

## CASE REPORT

# Synchronous Surgical Resection of Double Primary Hepatocellular Carcinoma and Renal Cell Carcinoma

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This paper presents a case of a 53 year old, Filipino male, known to have Chronic Hepatitis B infection, presenting with bloatedness and unintentional weight loss attributed to a 21.3cm x 18.2cm x 16.6cm right liver mass with radiographic features pathognomonic for Hepatocellular Carcinoma. An incidental finding of a right renal mass measuring 3.5cm x 3.2cm x 3.4cm is seen in the inferoposterior pole was noted. Multidisciplinary team collectively decided to proceed with outright surgical resection of both hepatic and renal masses over preoperative biopsies of the masses. Histopathologic report of the Right Hemihepatectomy and Right Partial Nephrectomy confirmed the occurrence of a Double Primary Malignancy of Hepatocellular Carcinoma Stage IB and Renal Cell Carcinoma Stage I. The postoperative course is unremarkable, and given a locoregional disease, the patient will undergo active surveillance for tumor recurrence. To the best of the authors' knowledge, this is the first case of double primary malignancy of the liver and kidney to be diagnosed and simultaneously resected in the Philippines. Improved prognosis of cancer patients and diagnostic modalities contributed to increasing number of reported cases with multiple primary malignancy. In the absence of a set standard of care, multidisciplinary approach has become of greater value in balancing the risks and benefits of selected timely interventions to the patients.

**Keywords:** Double primary, hepatocellular carcinoma, renal cell carcinoma

### Introduction

The development of malignancies with double primary has become more common in the recent years due to genetic susceptibility, environmental and iatrogenic factors. Improved patient survival with different treatment modalities of patients with a primary malignancy also gives a window for a development of a second malignancy.<sup>1</sup>

This papers presents a case of hepatocellular carcinoma and renal cell carcinoma that was able to fulfill the three criteria set by Warren and Gates in 1932 to describe multiple primary malignancies,

namely: 1) each tumor must present a definite picture of malignancy; 2) must be histologically distinct and 3) that one is a metastasis of another must be excluded.

Furthermore, this paper presents a case of double primary malignancy treated synchronous surgical resection.

### The Case

This is a case of 53-year old male who complained of episodic bloatedness and unintentional weight

loss for a year prior to consult. Persistence of the symptoms were attributed to an ultrasonographic finding of a 20 by 16 centimeter right hepatic lobe mass. Patient is of good functional capacity with no report of any genitourinary complaints during all of his outpatient consultations. Only a pertinent physical finding of an enlarged liver span was recorded.

He is known to have Chronic Hepatitis B. His surgical history only included a previous appendectomy. The patient's mother had liver cirrhosis from Hepatitis B. He is a non-smoker, but reported of consuming 2-3 servings of alcoholic beverage per week for approximately 4 years during his previous employment as a seafarer.

The patient was referred to a tertiary hospital for further management of the previously noted hepatic mass, and an incidental finding of a right renal mass visualized on the auxiliary CT imaging done. The liver mass was characterized to be hypodense with minimal enhancement on the intravenous contrast CT scans, whereas the renal mass was said to be hyperdense with equivocal features for a primary renal pathology or a metastatic disease.

### Radiologic Imaging

A repeat triple-phase upper abdominal CT scan was done in the hospital a month after the initial consult exposing the previously noted large

heterogenous predominantly hypodense right liver mass with central areas of necrosis (Figure 1). The same mass exhibited the pathognomonic arterial phase enhancement with delayed washout of a Hepatocellular Carcinoma. The inferoposterior exophytic heterogeneously enhancing right renal mass was also visualized (Figure 2).

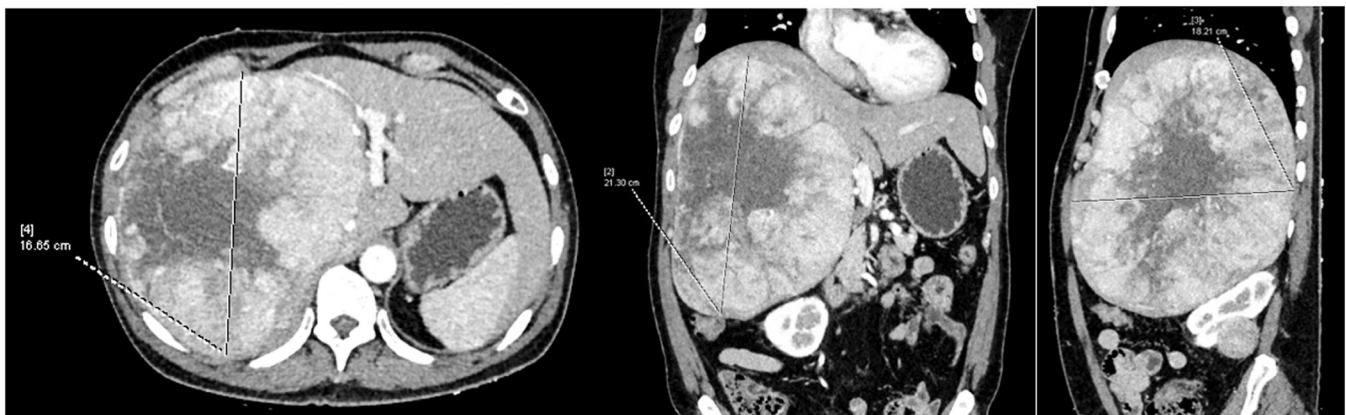
### Multidisciplinary Management

A multi-disciplinary conference was conducted to discuss the case with an initial impression of Hepatocellular Carcinoma, and primary versus metastatic right renal mass.

With the medical status of the patient considered, patient was deemed as a good candidate for definitive surgical resection. He can be classified as Child-Pugh Class A, (Score 5) given that his serum bilirubin was 1.0 mg/dL, serum albumin was 4.0 g/dL, and prothrombin time (INR; International Normalized Ratio) was 1.17. No sign suggestive of ascites nor encephalopathy was elicited. Other than the resectable right renal mass, ancillary studies revealed no evidence of distant metastasis.

### Operative Course

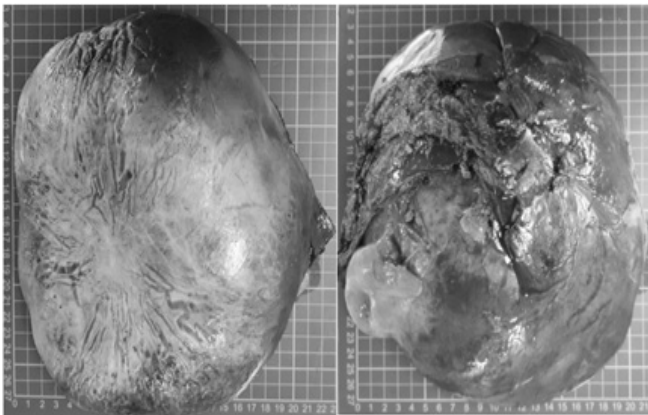
Open Right Hemihepatectomy and Right Partial Nephrectomy was done on the patient.



**Figure 1.** The coronal, axial, and sagittal films of the triple phase contrast study of the upper abdomen are shown above. The liver is markedly enlarged with smooth contours. The 21.3 x 18.2 x 16.6 cm (CCxWxAP) heterogenous predominantly hypodense mass with central areas of necrosis is seen occupying most of the right liver lobe. The mass exhibits early arterial enhancement with washout in the delayed phases.



**Figure 2.** A heterogeneously enhancing solid mass measuring 3.5cm x 3.2cm x 3.4cm is seen in the inferoposterior pole of the right kidney. The mass is more than 50% exophytic and is more than 7mm from the collecting system.



**Figure 3.** The Right Hemihepatectomy specimen measuring 21cm x 17cm x 10cm and weighing 2,300 grams. Cut sections reveal a well delineated, lobulated, cream-yellow to tan smooth mass with at least 2cm parenchymal section margins.

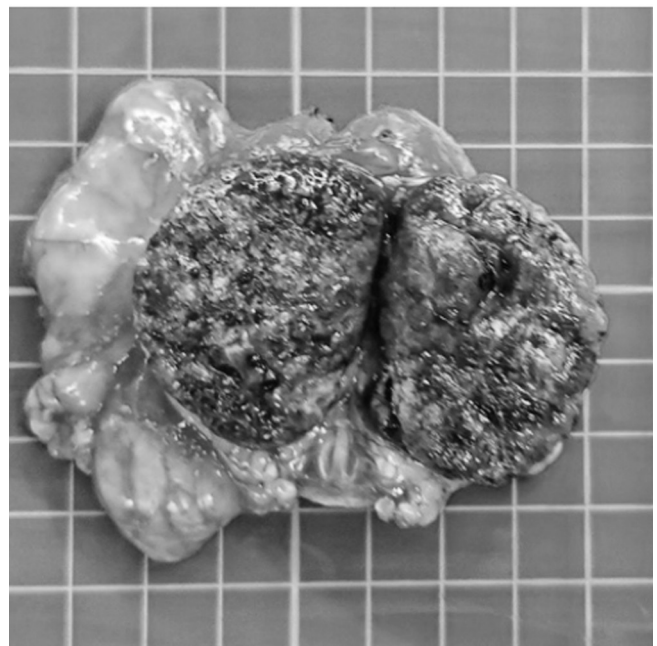
Intraoperatively, no evidence of gross metastatic lesion was seen and no other hepatic lesion was detected via intraoperative ultrasonography. The liver and renal specimen are shown in Figures 3 and 4.

The postoperative course of the patient was uneventful with note of stabilization of the liver function tests 5 days after the operation. Creatinine level was maintained at 0.8 md/dL. He was discharged on his 7th hospital day.

## Histopathology

The hepatic mass was reported by the pathologists as Hepatocellular carcinoma, moderately differentiated, 20cm in greatest dimension confined in the liver. Resection margins, lymphovascular space and gallbladder are all negative for tumor.

On the other hand, the right renal mass was reported as Clear Cell Renal Cell Carcinoma, WHO/ISUP Grade 3, 3.5 cm in widest dimension confined in the kidney. Renal parenchymal resection margins, perinephric fat and lymphovascular space are negative for tumor as well.

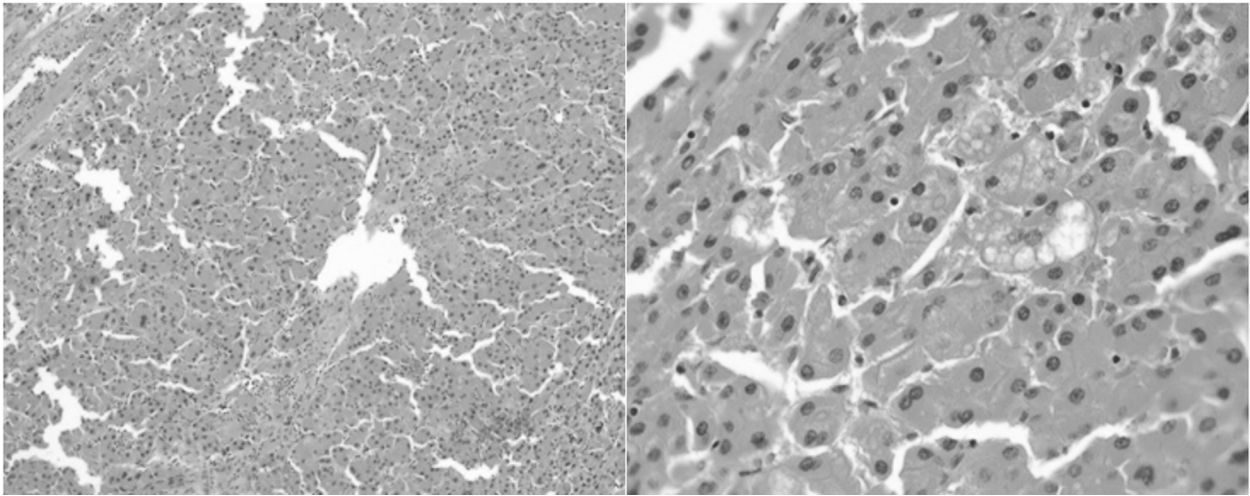


**Figure 4.** The Right Partial Nephrectomy specimen measuring 6cm x 5cm x 3cm revealed a well circumscribed cream yellow ovoid mass with areas of hemorrhage and necrosis. The mass is seen 0.5cm from the nearest parenchymal resection margin with 1 to 1.5cm thick attached perinephric fat.

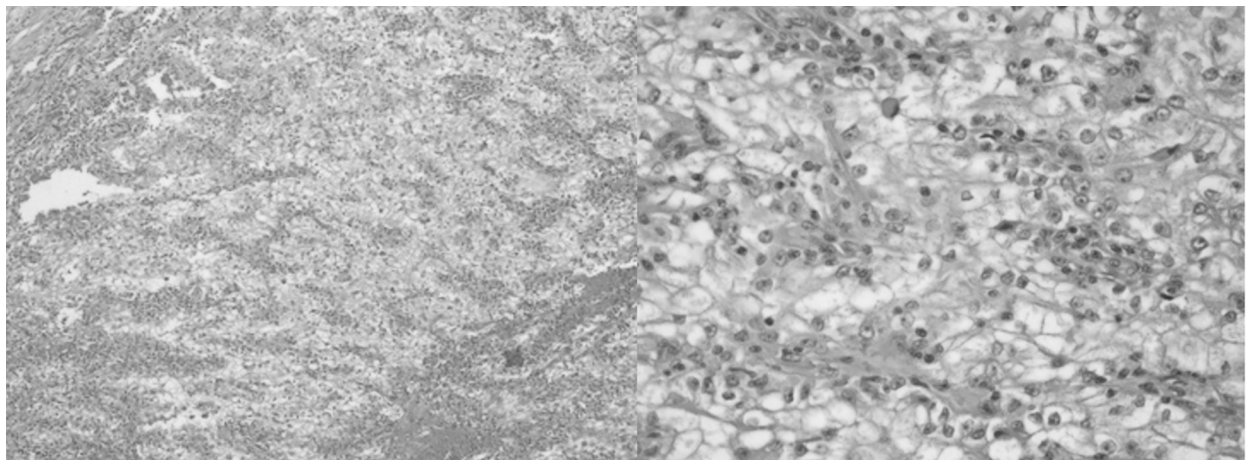
## Postoperative Diagnosis and Plan

Based on the intraoperative findings and histopathology report, the patient has Hepatocellular Carcinoma Stage IB (pT1bN0M0) by American Joint Committee on Cancer (AJCC) Prognostic Stage Groups, with synchronous Clear Cell Renal Carcinoma Stage I (pT1aN0M0) by AJCC.





**Figure 5.** Histologic sections from the hepatic mass show trabeculae of polygonal neoplastic cells with large round to ovoid nuclei, occasional distinct nucleoli and ample eosinophilic cytoplasm



**Figure 6.** Histologic sections from the renal mass is composed of alveolar, nests and sheets of malignant cells. The neoplastic cells have large round to ovoid nuclei with occasional irregular nuclear border, prominent nucleoli, and ample clear to eosinophilic granular cytoplasm.

Active surveillance with imaging and tumor markers are being recommended by current National Comprehensive Cancer Guidelines Version 2.2019 for both of the current stage of the patient's malignancy.<sup>3</sup>

On follow-up, the patient reported resolution of his chief complaint of bloatedness. He maintained his good functional status with Eastern Cooperative Oncology Group (ECOG) Score of 0. Patient is amenable to surveillance plan of chest and multiphasic abdominal imaging every 3-6 months for the first 2 years.

## Discussion

Complying with the three criteria for a definite Multiple Primary Malignancy has been the challenge for this case preoperatively. For such a diagnosis to be called, the two primary tumor must present a definite picture of malignancy, must be histopathologically distinct, and must exclude that one tumor is a metastasis of the other.

For this case, a primary malignancy of the liver is reasonable. Hepatocellular carcinoma (HCC) is known as one of the most common causes of

cancer deaths worldwide. The predisposition of the patient from chronic Hepatitis B infection further supports the development of chronic liver disease and subsequent development of HCC. The mass effects of the large hepatic mass can cause compression of the stomach leading to his complaint of bloatedness. The patient, on the other hand, has presented no symptoms directly implicated for a tumor of renal in origin. Renal carcinoma, particularly those that are locally advanced, will present with the classical triad of flank pain, hematuria and palpable abdominal renal mass.<sup>4</sup>

Postoperatively, both tumors were proven to be histopathologically distinct. The hepatic mass showed trabeculae of polygonal neoplastic cells with large round to ovoid nuclei, occasional distinct nucleoli and ample eosinophilic cytoplasm, while the classic clear cell histologic appearance of a renal cell carcinoma involving neoplastic cells with clear cytoplasm that are arranged in nests with intervening blood vessels was seen in the renal specimen. This histopathologic dissimilarity also supported the criterion that one mass is not a metastasis of the other.

Deciding on whether to manage this case as a double primary or a disseminated malignancy has been the foremost dilemma for the case in the preoperative period. Clinical presentation, known patient risk factors and the pathognomonic imaging findings are all favoring an advanced hepatic cellular carcinoma, except that the most documented common sites of extrahepatic metastases of HCC include the lungs, intraabdominal lymph nodes, bone and adrenals. Although theoretically plausible, a proof of a distant metastasis to the kidneys can greatly affect the choice of treatment for the patient. Current guidelines edict that after a biopsy confirming a metastatic disease, supportive therapy, clinical trials and best supportive care are the treatment options for a HCC patient. Whereas resection if deemed feasible is the preferred management for a potentially resectable disease for a good surgical candidate.

The decision to proceed with surgery was highly influenced by the treatment guidelines for renal cell carcinoma. This is one of the few types of malignancy in which surgical resection of the primary tumor and metastasectomy are being recommended.<sup>3</sup> Although, current oligometastatic sites amenable to this approach only include the lung, bone and brain, the multidisciplinary team of

this case decided to extend this guideline to include the operably resectable liver mass.

Both the Hepatic and Renal masses were deemed resectable. The patient has adequate future liver remnant and deemed medically fit for a major operation. The solitary hepatic mass has shown no evidence of major vascular invasion on his preoperative scans.

The five-year survival rate is currently marked at around 80% for Renal Cell Carcinoma Stage I<sup>3</sup> and over 50% for post-liver resection HCC cases. However, it must be noted that no single staging system can be used in prognosticating the survival of patients with hepatocellular carcinoma due to complex multiple factors like tumor extent and residual liver function.

Partial Hepatectomy and Partial Nephrectomy was potentially curative therapy for the patient's HCC and RCC, respectively. Given the limited data to prognosticate a case with double primary malignancy, active surveillance with imaging and tumor markers may be done for earlier identification of disease recurrence.

## Conclusion

Improved prognosis of cancer patients and diagnostic modalities contributed to increasing number of reported cases with multiple primary malignancy. In the absence of a set standard of care, multidisciplinary approach has become of greater value in balancing the risks and benefits of selected timely interventions to the patients.

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