

## Case Report

# Synchronous Occurrence of Hepatocellular Carcinoma and Renal Cell Carcinoma: A Case Report

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### Abstract

The coexistence of two primary tumors is very rare. Additionally, hepatocellular carcinoma (HCC) and renal cell carcinoma (RCC) are even less frequent. An 81-year-old male patient had HCC and RCC synchronously. Surgery was performed primarily, as both tumors were suitable for resection. Adverse effects were observed during the patient's follow-up with adjuvant chemotherapy, and the treatment regimen was changed. This report presents the seventh case describing the treatment of synchronous double cancers of HCC and RCC. Although this rare condition shortens the patient's life expectancy, our patient is

alive even though he has a liver recurrence in the third month and is followed up to the 20<sup>th</sup> month.

**Keywords:** Synchronous tumor; Hepatocellular carcinoma; Renal cell carcinoma; Case report

### Background

The presence of two different tumors in a single patient is a rare condition. The incidence rate of hepatocellular carcinoma (HCC) associated with extra hepatic primary malignancy varies from 0.22% to 25.7% <sup>[1]</sup>. When the patient has two tumors in different sites, it should be realized whether cancers are the two primary

cancers or the other's metastasis. The life expectancy of the patient and the prognosis of the cancers should be taken into consideration for appropriate treatment planning. Here, we present the clinical course of a patient with HCC and renal cell carcinoma (RCC).

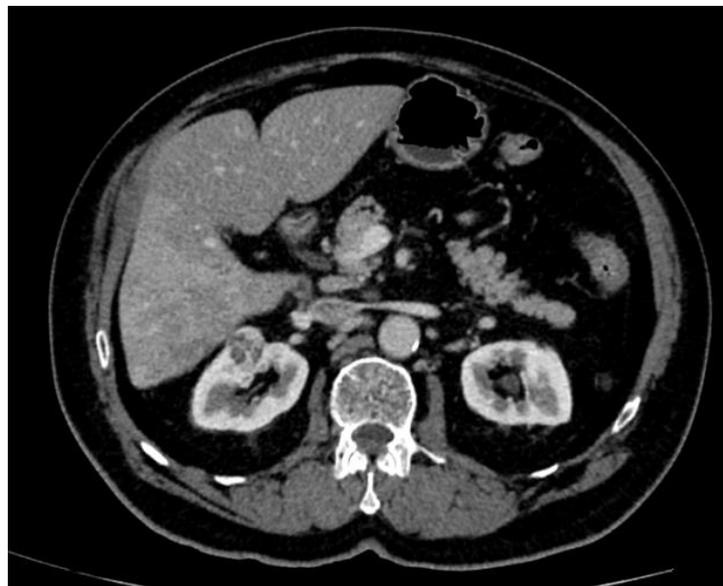
### **1. Case Presentation**

An 81-year-old male was referred to our hospital with liver and kidney lesions determined in routine medical examination. The patient's past medical history was remarkable for hypertension, absence of hepatitis or cirrhosis, absence of significant weight loss (<10%), and no gross hematuria. His physical examination was unremarkable. Laboratory examinations all ranged in normal limits, including routine blood chemistry, complete blood count, liver and kidney function tests, and urine analysis. Alpha-fetoprotein (AFP) was in the normal range, and the tumor marker Ca19-9 value was higher than normal (62 U/mL). Computed tomography (CT) revealed a mass lesion in segments 6 and 7 of the liver, 64x60 mm in size, with a heterogeneous appearance without significant contrast in the arterial phase (Figure 1A), and a tumor thrombus was observed in the right portal vein (Figure 1A). It was considered HCC and staged as stage C of Barcelona Clinic Liver Cancer (BCLC) due to portal vein tumor thrombus (PVTT). A second mass lesion, 26x24 mm in size, was also detected in the anterior part of the right kidney. It was found to be compatible with RCC (Figure 1B). Simultaneous posterior liver sectorectomy under intermittent portal triad clamping (PTC, 29 minutes) and right radical nephrectomy was

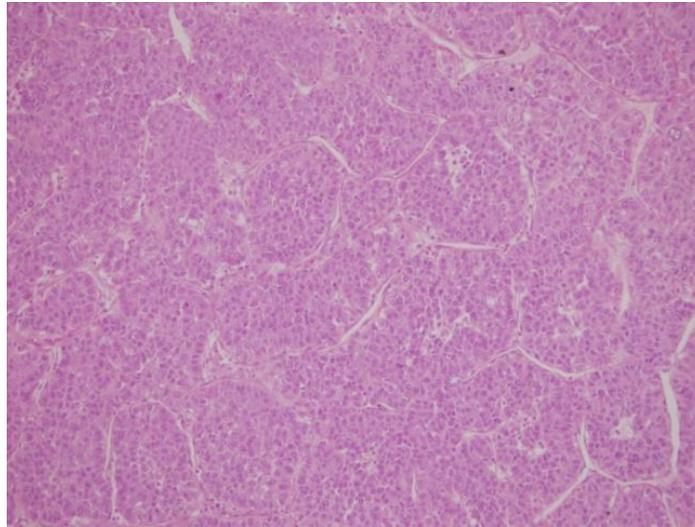
performed. The tumor thrombus was also removed with thrombectomy. Pathological examination revealed moderately differentiated (G2) HCC (with necrosis, lymphovascular and capsular invasion (Figure 2A)) and Fuhrman Grade 1 clear cell renal cell carcinoma (localized middle pole of right kidney (Figure 2B) and limited in the renal parenchyma (pT1N0M0)). The tumor distance from the surgical margin of the liver was 2.5 cm. Transient elevation of creatinine levels in the early postoperative period was controlled with medical treatment. The patient was discharged on the 18th postoperative day without any additional events. Three months after the operation, control magnetic resonance imaging (MRI) of the liver revealed a new mass lesion in segments 2 and 3 (47x30 mm in size). The diagnosis of HCC recurrence was confirmed by percutaneous liver biopsy. Hence, selective hepatic transarterial chemoembolization (TACE) was performed for HCC recurrence, and sorafenib treatment was started (Figure 3). However, it was discontinued 3 weeks later due to drug-related side effects, including widespread nonpalpable petechia and purpura, erythema on the trunk, and hematuria. Skin biopsy revealed perivascular lymphocytic infiltrate with erythrocyte extravasation compatible with vasculitis (Figure 4). A week after cessation of sorafenib and starting of intravenous prednisolone treatment, skin lesions were significantly regressed. At the 18-month follow-up, diffuse recurrence of HCC was observed in the liver on tomography images. After 20 months of surgery, the patient is still alive with no distant metastasis.



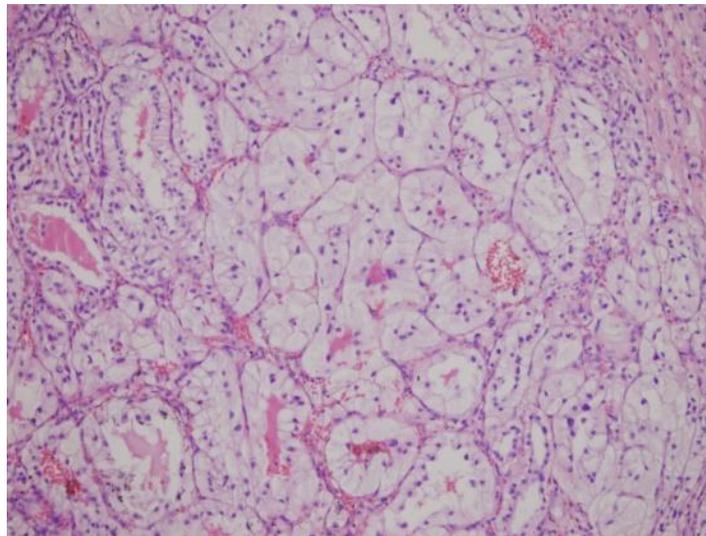
**Figure 1A:** Preoperative localization of HCC and portal vein tumor thrombosis



**Figure 1B:** Preoperative RCC on the right kidney



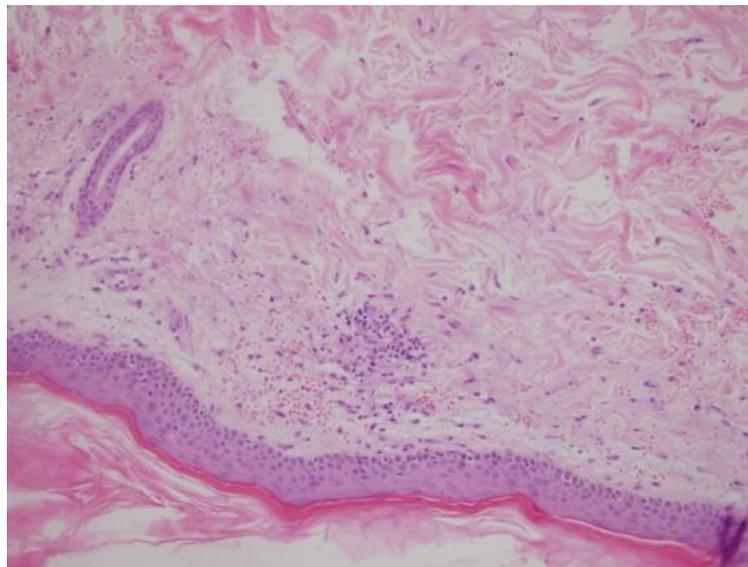
**Figure 2A:** Hepatocellular carcinoma with macrotrabecular growth pattern (H&E; x200).



**Figure 2B:** Renal cell carcinoma composed of neoplastic cells with clear cytoplasm and a nested growth pattern (H&E;x200).



**Figure 3:** Left hepatic artery and pathological tumoral staining. Catheterization of the anastomosis with a peripheral microcatheter and TACE with doxorubicin-eluting beads (DEB-TACE) were performed, and the pathological staining was removed.



**Figure 4:** Skin biopsy demonstrating perivascular lymphocytic infiltration with erythrocyte extravasation (H&E; x200)

## **2. Discussion and Conclusions**

As indicated by us and in other studies, HCC is a disease among the elderly population in Turkey. In contrast to Asian and Western countries, the median tumor size at the time of diagnosis was found to be larger than 5 cm [2-4]. The accumulation of patients in BCLC stages B and C is not considered bizarre. The European Association for the Study of the Liver (EASL) and the American Association for the Study of Liver Diseases (AASLD) guidelines recommend noncurative therapies for BCLC stages B and C [5]. However, we followed an aggressive policy in the treatment of intermediate and advanced stages of HCC [4]. The background of our policy has been well described in the literature [6,7]. Macrovascular invasion is a well-recognized characteristic of HCC. The presence of tumor thrombi is reported in 35% of cases in the portal vein (PVTT) and 2% of cases in the hepatic vein [8,9]. Thrombectomy is a feasible method for clearance of tumor remnants within the vessel during liver resection, and it is safely performed for PVTT under inflow control. Patients with BCLC stage B and stage C tolerate hepatic resection with low mortality, acceptable morbidity, and survival benefits in the current era. On the other hand, surgical treatment stands out as the most important modality in RCC treatment and is curative in patients in the localized stage. It has been stated that there is no age limit for radical nephrectomy, and it can be applied safely even in elderly patients [10]. There were six cases with the synchronous occurrence of HCC and RCC reported in the literature (Table 1) [11-16]. The median age was 55 years (42-72). Underlying chronic liver disease was determined in 4 of 6 patients. Half of the patients presented without symptoms. Many of the HCC lesions were in the right lobe of the liver (66.7%). The median diameter of the HCC was 110 mm (28-151). The RCC lesions were equally distributed both in the

right and the left kidneys. The median diameter of the RCC was 37 mm (16-43). Half of the patients were considered to have BCLC stage B disease. There was no uniform approach observed in the treatment of these cases. Surgical treatment was applied in combination with interventional treatments (n=2), chemotherapy, and radiation treatment (n=1) or alone (n=1). Simply, radiofrequency ablation (RFA) was used in two of the cases without any intervention against RCC. Sorafenib treatment was preferred in one of the six cases. The follow-up periods of these cases were limited. Therefore, it is difficult to reach generalized comments regarding the impact of treatment on patient prognosis. Sorafenib is considered the standard systemic therapy for HCC. According to some researchers, it is recommended as a first-line treatment option for patients with BCLC stage C HCC [5]. However, sorafenib treatment induces some adverse effects, including hand-foot skin reaction, hypertension, diarrhea, anorexia, fatigue, and weight loss. Dose reduction or discontinuation of the therapy may be needed to improve patient quality of life. Sorafenib-related vasculitis is an exceedingly rare dermatological event [17]. A couple of cases have been reported in the literature. Interruption of sorafenib treatment with or without steroid therapy was preferred to eliminate vasculitis. In conclusion, this report presents the seventh case describing the treatment of synchronous double cancers of HCC and RCC. Cumulative data indicated that HCC is the predominant cancer, and it should be taken into consideration for planning the treatment of both cancers. If the stages of double cancers are suitable for surgical treatment, it should be performed primarily. Clinicians should also consider the probability of rare adverse events such as vasculitis during the administration of sorafenib.

Author (Ref.)	Age/Gender	Hepatitis/Cirrhosis	Clinical symptoms	Location of HCC and RCC	Tumor Size on CT scan	BCLC*	Preoperative treatment	Operative Treatment	Postoperative treatment	Follow-up
Shetty [11]	57 Y/M	N/A	Asymptomatic	The right lobe of the liver, mid-pole right kidney	HCC: 118×113mm; RCC: 37×35mm	B	Chemoembolization (cisplatin and gel foam)	Right hepatectomy and after two months Right radical nephrectomy	N/A	N/A
Lee [12]	53Y/M	Alcoholic cirrhosis	General weakness	Segment II of the liver, left kidney	HCC: 28mm; RCC: 19mm	A	RFA	-	-	1 month
Gang [13]	72Y/M	Hepatitis B and Cirrhosis	Asymptomatic	Segment V of the liver, The lower pole of the left kidney	HCC: N/A; RCC: N/A	N/A	RFA	-	Oral medication (Sorafenib 2x400mg)	10 Month (Died)
Zhang [14]	63Y/M	Hepatitis B and Cirrhosis	Right upper quadrant abdominal pain	Right hepatic posterior lobe, The lower pole of the right kidney	HCC: 93×87mm; RCC: 16×15mm	B	Five courses of interventional treatment	Right Hemi hepatectomy and Partial wedge nephrectomy	One course of interventional treatment	6 month
Sun [15]	42Y/M	Hepatitis B	Poor appetite and Abdominal discomfort	Left lateral hepatic lobe, left kidney	HCC: 151×70mm; RCC: 43×42mm	B	-	Left Hemi hepatectomy and Left nephrectomy	-	4 month
Hou [16]	53Y/M	No	Asymptomatic	Left lateral hepatic lobe, The lower pole of the right kidney	HCC: 110×94mm; RCC: 43×38mm	A	-	Left Hemi hepatectomy and Right radical nephrectomy	Adjuvant chemoradiation therapy	18 month
Current	81Y/M	No	Asymptomatic	Right hepatic posterior lobe, mid-pole right kidney	HCC: 64×60mm; RCC: 26×24mm	C	-	Posterior sectorectomy, Portal Vein Thrombectomy and Right radical nephrectomy	TACE and Oral medication (Sorafenib 2x400mg)	20 month

Ref., References; Y, Years; M, Male; N/A, Not available; HCC, Hepatocellular carcinoma; RCC, Renal cell carcinoma; RFA, Radiofrequency ablation; TACE, transarterial chemoembolization; \*: Patients' Barcelona Clinic Liver Cancer (BCLC) stages calculated by parameters found on papers

**Table 1:** Summary of coexisting hepatocellular carcinoma and renal cell carcinoma cases reported in the English literature [16]

**List of abbreviations**

- HCC Hepatocellular carcinoma
- RCC Renal cell carcinoma
- AFP Alpha-fetoprotein
- CT Computed tomography
- BCLC Barcelona Clinic Liver Cancer
- PVTT Portal vein tumor thrombus
- PTC Portal triad clamping
- MRI Magnetic resonance imaging
- TACE Transarterial chemoembolization
- EASL European Association for the Study of the Liver
- AASLD American Association for the Study of Liver

**Diseases**

- RFA Radiofrequency ablation

**Declarations**

**Ethics approval and consent to participate**

Ethical approval is not required for this case report, and ethical approval has been obtained for our case series, including this study. In addition, written consent was obtained from the patient and his relatives for the case presentation in their native language.

**Consent for publication**

Written and signed consent for publication was

obtained from the patient and his relatives.

#### Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request. All patient data are in the hospital database.

#### Competing interests

The authors have no conflicts to disclose.

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No funds, grants, or other support were received.

#### Authors' contributions

KE, MER, and ST conceived and designed a case report. ST, AC, and FC operated. UC evaluated cross-sectional studies and biopsy results. KE wrote the manuscript. All authors read and approved the manuscript.

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Not applicable

#### References

1. Wong LL, Lurie F, and Takanishi DM Jr. Other primary neoplasms in patients with hepatocellular cancer: prognostic implications? *Hawaii Med J* 66 (2007): 206-208.
2. Can A, Dogan E, Bayoglu IV, et al. Multicenter epidemiologic study on hepatocellular carcinoma in Turkey. *Asian Pac J Cancer Prev* 15 (2014): 2923-2927.
3. Akkiz H, Carr BI, Kendal YK, et al. Characteristics of hepatocellular carcinoma aggressiveness factors in Turkish patients. *Oncology* 94 (2018): 116-124.
4. Tomas K, Oguz S, Topaloglu S, et al. Is it rational to perform liver resection for patients with intermediate and advanced stages of hepatocellular carcinoma? *The American Surgeon* 86 (2020): 313-323.
5. Bruix J, Reig M, Sherman M. Evidence-based diagnosis, staging, and treatment of patients with hepatocellular carcinoma. *Gastroenterology* 150 (2016): 835-853.
6. Kim KM, Sinn DH, Jung SH, et al. The recommended treatment algorithms of the BCLC and HKLC staging systems: does following these always improve survival rates for HCC patients? *Liver Int* 36 (2016): 1490-1497.
7. Torzilli G, Belghiti J, Kokudo N, et al. A snapshot of the effective indications and results of surgery for hepatocellular carcinoma in tertiary referral centers: is it adherent to the EASL/AASLD recommendations? *Ann Surg* 257 (2013): 929-937.
8. Amitrano L, Guardascione MA, Brancaccio V, et al. Risk factors and clinical presentation of portal vein thrombosis in patients with liver cirrhosis. *J Hepatol* 40 (2004): 736-741.
9. Ogren M, Bergqvist D, Björck M, et al. Portal vein thrombosis: prevalence, patient characteristics, and lifetime risk: a population study based on 23,796 consecutive autopsies. *World J Gastroenterol* 12 (2006): 2115-2119.
10. Ljungberg B, Albiges L, Abu-Ghanem Y, Bensalah K, et al. European Association of Urology Guidelines on Renal Cell Carcinoma: The 2019 Update. *Eur Urol* 75 (2019): 799-810.

11. Shetty GS, Bhalla P, Desai SM, et al. Synchronous hepatocellular carcinoma with renal cell carcinoma: a case report and review of literature of multiple synchronous primary malignancies. *Indian J Surg* 75 (2013): 290-292.
12. Lee YS, Kim JH, Yoon HY, Choe WH, Kwon SY, Lee CH. A synchronous hepatocellular carcinoma and renal cell carcinoma treated with radio-frequency ablation. *Clin Mol Hepatol* 20 (2014): 306-309.
13. Gang G, Hongkai Y, Xu Z. Sorafenib combined with radiofrequency ablation in the treatment of a patient with renal cell carcinoma plus primary hepatocellular carcinoma. *J Cancer Res Ther* 11 (2015): 10-26.
14. Zhang W, Wang Q, Jiang YX, et al. Simultaneous double primary clear cell carcinomas of liver and kidney: a case report and review of literature. *Int J Clin Exp Pathol* 8 (2015):995-999.
15. Sun JJ, Yang TB, Yang YH, Liu WF, Song JX. Synchronous double primary malignancies of the liver and kidney: a case report. *Oncol Lett* 11 (2016): 2057-2060.
16. Hou S, Wang L, Qi S. Synchronous hepatocellular carcinoma with renal cell carcinoma: a case report and review of literature. *Int J Clin Exp Med* 10 (2017): 11026-11032.
17. Prejac J, Kekez D, Belev B, et al. Leukocytoclasticvasculitis associated with sorafenib treatment for hepatocellular carcinoma. *Anti-Cancer Drugs* 31 (2020): 76-77.



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