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Case Report

Simultaneous double primary clear cell carcinomas of liver and kidney: a case report and review of literature

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Abstract: Reported herein are simultaneous double primary clear cell carcinomas arising from liver and kidney. A 63-year-old man underwent a partial wedge nephrectomy of the right kidney in a surgical resection for hepatocellular carcinoma. Coincidently, on histology the tumors in liver and kidney were consisted of clear cancer cells, which arranged in haphazardly intermixed pattern without capsules. Immunohistochemically, the clear neoplastic cells in the liver were positive for HepPar-1, GPC3, and negative for nephrogenic markers; however, renal clear neoplastic cells were positive for CD10, RCC and Pax-8, but negative to liver-derived markers. These findings led to the diagnosis of simultaneous double primary clear cell carcinomas of kidney and liver. Multiple primary carcinomas of kidney and liver, especially both are primary clear cell carcinomas, are extremely rare neoplasms, only 1 case has been reported previously until now. To our knowledge, this is a report of multiple primary carcinomas arising from the liver and kidney and reminders us of differentiation diagnosis with carcinoma metastasis.

Keywords: Hepatocellular carcinoma, renal cell carcinoma, synchronous primary malignancies, clear cell carcinoma

Introduction

Multiple primary malignant neoplasms are extremely rare in the hepatocellular carcinoma patients. We herein report a case of simultaneous double primary clear cell carcinomas of liver and kidney of a 63-year-old male, an infrequent multiple primary tumors with the literature review to understand it better.

Case presentation

A 63-year-old male was admitted to our hospital with space-occupying lesions in the liver and kidney in his a routine medical examination. The patient had suffered from right upper quadrant abdominal pain without any obvious incentive cause for 45 months, such as constant dull pain and radiating back pain. Nothing remarkable was found in additional investigations. Laboratory results such as routine blood chemistry, complete blood count, kidney and liver function tests, and urine analysis were all ranked in normal limits. Hepatitis B Test showed that hepatitis B surface antigen (HBsAg) was positive, but hepatitis B surface antibody (anti-HBs/HbsAb) was negative. The result of alpha-fetoprotein (AFP) was 1200 ng/ml.

Enhanced computerized tomography (CT) examination of the abdomen revealed space-occupying lesions in the liver and kidney. CT scan found a 9.3 cm × 8.7 cm heterogeneously contrast enhancing hepatic neoplasm in the posterior lobe with irregular lesion edges on arterial phase (**Figure 1A**). However, the enhancement deduces on portal phase and delayed phase gradually. Another 1.6 cm × 1.5 cm round-like kidney mass with heterogeneous intensity occupied the lower portion of right kidney but no indication of local invasion or lymphnode metastases (**Figure 1B**). Heterogeneous obvious gridding enhancement on arterial phase with gradually reduction on portal phase

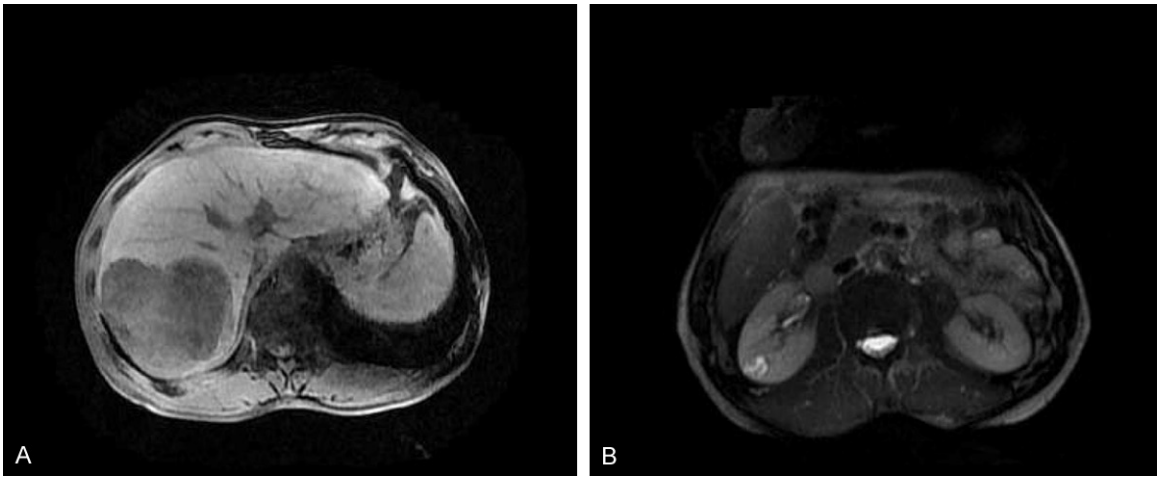

Figure 1. Contrast-enhanced computerized tomography (CT) scanned images of the abdomen at portal venous phase. A. A 9.3 cm × 8.7 cm mass in the hepatic posterior lobe. B. Another 1.6 cm × 1.5 cm mass occupying the lower portion of right kidney without local invasion or lymphnode metastases.

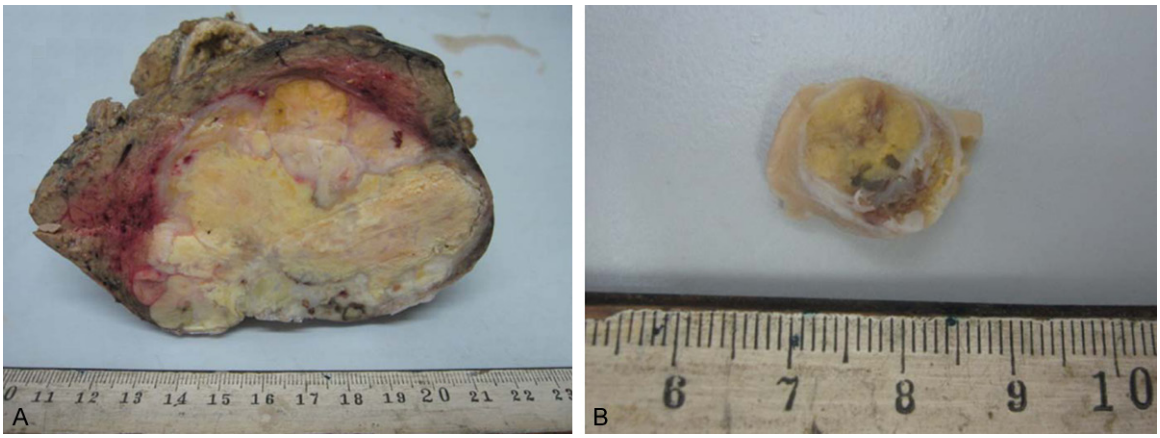

Figure 2. Grossly observation: A. A 7 cm × 5 cm boundary clear but unencapsulated tumors were found in the liver tissue in white to gray-yellow color, which had already invaded liver capsule. B. A circumscribed and pliable tumor (1.2 cm × 1 cm) was found in bisected section of the kidney specimen, of which the border was clear.

delayed phase. The percutaneous needle biopsy of the hepatic tumor diagnosed as hepatocellular carcinoma. Clinical presumptive diagnosis was primary hepatocellular carcinoma (T3N0M1) metastasis to right kidney. Subsequently he received five courses of interventional treatment before surgical resection in the next 44 months.

Surgical resection for hepatocellular carcinoma was performed on the right hepatic posterior lobe of segments VI and VII plus partial of the right diaphragm. Small-nodules were found in the surface of the cirrhosis liver. The hepatic tumor was localized at the VI, VII segments of the right hepatic posterior lobe, of which the size was about 10 cm × 9 cm × 9 cm. The neoplasm had extruded liver capsule and invaded the right diaphragm ranged from about 3 cm × 5 cm, the back bottom of the tumor had invaded the peritoneum ranged from 2 cm × 3 cm. A hard nodule with a size about 2 cm × 2 cm was seen on the posterolateral of the right kidney. In case of the risk of impaired renal function, a partial wedge nephrectomy of the right kidney was performed.

Pathologic findings

Grossly, the resected specimen (11 cm × 10 cm × 6 cm) of the hepatic neoplasm with attached partial diaphragm and peritoneum

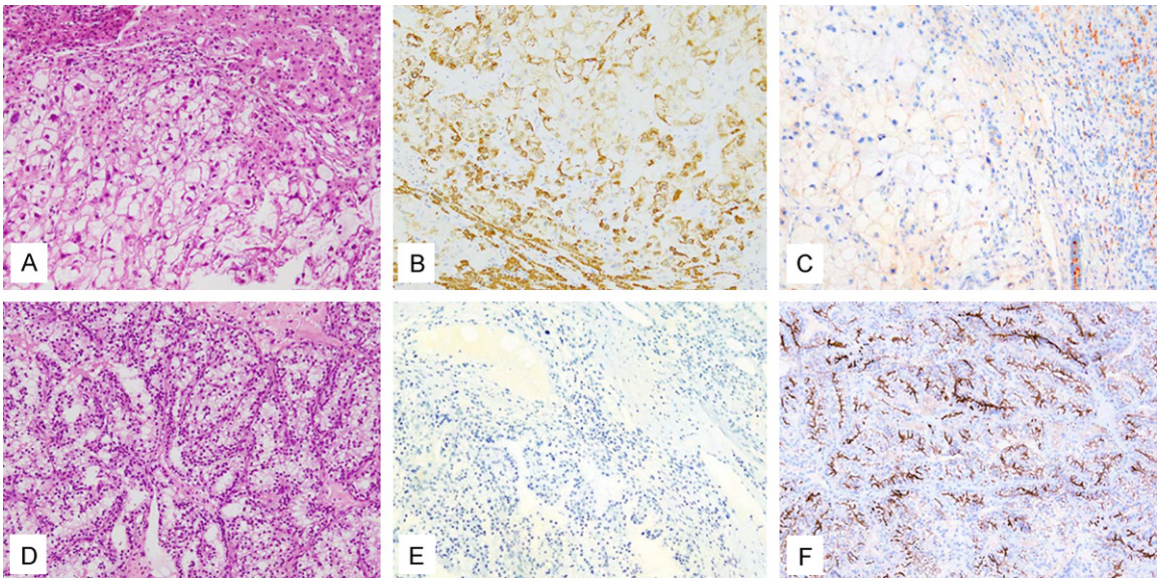

Figure 3. Histopathological observation: A. Bulky cancer cell with clear cytoplasm were found in liver tumor by HE staining (× 200); B. hepatocellular carcinoma cells were positive for HepPar-1 (× 200); C. hepatocellular carcinoma cells were negative for CD10 (× 200). D. HE staining of renal tumor shows that the cancer cells were small and acinar-like arranged (× 200). E. Renal cancer cells were negative for HepPar-1 (× 200); F. Renal cancer cells were strongly positive for CD10 (× 200).

Table 1. Immunohistochemistry results of liver and renal tumors

	HepPar-1	GPC3	AFP	CA IX	CD10	RCC	CK7	Pax-2	Pax-8	P504S	TFE3	SMA	s100	HMB45	melanA
Liver tumor	+	+	-	-	-	-	-	-	-	+	-	-	-	-	-
Renal tumor	-	-	-	+	+	+	+	+	+	+	-	-	-	-	-

was received. The specimen was of slightly granular surface, bisected to reveal a 7 cm × 5 cm boundary clear but unencapsulated tumor in white to gray-yellow color, which had already invaded liver capsule (**Figure 2A**). Another resected specimen from the right kidney (2.5 cm × 1.8 cm × 1 cm) was attached with partial kidney tissue. A circumscribed and pliable tumor (1.2 cm × 1 cm) was found in bisected section, which is in gray-yellow color was seen during section, with a size, tough, the border was clear (**Figure 2B**).

Microscopically, the neoplastic cells of the hepatic neoplasm arranged in sheet, more than 90% of which were of clear cytoplasm. Laminar necrosis could be seen. Bulky tumor cells were round or polygonal shape, which were characterized with rich foamy cytoplasm and small, round or irregular nuclei, condensed chromatin but indistinct nucleolus (**Figure 3A**). Thin-walled vessels were enriched in scarce interstitial substance. Tumor tissue without capsule had locally invaded the surrounding liver tissues. The hepatic tissue around the lesions was slightly sclerotized.

The tumor cells of the kidney neoplasm arranged in acinar, cystic and solid sheet. The tumor cells were of medium size with clear cytoplasm, spherical and irregular nucleus. Nucleoli were not obvious, and Fuhrman nuclear grade II (**Figure 3B**).

Immunohistochemically (**Table 1**), the hepatic carcinoma cells exhibited high immunoreactivity for HepPar-1 (**Figure 3C**) and GPC3, and negative for CA IX, CD10 (**Figure 3D**), RCC and Pax-8 (Supplementary Figure 1). The renal clear cell carcinoma showed positive for CA IX, CD10 (**Figure 3F**), RCC and Pax-8, while negative for HepPar-1 (**Figure 3E**) and GPC3 (Supplementary Figure 1).

Owing to the difference in their variable histological appearances and the immunohistochemical results, a final diagnosis of simultane-

ous double primary clear cell carcinomas of the liver and kidney was confirmed: hepatocellular carcinoma (clear cell type) in right posterior lobe of liver and clear cell renal cell carcinoma in right kidney. Another intervention treatment was performed for the hepatocellular carcinoma since then. The patient is still alive and well without evidence of local recurrence and distant metastasis for 6 months after the operation.

Discussion

Multiple primary malignant neoplasms are referred to the same patient simultaneously or successively suffers from two or more primary malignancies of different histological types, which can affect multiple tissues and organs [1]. Currently the most accepted criteria for diagnosing primary malignant tumors are: 1) each tumor should be histologically confirmed as malignant; 2) each tumor occurs in different parts or organs; 3) the histological, cytological and morphological feathers as well as immunohistochemical phenotype of each tumor should be completely different; 4) the possibility that one tumor is the metastasis of another, must be completely excluded clinically, radiologically and pathologically [2].

The incidence rate of hepatocellular carcinoma associated with extrahepatic primary malignancy is varying from 0.22%~25.7% [2, 3]. The extrahepatic primary malignant tumors occurred at different locations. It is commonly associated with the tumors of the genitourinary system (mainly prostate cancer) and colorectal cancer in western countries [2, 3]. But in China, the digestive system neoplasms were the most common extrahepatic primary neoplasms (17 cases, 85%), according to the report from Hua Yu et al with 20 hepatocellular carcinoma. Due to the ease of hematogenous metastasis of hepatocellular carcinoma and other metastatic malignant tumors metastasis to liver, the possibility of metastatic tumors (metastasis extrahepatic/hepatocellular carcinoma) must be excluded before making a diagnosis of multiple primary carcinomas, in which immunohistochemical stains plays very significant role for differential diagnosis. It is extremely rare reported that two primary cancers simultaneously occur in the liver and kidney [4-8]. It was even rarer for both were clear cell carcinomas, and only one case was reported in the literature previous [6]. During pathological diagnosis, it is difficult to distinguish between the clear-cell hepatocellular carcinoma and the metastatic clear cell renal cell carcinoma if relying solely on morphological characteristics [9-13]. So obtaining a wide range of sections, carefully searching for typical hepatocellular carcinoma and leveraging immunohistochemical stains, such as HepPar-1, GPC3 and CD10, will play important roles in differential diagnosis [8, 11, 14, 15]. The case reported here with a diagnosis history of “hepatitis B” and “cirrhosis”, also found neoplasm in liver (diameter 10 cm) and kidney (2 cm), which initially clinical diagnosed with primary hepatocellular carcinoma with right kidney metastasis. During pathological diagnosis, clear-cytoplasm neoplastic cells were observed in both neoplasms from liver and kidney. Clear cell carcinoma is the most common type of renal cell carcinoma, so initially clear cell renal cell carcinoma with metastasis to liver was considered. However, immunohistochemical staining results showed that clear neoplastic cells of the liver were HepPar-1, GPC3 positive, and CD10, RCC and Pax-8 as well as other nephrogenic markers were negative; however, renal clear neoplastic cells were CD10, RCC and Pax-8 positive, but negative to the liver-derived markers Heppar-1 and GPC3, supported the diagnosis that both tumors in the liver and kidney were primary.

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Disclosure of conflict of interest

None.

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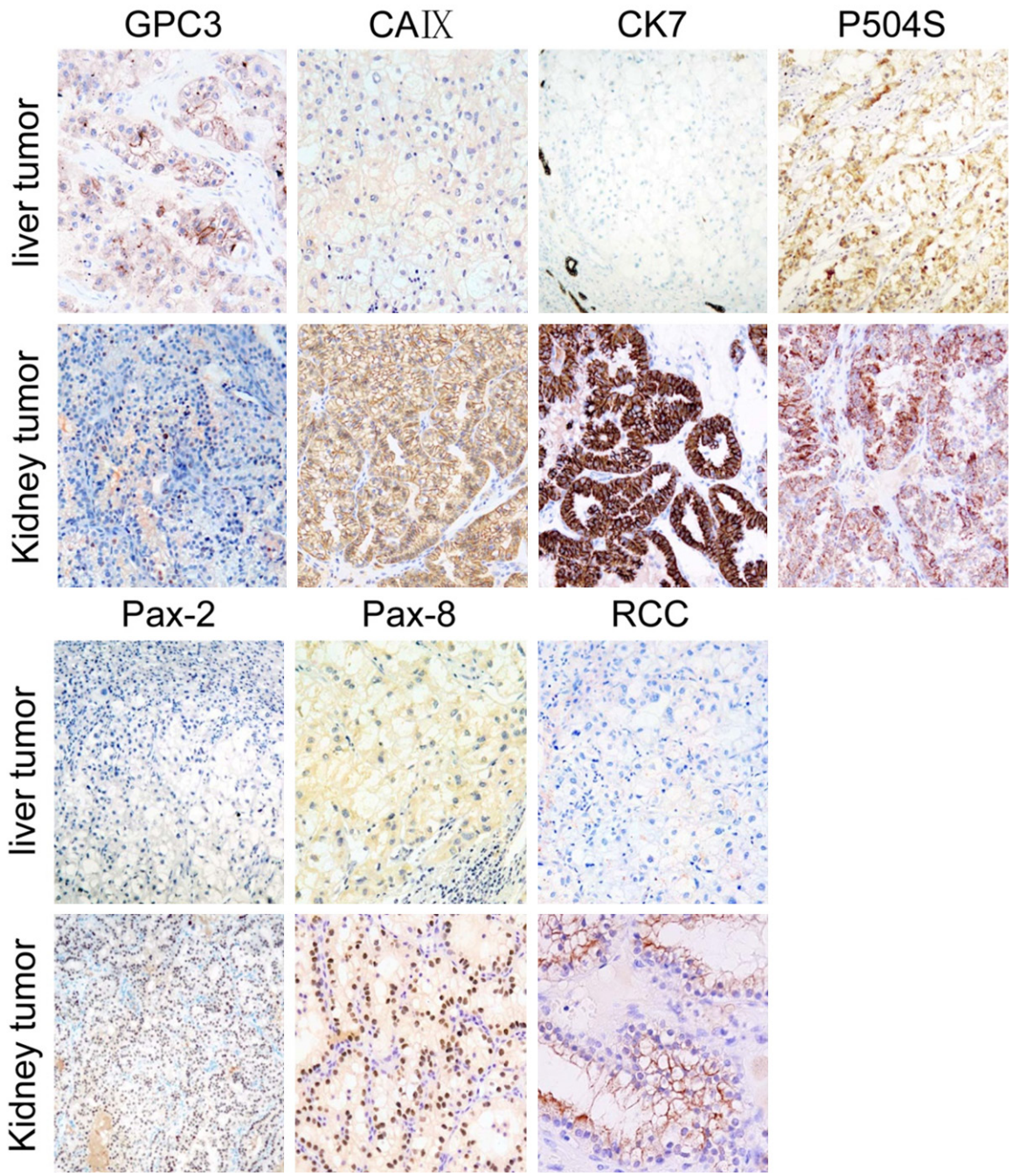

Supplementary Figure 1. Histopathological observation: hepatocellular carcinoma cells were positive for GPC3 and P504S, negative for CK7, CA IX, RCC, Pax-2 and Pax-8 (× 200). Renal cancer cells were negative for GPC3, positive for P504S, CK7, CA IX, RCC, Pax-2 and Pax-8 (× 200).