Hepatocellular carcinoma disguised as liver abscesses

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ABSTRACT

The incidence of hepatocellular carcinoma (HCC) is growing rapidly in the United States. Nonalcoholic fatty liver disease and nonalcoholic steatohepatitis are being increasingly recognized as known risk factors for the development of HCC. However, this risk seems to be associated with their progression to cirrhosis. This case demonstrates an unusual initial presentation of HCC masquerading as liver abscesses in a previously healthy woman with nonalcoholic fatty liver disease without cirrhosis. Our patient's clinical presentation was suspicious for an infectious etiology due to her ongoing fever in the setting of possible zoonotic transmission, because she had just acquired two unvaccinated kittens. Abscess-like clinical presentation can be seen in HCC and is due to neoplasm-associated granulocytosis. Fever is due to pyrogen production by malignant tumor cells or by macrophages. Therefore, HCC can be difficult to differentiate from a hepatic abscess, and aspiration of malignant cells may be needed for an accurate diagnosis. Although the incidence of HCC in nonalcoholic fatty liver disease without cirrhosis is low or unknown, surveillance for HCC should be considered due to the higher prevalence of nonalcoholic fatty liver disease in the developed world and its potential risk for HCC.

KEYWORDS Hepatic abscess; hepatocellular carcinoma; liver biopsy; low-density hepatic lesions; noncirrhotic HCC; pyogenic liver abscess

The incidence of primary liver cancer, most commonly hepatocellular carcinoma (HCC), is growing rapidly in the United States. HCC is expected to be the third leading cause of cancer-related mortality by the year 2030.¹ This high mortality rate is in parallel to the rest of the world, where primary liver cancers are the second most common cause of cancer-related mortality.¹ A majority of patients diagnosed with HCC are known to have risk factors, such as hepatitis B viral infection, chronic hepatitis C viral infection, hereditary hemochromatosis, and cirrhosis.² Nonalcoholic fatty liver disease and nonalcoholic steatohepatitis are also increasingly being recognized as known risk factors for the development of HCC.³ However, this risk seems to be associated with their progression to cirrhosis, though cases of HCC in noncirrhotic livers have also been reported.^{3,4} This case demonstrates an unusual initial presentation of HCC masquerading as liver abscesses in a previously healthy woman without cirrhosis.

CASE REPORT

A 64-year-old woman presented with fever, chills, diaphoresis, fatigue, and malaise followed by daily episodes of nonbloody diarrhea for 1-week duration. Her symptoms were unrelenting and did not

improve with ibuprofen or acetaminophen. She developed abdominal discomfort described as a burning sensation, which prompted her to seek medical attention. She had suffered bites and scratches from her two recently acquired unvaccinated kittens. She had no recent travel, antibiotic use, or medication changes. Her past medical history included nonalcoholic fatty liver disease, hypertension, hyperlipidemia, obesity, iron deficiency anemia, and colon polyps.

Her vital signs were concerning for tachycardia and a fever of 101.2°F. Physical exam was unremarkable except for some healing scratches on her bilateral upper extremities. Laboratory work showed leukocytosis, microcytic anemia, thrombocythemia, and an elevated hemoglobin A1c. Computed tomography of the abdomen with intravenous contrast showed numerous low-density liver lesions resembling abscesses, with the largest measuring up to 4 cm. Based on her clinical symptoms and imaging, these findings were most concerning for liver abscesses but cat-scratch disease and malignancy were also on the differential. Blood cultures were obtained prior to initiation of broad-spectrum antibiotics, including azithromycin. However, she continued to have a fever despite antibiotic treatment. Blood and stool cultures, stool ova and cysts, and *Bartonella* serologies were obtained, which were all negative. Hepatitis B and C test results were negative.

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Received November 16, 2017; Revised January 8, 2018; Accepted January 9, 2018.

Interventional radiology attempted a liver lesion aspiration; however, no significant fluid could be aspirated. A core biopsy was then performed and preliminary results were consistent with a metastatic adenocarcinoma. The pathologist noted that there was not a significant component of background fibrosis. The collected specimen was also sent for bacterial, fungal, and acid-fast bacilli cultures along with *Bartonella* polymerase chain reaction, which were negative. Her antibiotics were discontinued. Colonoscopy was performed to evaluate for primary lower gastrointestinal malignancy, which was not discovered. Computed tomography of the chest also did not show evidence of primary or metastatic neoplasia within the thorax. Computed tomography of the head was negative for cranial malignancy. Her alpha-fetoprotein level was 2 ng/mL. Final pathology results were eventually received, which revealed a poorly differentiated carcinoma. Histomorphology and immunostaining pattern were consistent with HCC, favoring a primary liver malignancy instead.

DISCUSSION

The hitherto described patient had HCC without any known, traditional risk factors. Although she did have a diagnosis of nonalcoholic fatty liver disease, she had not progressed to cirrhosis of the liver. One study examined multiple case series, cohort, case-control, and cross-sectional studies and concluded that there was minimal risk for HCC in nonalcoholic fatty liver disease or nonalcoholic steatohepatitis cohorts with few or no cases of cirrhosis.³ Interestingly, patients diagnosed with nonalcoholic fatty liver disease/nonalcoholic steatohepatitis-associated HCC tend to also have manifestations of metabolic syndrome, such as diabetes mellitus, hypertension, dyslipidemia, and coronary artery disease.⁵ Therefore, a higher suspicion for HCC with early interventions may be warranted in this population due to higher prevalence of metabolic syndrome in the developed world.⁵ Our patient had hypertension, hyperlipidemia, obesity, and a new diagnosis of diabetes mellitus.

Our patient's clinical presentation was suspicious for an infectious etiology due to her ongoing fever, history of possible zoonotic transmission, and findings on computed tomography.^{6,7} Her imaging showed numerous low-density liver

lesions, which are characteristic of pyogenic liver abscesses and known as the "cluster sign."⁸ A typical feature of HCC on computed tomography includes an intense enhancement in the arterial phase followed by a rapid contrast washout in the late portal venous phase leading to hypoattenuating lesions.⁹ Therefore, HCC can be difficult to differentiate from a hepatic abscess, and a biopsy of malignant cells may be needed for an accurate diagnosis.^{10,11} Although our patient's presentation was suspicious for an infectious etiology, HCC was lurking in disguise.

1. Makarova-Rusher OV, Altekruze SF, McNeel TS, et al. Population attributable fractions of risk factors for hepatocellular carcinoma in the United States. *Cancer*. 2016;122:1757–1765. doi:10.1002/cncr.29971.
2. Davila JA, Morgan RO, Shaib Y, McGlynn KA, El-serag HB. Hepatitis C infection and the increasing incidence of hepatocellular carcinoma: a population-based study. *Gastroenterology*. 2004;127:1372–1380. doi:10.1053/j.gastro.2004.07.020.
3. White DL, Kanwal F, El-serag HB. Association between nonalcoholic fatty liver disease and risk for hepatocellular cancer, based on systematic review. *Clin Gastroenterol Hepatol*. 2012;10:1342–1359. doi:10.1016/j.cgh.2012.10.001.
4. Baffy G, Brunt EM, Caldwell SH. Hepatocellular carcinoma in non-alcoholic fatty liver disease: an emerging menace. *J Hepatol*. 2012;56:1384–1391. doi:10.1016/j.jhep.2011.10.027.
5. Ertle J, Dechêne A, Sowa JP, et al. Non-alcoholic fatty liver disease progresses to hepatocellular carcinoma in the absence of apparent cirrhosis. *Int J Cancer*. 2011;128:2436–2443. doi:10.1002/ijc.25797.
6. Li C, Li G, Miao R, et al. Primary liver cancer presenting as pyogenic liver abscess: characteristics, diagnosis, and management. *J Surg Oncol*. 2012;105:687–691. doi:10.1002/jso.22103.
7. Chong V, Lim K. Pyogenic liver abscess as the first manifestation of hepatobiliary malignancy. *Hepatobiliary Pancreat Dis Int*. 2009;8:547–550.
8. Jeffrey RB, Tolentino CS, Chang FC, Federle MP. CT of small pyogenic hepatic abscesses: the cluster sign. *Am J Roentgenol*. 1988;151:487–489. doi:10.2214/ajr.151.3.487.
9. Saar B, Kellner-Weldon F. Radiological diagnosis of hepatocellular carcinoma. *Liver Int*. 2008;28:189–199. doi:10.1111/j.1478-3231.2007.01655.x.
10. Huang CI, Wang LY, Yeh ML, et al. Hepatocellular carcinoma associated with liver abscess. *Kaohsiung J Med Sci*. 2009;25:537–543. doi:10.1016/S1607-551X(09)70546-7.
11. Kim JW, Shin SS, Heo SH, Lim HS, Hur YH, Kim JH. Hepatic abscess mimicking hepatocellular carcinoma in a patient with alcoholic liver disease. *Clin Mol Hepatol*. 2013;19:431–434. doi:10.3350/cmh.2013.19.4.431.