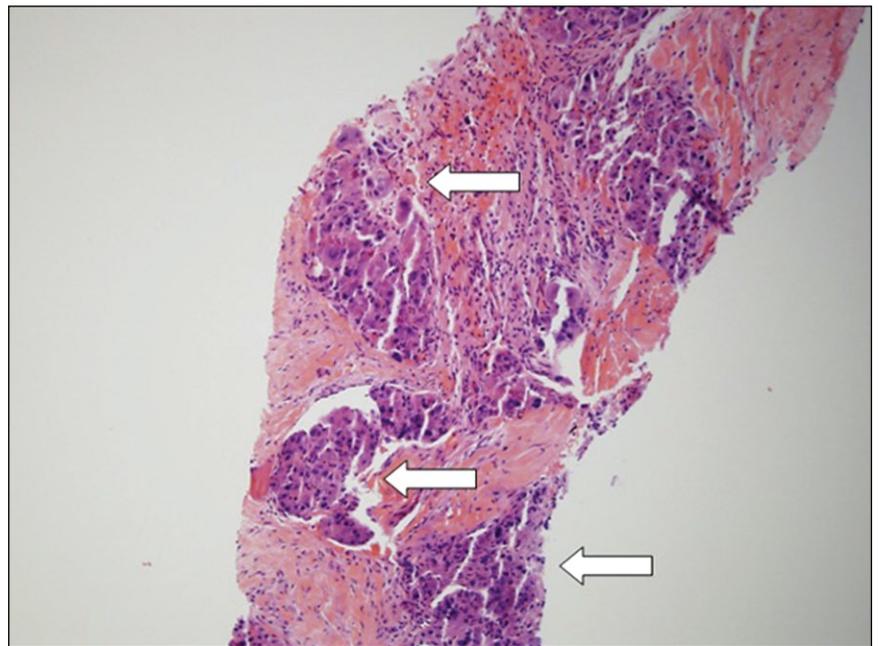


Figure 3. A tissue biopsy from the abdominal muscle lesion confirms well-differentiated, intramuscular, metastatic HCC in the area of the previous biopsy's needle tract.

Continued on page 38

Continued from page 36

and management of HCC in veterans were developed by the VA Hepatitis C Resource Centers.<sup>13</sup> For patients with liver lesions smaller than 1 cm, the guidelines call for intensive surveillance with ultrasound every 3 to 4 months. Clinicians may resume routine surveillance after lesion stability

that do not fulfill typical imaging criteria, especially if the AFP level is less than 200 ng/mL.

Arriving at a diagnosis of HCC can be a difficult task. A multidisciplinary, center-specific approach is encouraged. Decisions to pursue biopsy for HCC diagnosis should be based on

*verse effects—before administering pharmacologic therapy to patients.*

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has been documented for 1 to 2 years. Patients with masses between 1 and 2 cm should have 2 dynamic imaging studies (CT or MRI), while patients with masses larger than 2 cm require only a single, characteristic dynamic imaging study. In the absence of typical vascular findings (arterial enhancement and venous washout) on CT or MRI, image-guided needle biopsy of the mass may be indicated.

### IN SUMMARY

Needle biopsy of suspected HCC lesions is not without risk. As described in this case, the procedure may allow the tumor to seed the needle tract, precluding such curative therapies as hepatic resection, RFA, or liver transplantation in otherwise appropriate patients. Biopsy should be performed on suspected HCC lesions in patients without documented cirrhosis and may be considered in patients with cirrhosis and nodules

patient-specific risks and benefits, taking into account both the risks of providing unnecessary HCC treatment to a patient without established HCC and the risk of inducing metastasis and incurable disease through needle tract seeding.

### Author disclosures

*The authors report no actual or potential conflicts of interest with regard to this article.*

### Disclaimer

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