CASE IN POINT

A Case of Metastatic Chromophobe Renal Cell Carcinoma Masked as Suspected Hepatic Abscesses

Jake A. Cresta, MD[a]; Michael A. Pavio, MD[b]; Jamie L. Lombardo, MD[b]; John G. McCarthy, MD[a]; Allison M. Bush, MD[b]

Background: Characterizing multiple hepatic lesions on cross-sectional imaging, particularly differentiating abscesses from metastatic lesions, can be challenging.
Case Presentation: A male aged 53 years with a history of chromophobe renal cell carcinoma presented with fevers and abdominal pain and was found to have multiple hepatic lesions concerning for hepatic abscesses. The lesions initially evaded diagnosis on imaging, laboratory tests, and biopsy, but ultimately were determined to be a rare case of metastatic chromophobe renal cell carcinoma of the liver.
Conclusions: The finding of multiple new liver lesions on imaging during a febrile illness is concerning for hepatic abscess or malignancy, which can be difficult to diagnose with imaging alone. Differentiation between infectious and neoplastic etiologies may require additional imaging and/or tissue sampling.

Author affiliations can be found at the end of this article.
Correspondence: Jake Cresta (jcresta15@gmail.com)

Fed Pract. 2024;41(suppl 2). Published online March 20. doi:10.12788/fp.0462

Finding new liver lesions on imaging during a febrile illness may indicate hepatic abscesses or malignancy. These can be difficult to diagnose with imaging alone. Differentiating between infectious and neoplastic etiologies may require additional images and/or tissue samples.

Hepatic abscesses are more commonly seen with other abdominal or biliary infections while metastatic disease usually presents in patients with active cancer or on surveillance imaging. While renal cell carcinoma (RCC) is the most common malignant neoplasm of the kidney, chromophobe renal cell carcinoma (chRCC) is a rare subtype that comprises only 5% of RCC cases.[1] We present a case of a patient with numerous new liver lesions and fever, initially thought to be hepatic abscesses, who was found to have metastatic chRCC.

CASE PRESENTATION

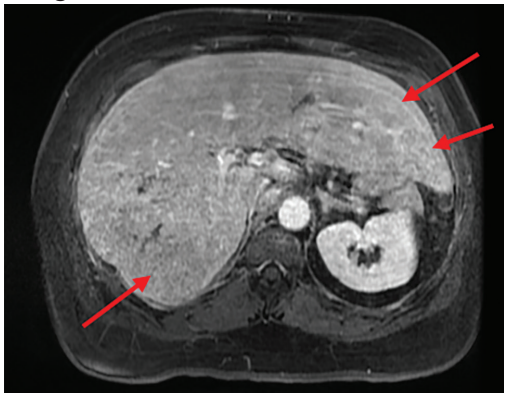
A 53 year-old male with a history of stage 2 chRCC and right radical nephrectomy 2 years prior presented to the emergency department following 1 week of drenching night sweats, fatigue, and subjective fevers. In addition, the patient reported gradually progressive, dull, right upper-quadrant abdominal pain. He noted no other acute medical complaints at the time of presentation. His history was notable for hyperlipidemia. His only surgery was the nephrectomy 2 years earlier. The patient reported no alcohol, tobacco, or drug use, any recent travel, or pet or animal exposure. On admission, he was afebrile with normal heart rate and was normotensive. His physical examination was remarkable for hepatomegaly with right upper-quadrant abdominal tenderness to palpation with a negative Murphy sign. There were otherwise no abnormal cardiovascular, respiratory, or skin findings.

Laboratory tests during initial evaluation were notable for hemoglobin of 10.0 g/dL, white blood cell count of 16.7×10^3 µL, alkaline phosphatase of 213 U/L, aspartate aminotransferase of 185 U/L, and alanine aminotransferase of 36 U/L. Screening tests for viral hepatitis A, B, and C were negative. Additional tests for HIV, rapid plasma reagin, Epstein-Barr virus, cytomegalovirus, and toxoplasma were negative. Tests for antimitochondrial, antismooth muscle, and serum antinuclear antibodies were negative.

Chest X-ray did not reveal any acute cardiopulmonary process. Computed tomography with contrast of the abdomen and pelvis demonstrated numerous hypodensities within the right hepatic lobe. Right upper-quadrant ultrasound demonstrated multiple hyperechoic foci throughout the liver. confluent decreased T1 signal lesions with peripheral gadolinium hyperenhancement were evident on Gadolinium-enhanced T1-weighted magnetic resonance imaging (MRI) with fat saturation demonstrated numerous (Figure 1).

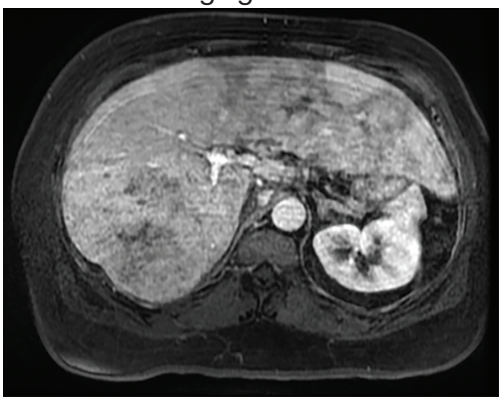
Liver biopsy and tissue cultures demonstrated normal hepatic tissue and no organism growth. Blood cultures demonstrated no growth. The patient was empirically treated with IV ceftriaxone 1 g daily and metronidazole 500 mg every

FIGURE 1 Initial Gadolinium-Enhanced T1-Weighted Magnetic Resonance Image With Fat Saturation



Numerous confluent decreased T1 signal lesions with peripheral gadolinium hyperenhancement can be seen.

FIGURE 2 Follow-Up Gadolinium-Enhanced T1-Weighted Magnetic Resonance Imaging With Fat Saturation



Interval increase in size and number of innumerable confluent hepatic lesions can be seen.

8 hours for suspected hepatic abscesses after he was admitted to the hospital.

The patient's symptoms initially improved following antibiotic treatment; however, he reported recurrence of the initial symptoms 2 months later at a follow-up appointment with gastroenterology. Liver-associated enzymes also remained elevated despite 4 weeks of antibiotic treatment. Repeat gadolinium-enhanced T1 fat-saturated MRI demonstrated an interval increase in size and number of confluent hepatic lesions throughout the liver (Figure 2).

A repeat liver biopsy revealed metastatic chRCC (Figures 3 and 4) that was both morphologically and immunohistochemically similar to the first pathologic diagnosis made following nephrectomy. The first liver biopsy likely did not sample the metastatic lesions that were present but instead sampled the surrounding normal liver. The patient was initiated on lenvatinib and everolimus therapy with oncology, a recommended regimen per the National Comprehensive Cancer Network for patients with nonclear cell RCC.[1]

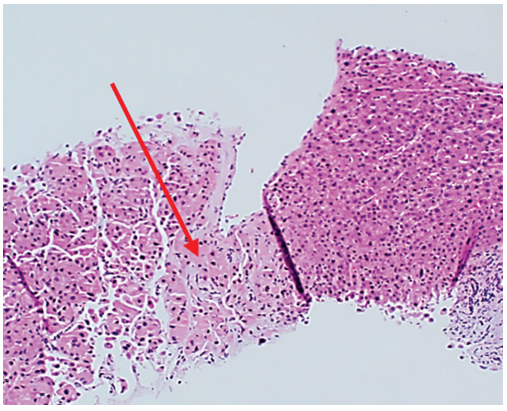
DISCUSSION

Chromophobe RCC is a rare form of RCC that has a recurrence-free survival of > 80% when treated in early stages.[2] These neoplasms represent only 3000 to 6000 new cases of RCC annually, with an even lower incidence (6% to 7%) resulting in metastatic disease. The liver is the most common site of metastases (39%).[2] Previously reported metastatic chRCC hepatic lesions have been incidentally noted on imaging with asymptomatic clinical presentations. In contrast to our patient, most documented cases report metastatic chRCC as a solitary hepatic lesion.[3-7]

A noteworthy genetic association with ChRCC is the Birt-Hogg-Dubé syndrome, which is an autosomal-dominant genetic disorder that results from germline mutations in the tumor suppressor folliculin gene located on chromosome 17.[8] This syndrome is characterized by the development of various benign and malignant tumors, particularly chRCC. Our patient appeared to have a sporadic chRCC with the absence of other tumors and negative family history for malignancies. On his initial staging imaging, in accordance with National Comprehensive Cancer Network guidelines, our patient was identified only as having a 10-cm right renal mass and 1 benign regional lymph node with an otherwise unremarkable computed tomography of the chest, abdomen and pelvis, corresponding to stage 2 cancer.

Common causes of hepatic abscesses, the other potential diagnosis of concern for the patient, were biliary infections, portal vein ascension from abdominal sources, arterial translocation due to bacteremia, and local invasion due to suppuration of adjacent tissue.[9] Incidence for hepatic abscesses increases with comorbidities such as diabetes, cirrhosis, malignancy, immunosuppression, and malnutrition.[10] *Candida* is also a common culprit when there are multiple, small abscesses, often in immunocompromised patients.[11]

FIGURE 3 Hematoxylin-Eeosin Stain



Original magnification ×10. The metastatic lesion is present on the left side of the image compared to the normal liver parenchyma on the right. Note how similar chromophobe renal cell carcinoma cells are to hepatocytes. They both demonstrate abundant eosinophilic cytoplasm; however, there is a subtle change in the size of the cells, architectural arrangement, and quality of the cytoplasm.

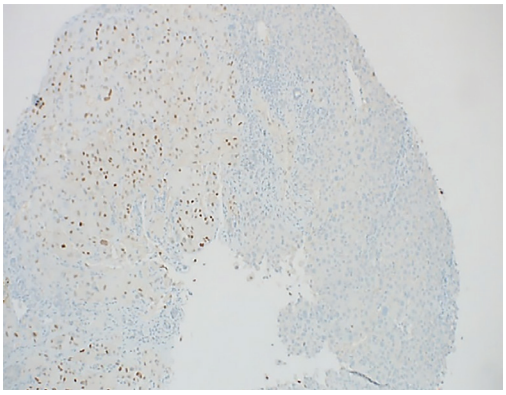
Given the high mortality rates associated with hepatic abscesses, prompt treatment is imperative.[10,12] Since the clinical signs and symptoms for hepatic abscesses are nonspecific (abdominal pain, fever, and malaise) and liver function tests can vary, the diagnosis primarily relies on imaging or tissue sampling.[9]

It can be difficult to distinguish abscesses from metastatic lesions based on imaging alone without microbiologic and pathologic confirmation.[11,13,14] There are certain radiologic characteristics that have been found to favor abscesses over metastasis, including parenchymal enhancement, arterial rim enhancement, and perilesional hyperemia.[15] However, previously described hallmark characteristics of hepatic abscesses, such as the "cluster sign" demonstrating early stages of abscess coalescence, have also been seen in some hepatic metastases.[16]

CONCLUSIONS

This patient highlights the presentation of a rare case of metastatic chRCC with multiple hepatic lesions. While often differentiated clinically, radiographically, or histologically, malignancy and abscess can be difficult to differentiate in a patient with fevers and leukocytosis with hepatic lesions.[17] Early diagnosis of hepatic abscesses and initiation of antibiotic therapy are essential. In cases when it is challenging to characterize the hepatic lesions, repeated tissue sampling and imaging can help direct therapy. Attention should be paid to a previous history of malignancy and should raise suspicion for metastatic disease, particularly with misleading imaging studies and tissue samples.

FIGURE 4 PAX8 Nuclear Stain Highlighting Cells of Renal Origin



Original magnification ×10. The cells in the malignant lesion on the left are positive, and the hepatocytes on the right are negative.

Acknowledgments

This case was presented as a poster presentation at the Tri-Service American College of Physicians Meeting, September 7-10, 2022, San Antonio, Texas.

Author affiliations

[a]Walter Reed National Military Medical Center, Bethesda, Maryland
[b]Naval Medical Center Portsmouth, Virginia

Author disclosures

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

Ethics and consent

Written informed consent for publication was obtained by the patient who was involved in this case.

References

1. National Comprehensive Cancer Network. Kidney cancer (version 2.2024). Accessed February 5, 2024. https://www.nccn.org/professionals/physician_gls/pdf/kidney.pdf
2. Vera-Badillo FE, Conde E, Duran I. Chromophobe renal cell carcinoma: a review of an uncommon entity. *Int J Urol*. 2012;19(10):894-900. doi:10.1111/j.1442-2042.2012.03079.x
3. Lordan JT, Fawcett WJ, Karanjia ND. Solitary liver metastasis of chromophobe renal cell carcinoma 20 years after nephrectomy treated by hepatic resection. *Urology*. 2008;72(1):230.e5-6. doi:10.1016/j.urology.2007.11.134

4. Talarico F, Buli P, Iusco D, Sangiorgi A, Jovine E. Synchronous nephrectomy and right hepatectomy for metastatic chromophobe renal cell carcinoma: report of a case and review of the literature. *Chir Ital*. 2007;59(2):257-261.
5. Aslam MI, Spencer L, Garcea G, et al. A case of liver metastasis from an oncocytoma with a focal area of chromophobe renal cell carcinoma: a wolf in sheep's clothing. *Int J Surg Pathol*. 2008;17(2):158-162. doi:10.1177/1066896908318741
6. Kyoda Y, Kobayashi K, Takahashi A, et al. Liver metastasis with portal vein tumor thrombosis as a late recurrence of chromophobe renal cell carcinoma. Article in Japanese. *Hinyokika Kiyo*. 2009;55(1):23-25.
7. Talarico F, Capizzi D, Iusco DR. Solitary liver metastasis of chromophobe renal cell carcinoma 17 years after nephrectomy. a case report and review of the literature. *Ann Ital Chir*. 2013;84(ePub):S2239253X13021816.
8. Garje R, Elhag D, Yasin HA, Acharya L, Vaena D, Dahmoush L. Comprehensive review of chromophobe renal cell carcinoma. *Crit Rev Oncol Hematol*. 2021;160:103287. doi:10.1016/j.critrevonc.2021.103287
9. Pearl R, Pancu D, Legome E. Hepatic abscess. *J Emerg Med*. 2005;28:337-339. doi:10.1016/j.jemermed.2004.08.024
10. Huang CJ, Pitt HA, Lipsett PA, et al. Pyogenic hepatic abscess. Changing trends over 42 years. *Ann Surg*. 1996;223(5):600-607; discussion 607-609.
11. Özgül E. Multiple pyogenic liver abscesses mimicking metastatic disease on computed tomography. *Cureus*. 2020;12(2):e7050. doi:10.7759/cureus.7050
12. Kuo SH, Lee YT, Li CR, et al. Mortality in Emergency Department Sepsis score as a prognostic indicator in patients with pyogenic liver abscess. *Am J Emerg Med*. 201331(6):916-921.
13. Lardière-Deguelte S, Ragot E, Amroun K, et al. Hepatic abscess: diagnosis and management. *J Visc Surg*. 2015;152(4):231-243. doi:10.1016/j.jviscsurg.2015.01.013
14. Halvorsen RA, Korobkin M, Foster WL, Silverman PM, Thompson WM. The variable CT appearance of hepatic abscesses. *AJR Am J Roentgenol*. 1984;142(5):941-946. doi:10.2214/ajr.142.5.941
15. Oh JG, Choi SY, Lee MH, et al. Differentiation of hepatic abscess from metastasis on contrast-enhanced dynamic computed tomography in patients with a history of extrahepatic malignancy: emphasis on dynamic change of arterial rim enhancement. *Abdom Radiol (NY)*. 2019;44(2):529-538.
16. Jeffrey RB Jr, Tolentino CS, Chang FC, Federle MP. CT of small pyogenic hepatic abscesses: the cluster sign. *AJR Am J Roentgenol*. 1988;151(3):487-489. doi:10.2214/ajr.151.3.487
17. Mavilia MG, Molina M, Wu GY. The evolving nature of hepatic abscess: a review. *J Clin Transl Hepatol*. 2016;4(2):158-168. doi:10.14218/JCTH.2016.00004