

letter

Hepatocellular carcinoma to renal cell carcinoma metastasis: a rare phenomenon with diagnostic challenges

To the Editor: The coexistence of two or more synchronous or metachronous malignancies in the same patient is not uncommon.¹ Tumor-to-tumor metastasis is, however, a rarer phenomenon.^{1,2} Probably, the first case reported in the literature was by Berent in 1902, in which squamous cell carcinoma of the jaw metastasized to renal cell carcinoma.³ Rabson et al found 50 reported cases of cancer-to-cancer metastasis in 1954.⁴ Petraki et al found 150 reported cases of tumor-to-tumor metastasis in 2003.¹ We report a case of hepatocellular carcinoma metastasized into renal cell carcinoma.

A 70-year-old non-local woman presented with intermittent abdominal pain. Four months prior to current presentation the patient was diagnosed with hepatocellular carcinoma (HCC) in her home country and received one cycle of chemotherapy. The patient decided to travel abroad to complete her treatment in our hospital. Computed tomography showed a right hepatic lobe mass that measured 7.7 cm with chemoembolization material and a cirrhotic liver (**Figure 1**). The left kidney showed an upper pole nodule that measured 3.5 cm (**Figure 1**). The right kidney and adrenal glands were unremarkable. Alpha-fetoprotein (AFP) was high (66.3 IU/mL). Clinical and radiological differential diagnoses included incidental renal cell carcinoma or metastatic hepatocellular carcinoma of the left kidney nodule. The patient was scheduled for frozen section of the left renal nodule and subsequent segmental resection of the hepatic mass.

We received segmental resection of the left kidney nodule that grossly measured 3.6 cm and showed a yellow

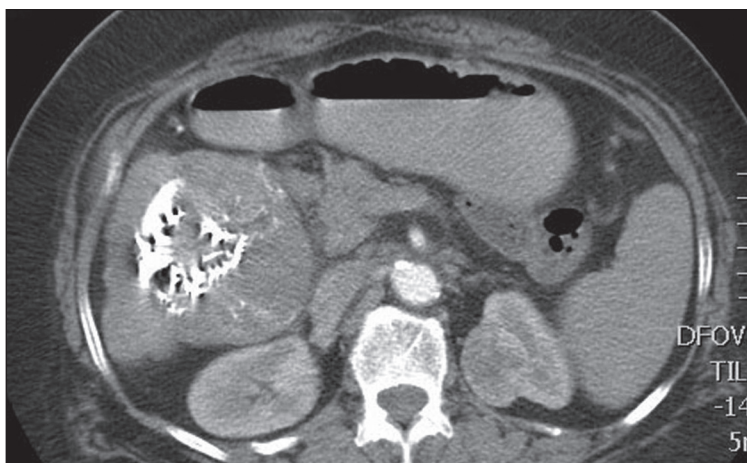


Figure 1. Computed tomography showed right liver lobe with large mass with chemoembolization material. The left kidney showed an upper pole nodule.

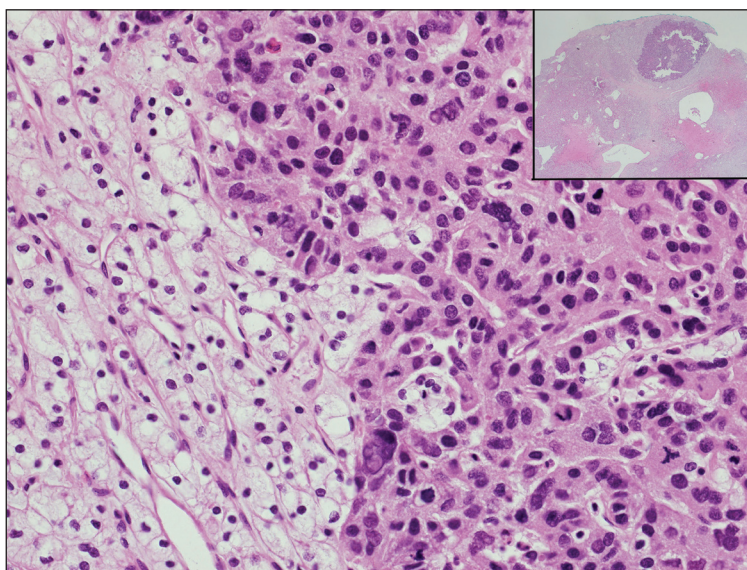


Figure 2. Inset showed left renal nodule composed of clear cell carcinoma with smaller eosinophilic nodule (hematoxylin and eosin stain, original magnification $\times 20$). The interface between the two tumors showed low-grade renal clear cell carcinoma and high-grade pleomorphic eosinophilic neoplasm with atypical mitotic figures. (Hematoxylin and eosin stain, original magnification $\times 400$).

low mass with areas of hemorrhage. A frozen section showed histologic features of clear cell carcinoma consistent with incidental renal cell carcinoma (RCC) of the left kidney. Subsequent permanent sections confirmed the frozen section diagnosis of low-grade conventional renal clear cell carcinoma. However, a smaller granular eosinophilic nod-

ule (measuring 2.5 mm) was found within the renal cell carcinoma nodule (**Figure 2**). This nodule showed a highly pleomorphic eosinophilic neoplasm with focal trabecular and pseudoacinar growth pattern lined by endothelial cells. High mitotic activity with atypical mitotic figures was present (**Figure 2**). Histologic differential diagnoses of the smaller

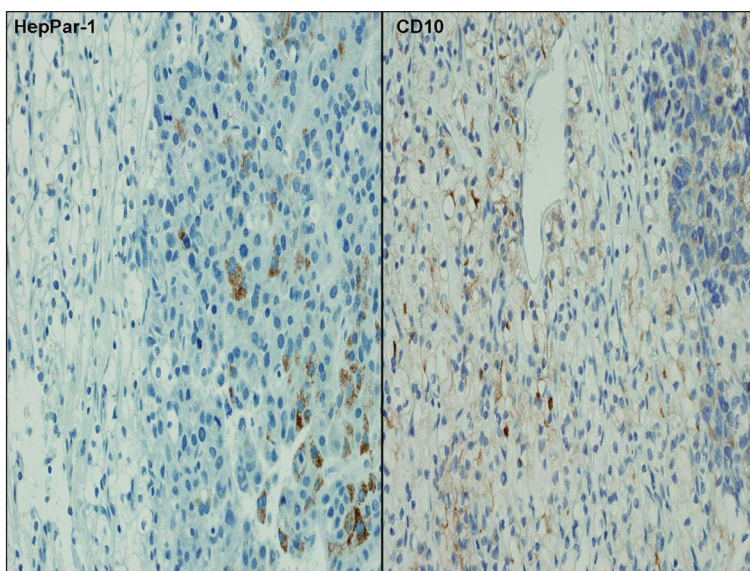


Figure 3. HepPar-1 showed positive neoplastic cells in the high-grade eosinophilic neoplasm with granular cytoplasmic staining. CD10 showed positive renal cell carcinoma cells with membrane staining. (Dako, Glostrup, Denmark, original magnification $\times 400$).

eosinophilic nodule included a focus of high-grade granular renal cell carcinoma, metastatic hepatocellular carcinoma or adrenal cortical cell carcinoma. Immunohistochemistry for CD10, HepPar-1, AFP and melan-A was done. The eosinophilic neoplastic cells of the small nodule were positive for HepPar-1 (Figure 3) and were negative for CD10, AFP and melan-A. The surrounding renal cell carcinoma cells were positive for CD10 (Figure 3) and negative for the remaining markers. We entertained the diagnosis of incidental low-grade renal cell carcinoma of the left kidney with metastatic HCC.

The liver mass was not resected because the patient developed severe life-threatening intraoperative bleeding and received several blood transfusions. The patient died two days after surgery because of uncontrolled hemorrhage. Because of social, ethical and religious restraints, postmortem examinations are not performed in our region, and therefore no autopsy study was carried out on the patient.

Tumor-to-tumor metastasis can

occur in patients with synchronous or metachronous simultaneous primaries.¹⁻⁴ This phenomenon is infrequent, but probably more common than previously reported.^{1,2} The receiving host neoplasm could be benign or malignant. The most common receiving malignancy is renal cell carcinoma.^{1,2,4} Other host neoplasms include sarcomas, meningiomas, thyroid neoplasms and pituitary adenomas.^{1,2,4} The most common donor neoplasm is primary lung carcinoma followed by breast, prostate and thyroid carcinomas.^{1,2,4} Other metastatic donor malignancies reported included squamous cell carcinoma of the head and neck region, melanoma, and colonic and gastric carcinomas, but HCC has not been previously reported.¹⁻⁴

The definition of one primary malignancy metastasizing to another primary neoplasm within the same patient should be based on certain criteria. Campbell et al⁵ proposed a set of criteria for the diagnosis of tumor-to-tumor metastasis which include: 1) the existence of more than

one primary tumor in the patient, 2) the recipient tumor must be a true neoplasm, 3) the donor tumor must be a true metastasis (direct contiguous spreading or collision tumor is not acceptable), and 4) lymphatic metastasis should be excluded. The reason why RCC was the most common host malignancy is unclear. Several theories have attempted to explain why non-metastasizing early renal cell carcinoma is the favorite host tumor in cancer-to-cancer metastasis.^{1,2} These mechanical and biochemical factors include: 1) the kidneys are vascular organs with abundant blood supply, 2) RCC is a very vascular neoplasm, 3) RCC provides a lipid and glycogen rich environment for tumor growth, 4) angiogenic or hormonal secretion by RCC cells, and 5) early low-grade RCC provides an aerobic oxygen-rich metabolic environment suitable for tumor growth. These hypotheses need validation by more probing studies that may shed light into the behavior and underlying pathogenesis of metastasizing cancers.

It is sometimes difficult to distinguish between renal cell carcinoma and HCC, particularly clear cell types. Clues to HCC might include the presence of focal trabecular and pseudoglandular growth pattern.⁶ The presence of bile pigments and Mallory bodies are helpful, but they are not always present particularly in high grade HCC.^{6,7} Immunohistochemistry with a small panel of HepPar-1 and CD10 can help.^{6,7} HepPar-1 is the most specific marker for hepatic differentiation.^{6,7} It can be patchy and variable sometimes, but shows characteristic granular cytoplasmic staining.⁶ HepPar-1 is almost always negative in RCC.^{6,7} CD10 is a good marker for RCC, but not specific. It can be positive in HCC, but usually shows a canalicular pattern in the trabecular areas as opposed to the brisk membrane stain-

ing in RCC.^{6,7} AFP is not specific and can be negative in HCC.⁶

In conclusion, tumor-to-tumor metastasis is an infrequent, but not a rare event. HCC-to-RCC metastasis is rare and can be considered as one of the rarest cancer-to-cancer metastasis. Sometimes, it can be morphologically difficult to distinguish between HCC and RCC. This could present diagnostic challenges to the pathologist, particularly on the frozen section. Simple immunohistochemistry panel of HepPar-1 and CD10 is helpful to distinguish between the two neoplasms.

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REFERENCES

1. Petraki C, Vaslamatzis M, Argyrakos T, Petraki K, Strataki M, Alexopoulos C, et al. Tumor to tumor metastasis. Report of two cases and review of the literature. *Int J Surg Pathol* 2003;11:127-135.
2. Sella A, Ro JY. Renal cell cancer: best recipient of tumor-to-tumor metastasis. *Urology* 1987;30: 35-38.
3. Berent W. Seltene Metastasenbildung. *Zentralbl Allg Pathol*. 1902; 13: 406-410.
4. Rabson SM, Stier PL, Baumgartner JC, Rosenbaum D. Metastasis of cancer-to-cancer. *Am J Clin Pathol*. 1954 May;24(5):572-9.
5. Campbell LV, Gilbert E, Chamberlain CR, Watne AL. Metastases of cancer to cancer. *Cancer* 1968;22:635-643.
6. Murakata LA, Ishak KG, Nzeako UC. Clear cell carcinoma of the liver: A comparative immunohistochemical study with renal clear cell carcinoma. *Mod Pathol* 2000;13:874-881.
7. Hou TC, Wu CC, Yang CR, Wang J. Synchronous renal cell carcinoma and clear cell hepatocellular carcinoma mimicking metastatic disease. *Path Res Pract* 2010;206:342-345.

CD123 monoclonal antibody in myelodysplastic syndrome

To the Editor: CD123 monoclonal antibody is an IL3Ra antireceptor useful in the diagnosis of hairy cell leukemia.¹ It is widely used to recognize minimal residual disease (MRD) in treated acute myeloid leukemia (AML). We studied 20 patients with a diagnosis of myelodysplastic syndrome (MDS). The most prominent clinical sign was leukopenia with variable lymphocytosis, and disease evolution of more than a year. Patient ages ranged between 32 to 81 years, and included 11 women and 9 men. Laboratory bone marrow findings were consistent with hypercellular and heteromorphous cytology with erythroid dysplasia and the presence of Pelger-Huett anomaly, with increased intermediate forms, immature myeloid series and macroplatelets. Serum iron and ferritin were measured and one marrow iron and biopsy were obtained. Flow cytometry monoclonal antibodies used included CD34 + CD123, CD38 + CD123, CD34 + CD117, CD34 + CD38, CD123, and p53 and Bcl2. These monoclonal combinations were studied to determine the presence of leukemic stem cells (LSC). The analysis showed evidence of CD123 in 12 patients, with more than 20% (range, 22%-66%). In the remaining 8 patients, CD123 was less than 20% (range, 6%-16%). The CD34 + CD117 combination findings corresponded with 16%-56%. The patient samples were also marked with CD38, with a presence of 39%-82%, indicating cellular activation. When compared with CD34 + CD123, the range was 20%-95%. Taking into account total positivity, all our patients had an increased presence of CD123, in addition to CD34 and CD117. Eleven (n=11)

patients presented with alterations in p53, and 14 had the presence BCL2 oncogene. Patients with more than 20% CD123 were treated with anti-methylation drugs. Our conclusions indicate that the use of CD123 with other immaturity markers corresponds with MDS and relates to the presence of LSC. The use of this marker may help in early identification and treatment of cases with higher potential for leukemic transformation. Limited but similar findings have been reported about the value of CD123, under comparable conditions.²

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REFERENCES

1. Del Giudice, Matutes E, Morilla R, Morilla A, Owusu-Ankomah K, Rafiq F, A'Hern R, Delgado J, Bazerbashi MB, Catovsky D. The diagnostic value of CD123 in B-cell disorders with hairy or villous lymphocytes. *Haematologica* 2004; 89(3): 303-308.
2. Jin L, Lee EM, Ramshaw HS, Busfield SJ, Peopl AG, Wilkinson L, Guthridge MA, Thomas D, Barry EF, Boyd A, Gearing DP, Vairo G, Lopez AF, Dick JE, Lock RB. Monoclonal antibody-mediated targeting of DC123, IL-3 receptor α chain, eliminates human acute myeloid leukemic stem cells. *Cell Stem Cell* 2009; 5(1): 31-42.