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Case Report

Simultaneous radical excision of synchronous primary hepatocellular carcinoma and renal clear cell carcinoma in an 80-year-old patient: a case report

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Abstract: Background: Synchronous multiple primary malignant tumors are still a rare occurrence, so the diagnosis and subsequent management are challenging to clinicians. Hepatocellular carcinoma (HCC) is one of the most common malignancies, and viral hepatitis and alcoholic liver cirrhosis have emerged as the leading causes of HCC. Renal clear cell carcinoma (RCCC) is also the most common histological type of renal carcinoma. There are only 5 reports about the coexistence of HCC and RCCC in the medical literature. But there is no report on an elderly patient with synchronous HCC and RCCC and without pre-existing liver disease who was simultaneously resected. Case presentation: We herein report a rare case of an 80-year-old man suffering from synchronous primary hepatocellular carcinoma (HCC) and renal clear cell carcinoma (RCCC) but without any past history of chronic viral hepatitis or alcoholic liver injury. Preoperative abdominal CT images revealed two solid masses respectively in the right hepatic lobe and the right kidney following the patient's 18-day history of right superior quadrant abdominal pain. In view of his good medical condition, the patient successfully underwent a simultaneous radical excision of HCC and a right nephrectomy in a single operation. Conclusion: 1) This is the first report of a patient who suffered synchronous primary HCC and RCCC but without any history of viral hepatitis or alcoholic liver cirrhosis, which reminds the clinicians to notice the link between HCC and RCCC especially in the elderly. 2) This is the first report of double primary HCC and RCCC that were simultaneously resected successfully in a patient over 80 years old, which suggests that age should absolutely not be considered an operational contraindication.

Keywords: Synchronous primary carcinoma, hepatocellular carcinoma, renal clear cell carcinoma, simultaneous radical excision, elderly patients

Background

Hepatocellular carcinoma (HCC) ranks as the sixth most common cancer worldwide and the third deadliest form of cancer [1]. It usually arises in a previously damaged organ, mostly in the setting of chronic viral hepatitis B or C and alcoholic liver cirrhosis [2]. However, synchronous extrahepatic primary malignant tumors are still a rare occurrence, so the diagnosis and subsequent management are challenging for clinicians. The most frequent extrahepatic primary malignancies (EHPM) associated with HCC are prostate cancer and colorectal cancer in North America and most of Europe and gastric and colorectal cancer in Asia [3]. The coexistence of HCC and RCCC is rare, and only 5 case reports of both synchronous prime tumors in the liver and kidneys could be found in the existing medical literature [4-8] (**Table 1**). These patients had histories of viral hepatitis or alcoholic liver cirrhosis, and one of them involved the same type of pathology with clear cell carcinomas [6]. Different treatments were chosen from among radio-frequency ablation, an interventional treatment blending resection, a stage operation, and organ transplantation [4, 5, 7]. Here, we describe the simultaneous excision case of an elderly male who suffered from synchronous primary HCC and RCCC but who had

Table 1. Summaries of the similar reported studies

	Age	Gender	Ananmnesis	Size and position of Liver tumor	Size and position of Kidney tumor	Treatment	Pathology
Case 1	57	Male	Alcoholic cirrhosis	Right lobe 11.8 × 11.3 cm	Upper portion of right kidney 3.7 × 3.5 cm	Staged procedure of hepatectomy and right radical nephrectomy	Hepatocellular and clear cell renal carcinoma
Case 2	52	Male	Hepatitis C virus-associated liver cirrhosis	Right lobe 2.7 × 2.2 cm	Upper portion of right kidney 1.7 × 1.2 cm	Liver transplantation and partial nephrectomy	Hepatocellular and renal cell carcinoma
Case 3	53	Male	Alcoholic cirrhosis	Left lobe 2.8 cm	Mid-pole of left kidney 1.9 cm	Transarterial chemoembolization and radio-frequency ablation	
Case 4	69	Male	Hepatitis C virus-associated liver cirrhosis	Right lobe 3 × 3 cm	Left kidney 10 × 5 cm	Left radical nephrectomy and segmental liver Resection	Clear cell hepatocellular and renal cell carcinoma
Case 5	42	Male	Hepatitis B virus infection and alcohol abuse	Left lobe 15 × 7 cm	Left kidney 4.3 × 4.2 cm	Left hepatectomy and partial gastrectomy, left nephrectomy	Hepatocellular and renal cell carcinoma

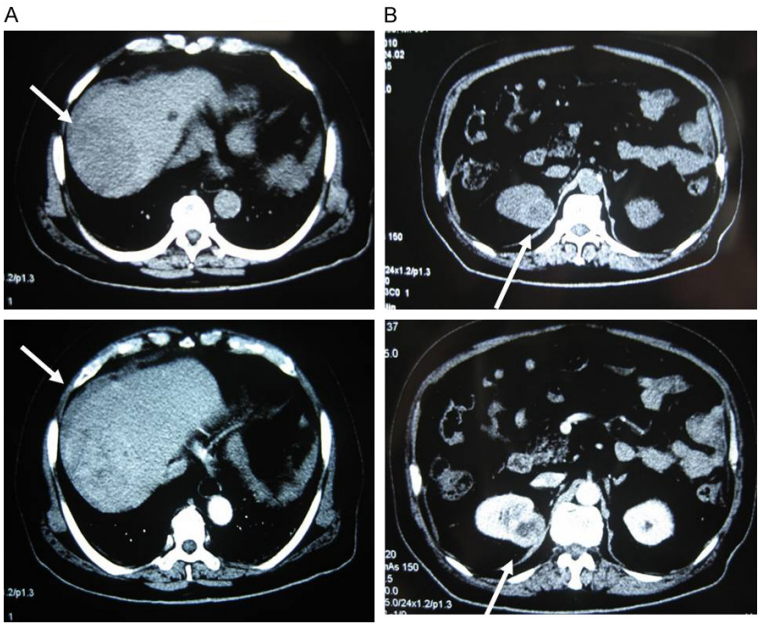

Figure 1. CT scans and contrast-enhanced CT findings. A low-density solid tumor is seen in the right hepatic lobe, and it shows a significant enhancement in isodensity (A. arrow) and a nonuniform enhancement of an irregular circular region in the right kidney (B. arrow).

no history of chronic viral hepatitis or alcoholic liver injury.

Case presentation

An 80-year-old man was admitted to the hospital with 18-day history of right superior quadrant abdominal pain but without any symptoms of fever, nausea, vomiting, diarrhea, or jaundice. The abdominal CT image revealed one 50 mm hypodense round-like mass in the right hepatic lobe representing a hepatoma, and another irregular circular region, approximately 40 mm with mildly lower density that had damaged the upper portion of the right kidney suggesting a second neoplasm. The CT images demonstrated both lesions with the enhancement of heterogeneous intensity (**Figure 1A**, **1B**). There were no lung nodules or mediastinal enlarged lymph nodes seen in the chest CT scan. The levels of tumor markers in the serum were determined, and the results showed that the α-fetoprotein (AFP) had risen to 1210 ng/ml (normal level ≤ 7.0 ng/ml), the carcinoembryonic antigen level was up to 4.58 ng/ml (normal level ≤ 3.4 ng/ml), the cancer antigen 125 level was up to 56.79 U/ml (the normal level ≤ 35 U/ml), and the carbohydrate antigen 19-9 was also elevated to 77.36 U/ml (the normal level ≤ 27 U/ml), but the serologic tests for hepatitis B and hepatitis C were negative. There were no lesions were seen in the gastroscopy or colonoscopy. The clinical presumptive diagnosis before the operation was co-existing space-occupying lesions, one in the right lobe of the liver considered to be primary HCC, and another in the right kidney thought to be primary RCCC based on the imaging tests and laboratory examinations. The T cell subsets were analyzed by flow cytometry and the results showed that the fraction of $CD3^+CD4^+$T cells and the ratio of CD4/CD8 were reduced (the $CD3^+CD4^+$T cells were 25.54%, normal: 40-51%; the CD4/CD8 cells were 0.85, normal: 1.33-1.99).

The routine blood examination of the renal function and liver function indices fell within the normal limits. Considering that there were no remarkable indications of local invasion or lymphonodus metastasis and the patient's generally good health, we performed radical surgical excision of both neoplasms in the right hepatic lobe and right nephrectomy. There was no obvious hepatic cirrhosis or evidence of cancer metastasis in the abdomen. The hepatic tumor was removed together with the liver tissue within about a range of 20 mm around the tumor. The hepatic portal interdicting was conducted just once with 12 minutes. Subsequently, a right nephrectomy was performed. The entire surgery lasted 105 minutes.

The excised hepatic tumor measured 30 × 50 × 45 mm in size with a complete pseudocapsule and showed a gray-white appearance on the surface, but with an absented malignant embolus. The right renal neoplasm was circumscribed in the pseudocapsule with a high tenacity and measured 15 × 35 × 30 mm, and it appeared a gray-yellow color on the lateral segment (**Figure 3**). There was no indication of an enlarged lymphonodus. The postoperative pathology reported that moderately differentiated HCC occupied the right hepatic lobe with no oncocytes at the cut edge (**Figure 2A**), and

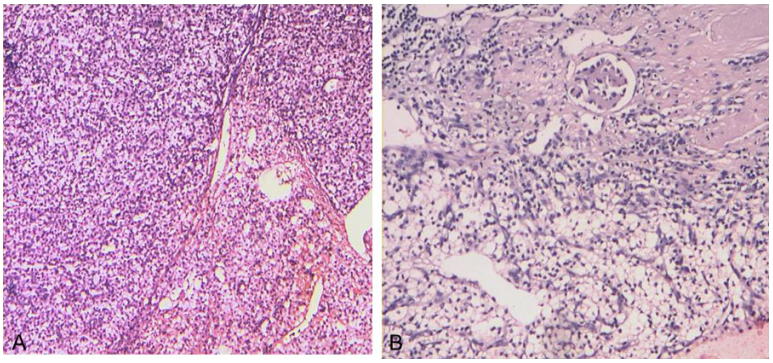

Figure 2. Histological analysis of the resected HCC and RCCC tumor tissues. Moderately differentiated hepatocellular carcinoma (A) and grade II renal clear cell carcinoma (B) were noted in the postoperative pathology report (H&E stain).

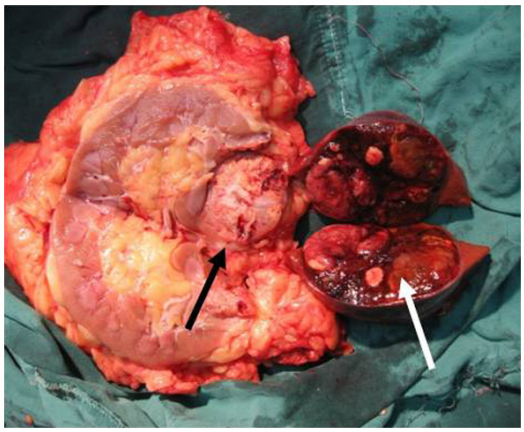

Figure 3. Gross appearance of HCC and RCCC. Right renal tumor showing gray-yellow color, measuring 15 × 35 × 30 mm with a pseudocapsule (black arrow), and a gray-white, solid tumor measuring 30 × 50 × 45 mm originating from the right lateral lobe of the liver (white arrow).

grade II RCCC captured the right kidney as well as the perinephric adipose capsule but neither the ureteral cut ends nor the adrenal body was affected (**Figure 2B**). The immunohistochemistry results reconfirmed both neoplasms were malignancies with tumor makers, concretely, and the tumor on the right lobe of the liver was positive for AFP and CD10, and the neoplasm of the right kidney was positive for CD10, epithelial membrane antigen (EMA), and vimentin. The values of ALT (465 U/L) and AST (373 U/L) were a little higher than normal on the first day, but then the ALT, AST and AFP levels recovered to their normal levels one week after the surgery. After a 12-month follow-up, the patient is currently healthy, with no evidence of local or distant recurrence.

Discussion

In most cases, the causes of liver cancer are long-term damage and cirrhosis due to the chronic inflammation of the hepatitis B or C virus, alcohol abuse, aflatoxins, autoimmunity, and nonalcoholic fatty liver disease. Moreover hepatic cancer resulting from the chronic hepatitis B virus may not involve cirrhosis like hemochromatosis and fibrolamellar HCC do. HCC accounts for most liver cancers and occurs more often in men than in women, and it is usually diagnosed in people age 50 or older [1, 2, 9]. Renal clear cell carcinoma accounts for 75-80% of all renal cell carcinomas and is the most common histological type [10]. But the coexistence of primary HCC and RCCC is rare. Synchronous multiple primary cancers are presumed to have a common genetic, hormonal, immunologic, environmental, or iatrogenic link and are less common than metachronous tumors. Only 5 case reports could be found in the medical literature on synchronous primary HCC and RCCC. All of them were related to patients with a history of alcoholic liver cirrhosis or viral hepatitis [4-8]. A recent large-scale study reported that HCC with prior, synchronous or metachronous extrahepatic primary malignancy (EHPM), manifested at an age > 60, an AFP level > 400 ng/ml, positive for HBsAg, Child-Pugh A cirrhosis, and earlier BCLC staging (Barcelona clinic liver cancer) are independent factors associated with EHPM [11]. We noticed that this patient was negative for both viral hepatitis and necrosis, even though he was 80. It was the most possible independent factors associated with one of the susceptible independent factors. The association of aging and cancer means there is more time for carcinogenesis to occur, older tissues being more susceptible to environmental carcinogens, and molecular changes in DNA signaling may favor the development of cancer [1]. We considered that the patient had an imbalance of his immune regulation ability. This presumption was supported by the distinctly declined percentage of his $CD3^+CD4^+$T cell subset and his rate of CD4/CD8 before the operation. It is well known that cellular immunity mediated by subsets of $CD4^+$T lymphocytes

plays an important role in the anti-tumor immunology process. Therefore a link between primary hepatic and renal carcinomas should be noted, especially in elderly patients.

The criteria for diagnosing co-existent primary malignant tumors are accepted as: each tumor should be in different parts or organs, confirmed as malignant, completely different morphologically, histologically and cytologically, as well as the immunohistochemical phenotype, and completely excludes the metastasis clinically, radiologically, and pathologically [3]. Our case showed that one mass with the enhancement of heterogeneous intensity using a CT scan occupied right lobe of the liver accompanied by a serum AFP level elevated to 1210 ng/ml, so that the primary hepatocellular carcinoma was diagnosed. Another heterogeneous lump involving the right kidney was revealed by contrast-enhanced CT and suggested renal carcinoma. The double primary carcinomas were confirmed to be different pathologic types in the postoperative pathology, but the metastases were excluded. The malignancies of both neoplasms were reconfirmed with the immunohistochemistry results, concretely, and the HCC was positive for AFP and CD10 and the RCCC was positive for CD10, EMA, and vimentin.

Due to the early diagnosis and an improvement in the treatment of cancer, the overall survival rate among cancer survivors is increasing. In addition, the incidence of secondary cancers has also increased. The clinical treatment makes it necessary for the patients suffering from coexisting carcinomas, especially HCC and RCCC, to consider the risks of simultaneous resection. Surgery remains the treatment option offering a potential cure for localized disease, especially in non-cirrhotic patients. In the five cases reported, radio frequency ablation (RFA) or RFA followed trans-arterial chemoembolization (TACE), the resections of masses and transplantations were treated according to the sizes of the tumors and general condition of the patients (**Table 1**). With regard to our case, we took into account the size of both tumors and the normal functions of the liver and kidneys, and we chose simultaneous surgical treatment.

Some studies showed that patients receiving curative treatment with surgery fared the same as those who were young, female, people with healthy livers, and those with less advanced TNM and BCLC stages, were independent factors for better survival [12]. As in this case, we couldn't conclude the relation between HCC with RCCC, but here we got the hint that the age should not rule out operations, as is the habitual understanding of some surgeons. Considering that being positive for vimentin is closely linked to tumorigenesis and metastasis, it is proper and crucial to choose the timely radical excision. In the future, the survival rates of HCC with EHPM should increase due to to earlier cancer detection and improved and timely cancer treatment.

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Disclosure of conflict of interest

None.

Abbreviations

HCC, hepatocellular carcinoma; RCCC, renal clear cell carcinoma; RCC, renal cell carcinoma; CT, computed tomography; AFP, α-fetoprotein; EMA, epithelial membrane antigen; ALT, alanine transaminase; AST, Aspartate transaminase.

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