Synchronous Hepatocellular Carcinoma with Renal Cell Carcinoma: A Case Report and Review of Literature of Multiple Synchronous Primary Malignancies

Guruprasad S. Shetty · Pankaj Bhalla ·
Samir M. Desai · Prasad K. Wagle · Hitesh S. Mehta

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Abstract Multiple synchronous primary malignancies have been reported since the 19th century. A number of proposed theories as to the predisposing factors have been discussed. The criteria to diagnose multiple primary malignancies have been revised by Warren and Gates. We hereby present a case of an asymptomatic individual detected with a synchronous hepatocellular carcinoma and a renal cell carcinoma, its presentation, diagnosis, and the management. The occurrence of synchronous hepatocellular carcinoma with renal cell carcinoma is very rare and only a few cases have been reported. Synchronous extrahepatic primary malignancies have been reported in a few studies across the world though with a varied incidence rate. The occurrence seems to be in the older age group without gender differentiation. The extrahepatic malignancies were more common in cirrhotic livers though the overall survival does not differ between patients with hepatocellular carcinoma alone and hepatocellular carcinoma with synchronous extrahepatic malignancies.

Keywords Hepatocellular carcinoma · Renal cell carcinoma · Synchronous primary malignancies

Case Report

A 57-year-old obese, nondiabetic, hypertensive, asymptomatic man was found to have a large echogenic mass in the right lobe of the liver and a right renal echogenic lesion on an ultrasound done during a health checkup. Contrast-enhanced computerized tomography (CECT) of the abdomen showed a well-circumscribed mass lesion in the liver with heterogeneous enhancement measuring 118 mm × 113 mm with evidence of another hypodense lesion measuring 37 mm × 35 mm arising from the mid-pole right kidney (Fig. 1). Liver function tests were marginally deranged with aspartate aminotransferase (AST) and alanine aminotransferase (ALT) being 95 and 70, respectively, which corrected subsequently after surgery. Alpha-fetoprotein was 546 IU/ml. He was a nonsmoker but consumed alcohol regularly. His viral profile was normal and he had no signs of any significant cardiorespiratory risks for surgery.

PET/CT confirmed a large lobulated mass with arterial and venous phase enhancement and patchy metabolic activity in segments V and VIII with extension into segments VI and VII as well, most likely representing a hepatoma. Another lobulated exophytic mass in the right kidney showed enhancement on arterial and venous phases, with mild metabolic activity suggesting a second primary neoplasm. There were no signs suggestive of any paraneoplastic syndromes. Cytology of the liver lesion, done to rule out the presence of a metastatic lesion, showed a well-differentiated hepatocellular carcinoma (HCC). Considering the size of the lesion and the risks associated with major hepatic resection, a preoperative chemoembolization using cisplatin and gel foam was done uneventfully. A CECT after 4 weeks revealed a smoothly heterogeneously nodular lesion with central necrosis with no significant change noted in size of hepatic lesion after chemoembolization (Fig. 1). With the associated cardiorespiratory risk, following an intraoperative bleeding during

All authors contributed equally to the article

G. S. Shetty (✉) · P. Bhalla · P. K. Wagle · H. S. Mehta
Department of Surgical Gastroenterology,
Lilavati Hospital & Research Centre,
A-791, Bandra Reclamation, Bandra (W),
Mumbai 400050, India
e-mail: shettyg@gmail.com

S. M. Desai
Department of Urology, Lilavati Hospital & Research Centre,
Mumbai, India

Fig. 1 CECT showing a mass in the right lobe of liver along with a right mid-pole renal lesion. The post-chemoembolization image shows no change in the size of the lesion

the right hepatectomy, a decision to do a staged procedure was taken. Two months later, in view of the presence of two simultaneous lesions on presentation and the revelation of the histopathology of the liver lesion, a right radical nephrectomy was done. The patient tolerated both procedures well, and the postoperative course was uneventful each time.

Histopathology, as confirmed with immunohistochemical studies, reported well-differentiated hepatocellular carcinoma of the liver, TNM stage T1N0M0. The renal pathology was a clear cell renal carcinoma, T1bN0M0 Furham's Nuclear Grade 1 (Fig. 2). The patient is now on regular follow-up and in good health.

Discussion

Multiple primary malignancies in a single patient were first reported by Billroth in 1879. He hypothesized that for multiple primary malignancies each tumor must have a different histological appearance, must arise in different location, and must produce its own metastasis [1]. In 1932, Warren and Gates modified these criteria as (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 [1].

The frequency of multiple primary tumors was reported as 3.7 % of all cancers, with no significant age difference between patients with single cancers and multiple malignancies. They identified eight reports of liver carcinoma

occurring synchronously with the mouth, esophagus, breast, bronchus, lung, prostate, kidney, and retroperitoneum [1].

Japanese population is prone to develop more than one primary malignancy. Yamamoto et al. reported that 15–20 % of Japanese patients with colorectal carcinoma developed more than one primary carcinoma [1]. This can be explained by gene susceptibility, longer lifespan, or medical advancement in chemotherapy and radiotherapy. Association of aging and cancer includes (1) time length of carcinogenesis; (2) older tissues being more susceptible to environmental carcinogens; (3) molecular changes in DNA signaling that may favor the development of cancer [1].

Smoking-related cancers such as prostate cancer and renal cell carcinoma (RCC) more often occur as more than one primary carcinoma. Head and neck cancer survivors are at an increased risk for another cancer of the respiratory or digestive tract [1].

Coexistence of renal cell carcinoma and hepatocellular carcinoma is extremely rare, and only a few case reports could be found in the literature [2, 3]. The association of HCC with extrahepatic primary malignancy (EHPM) has been reported from Taiwan, Japan, Germany, and the United States [4]. The incidence of HCC with EHPM ranged from 2.1 to 14.5 % in these studies. The discrepancies may be explained by the proportion of patients with disease diagnosed by biopsy and autopsy in the various studies [4].

Nzeako et al. found one or more EHPM in 74 of 1349 (5.5 %) patients with HCC. Of these patients, 65(4.8 %) had one EHPM, 7(0.5 %) had two tumors, and 1 each had three

Fig. 2 Histopathology showing well-differentiated hepatocellular carcinoma and the renal lesion was a clear cell renal carcinoma

and four tumors. Only 10 of 1349 (0.74 %) patients had primary renal cell carcinoma coexistent with HCC. HCC with coexistent EHPM occurred at an older age compared to HCC alone without any sex difference [4].

Patients having HCC with cirrhosis were 1.8 times more likely to have an EHPM than noncirrhotic HCC patients [4].

Nzeako et al. [4] reported the most common site of EHPM was the gastrointestinal system with adenocarcinoma of the colon as most common tumor, whereas Lin et al. and Takayasu et al. found gastric carcinoma was the most common tumor [4].

Kanemastu et al. noted that causes of death were due to complications of HCC and not due to EHPM [4]. Nzeako et al. found 1-year survival of 29.7 % with HCC patients and 21.8 % with HCC patients with EHPM, which is not statistically significant [4].

Conclusion

With the increase in longevity, patients have more chances of developing additional malignancies. The early detection of additional primary malignancies enables prompt

management and increases cure rates. The coexistence of RCC does not significantly change the survival rate of patients with HCC.

Conflicts of Interests None.

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