Case Report

Synchronous hepatocellular carcinoma and renal cell carcinoma in young woman with sarcoidosis: A case report

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ABSTRACT

Hepatocellular carcinoma (HCC) and clear cell renal carcinoma are both frequent cancers, especially in patients with risk factors such as cirrhosis in the first case or genetic mutations such as Li-Fraumeni syndrome in the second case; however, their synchronous appearance is very rare especially in young patients with no apparent predisposing factors. We describe the case of a 33-year-old woman with acute pain onset in right hypochondrium. The ultrasound (US) imaging and the contrast-enhanced computed tomography (CECT) of the abdomen revealed 2 abdominal masses: one in the VI-VII segments of the liver and the other one in the right kidney. The chest CECT study, acquired for staging purpose, detected multiple micronodules with patchy peri-bronchial distribution at both lungs. At the histological examination, the tumor arising from the right kidney was finally diagnosed as clear cell renal carcinoma, whereas the tumor arising from the right lateral hepatic lobe as HCC. The histological examination of lung lesions revealed sarcoidosis granulomas. The patient is still being followed up for the occurrence of lung and lymph node metastases from HCC 14 months later.

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Introduction

Multiple synchronous primary malignancies have been reported since XIX century [1].

The coexistence of hepatocellular carcinoma (HCC) and other primary malignancies ranges from 2.1% to 14.5% and is associated with chronic liver disease, older age and male gender, with a male-to-female ratio of 11:1 [2]. Gastrointestinal tumors are the most common extrahepatic primary malignancies associated with HCC [2].
The incidence of synchronous primary cancers with renal cell cancer (RCC) is about 3.7%, and the most common site are urogenital system and lung [3].

The coexistence of synchronous HCC and RCC is quite rare. We present the case of a young woman, with no predisposing factors, affected by synchronous HCC and RCC, treated with wedge heptatectomy and right nephrectomy.

Case report

A 33-year-old woman was admitted to the emergency department due to acute onset of abdominal pain in the right side without any reported trauma or other apparent causes.

The US abdominal examination revealed the presence of two masses: one at the right kidney, and the other one at the right lobe of the liver.

A contrast-enhanced computed tomography was then acquired and confirmed the two lesions. The one on the right kidney (Fig. 1) measured 7 cm and showed intense arterial enhancement. The lesion on the VI-VII hepatic segments (Fig. 2) measured 5 cm and showed arterial enhancement with washout in portal phase.

Also, an enhanced magnetic resonance imaging (MRI) study of the upper abdomen with hepato-specific contrast agent was performed and showed the same angio dynamic behavior of the lesions, which also had high signal intensity in DWI with high b-value (800) (Fig. 3).

The physical examination was completely silent. In anamnestic history, the patient reported psoriasis, previously treated, a mild smoke habit lasted for about 15 years, no alco-
hol abuse and a varied diet. At the time of symptoms presentation, no drug therapy was mentioned.

About family oncological history, the patient reported a bladder cancer in the paternal grandfather and a prostate cancer in the father.

At the admission, the serum biochemistry analysis was all in the normal range, except for CA125 and AFP a little over the norm, as follows: CEA 1.2 ng/ml (normal range, 0-5), CA 19-9 7.4 U/ml (normal range 0-37), CA 125 42.3 U/ml (normal range, 0-35), CA 15-3 19.5 U/ml (normal range, 0-23.5), AFP 13.4 ng/ml (normal range < 10).

After CT finding, further investigations were required for staging purposes: head and chest CT enhanced scan, bone scintigraphy, and liver and kidney biopsy for a definitive diagnosis.

The CT scan reported multiple areas of thickening with a tendency for peri-bronchial distribution to both lung fields; no lymphadenopathies, no brain lesions (Fig. 4). Bone scintigraphy was negative.

Liver and kidney biopsies revealed the presence of 2 primary synchronous malignancies: high grade HCC (G3, Edmondson classify) (Fig. 5) and clear cell renal carcinoma (nucleolar grade 3, WHO classify) (Fig. 6).

To characterize the lung lesions, the patient underwent to a wedge resection through video-assisted thoracoscopic surgery. Subsequent histological analysis showed that the lung lesions were not secondary nodules, as suspected, but sarcoidosis granulomas.

Genetic surveys were also carried out to identify a genetic syndrome that could explain the presence of a double neoplasm in young patient without familiar predisposition and in the absence of hepatopathy. However, no specific genetic syndrome was detected.

The patient was referred to surgeons for surgical treatment of the 2 neoplasms. During the surgery, she underwent an intraoperative hepatic contrast-enhanced ultrasound that depicted additional nodules at the II, III, and VIII hepatic segments of doubtful nature. Thus, she underwent a resection of HCC at VI and VII segments and an additional wedge resection of the above segments plus right nephrectomy. The histological analysis revealed that the lesion at the III segment was focal nodular hyperplasia, whereas the nodules at II and VIII segments turned out to be sarcoidosis granulomas.

The histopathologic stage of renal cancer was pT2a Nx Mx (G3) (AJCC 8th 2016).
Fig. 4 – Chest CT scan demonstrates multiple micronodular formations with peri-bronchial distribution to both lung fields (white arrows in pictures A-C); image D shows the lesions of the right lung at greater magnification. Histopathological analysis showed to be non-necrotizing granulomatous nodules of sarcoidosis.

Fig. 5 – Histopathology images of HCC at 10x (A) and 20x (B-D) magnification. Images A and B show tumor cells with enlarged nuclei with high replicative activity (black arrows); images C and D exhibit a macro trabecular growth pattern (arrowheads); Grade III based on Edmondson Class.
The postoperative course was uneventful, and the patient was discharged on day 9 post-surgery. Approximately 1 year after surgery, a follow-up CT scan shows the appearance of some solid nodular formations at the right lung, characterized by radiopharmaceutical uptake at the PET-CT scan as suspicious for secondary pulmonary nodules.

The patient underwent a wedge resection through video-assisted thoracoscopic surgery for nodule exeresis and the histological examination confirmed their secondary nature from HCC. The postoperative course was characterized by the appearance of PNX that resolved in the following days by drainage.

The patient started systemic therapy with Lenvatinib. Four months later, on follow-up CT scan, there was evidence of suspicious mediastinal lymphadenopathy. The patient underwent endobronchial ultrasound transbronchial needle aspiration (EBUS-TBNA).

Histological examination was diagnostic of lymph node metastasis from high-grade HCC.

Due to disease progression, the systemic therapy was switched to second line Sorafenib and then to Cabozantinib as third line.

To date, the patient is still being followed up and the disease is stable.

In addition to systemic therapy, the patient starts Prednisone for sarcoidosis, Amlodipine for hypertension, and Levothyroxine for hypothyroidism.

**Discussion**

Multiple primary malignancies are defined as synchronous when they present simultaneously or within 6 months following the first diagnosis [4].

With the increase in life expectancy and the development of improved diagnostic techniques, the frequency of multiple primary tumors has increased [4].

According to Warren and Gates’ criteria [5], in the diagnosis of multiple primary malignancies, the occurrence of metastatic cells must be excluded. Cancers must be histologically distinct and present a different nuclear grading status.

Our patient has synchronous HCC and RCC that have been confirmed by histopathological and immunohistochemical examinations after surgery.

Dac Hong et al. [6] reported 8 cases of synchronous HCC and RCC from English literature: all these patients were male, 5 had hepatitis B with or without cirrhosis; 6 of them underwent resection, while in 2 cases, the malignancies were treated with radiofrequency ablation.

Surgery resection with adjuvant chemotherapy still represents the gold standard in multiple primary tumors treatment [4].

All the reports confirmed that prognosis of patients with multiple primary malignancies and that of patients with HCC alone does not significantly differ, as the survival rate depends on HCC evolution [4] (Fig. 5, Fig. 6).

**Patient consent**

Patient was informed of the publication of the case report and an informed consent was obtained. Furthermore, the patient is aware that the name will not appear in the text of the article.

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