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Double primary hepatic cancer (sarcomatoid carcinoma and hepatocellular carcinoma): A case report

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Abstract. Primary liver sarcomatoid carcinoma (SC) is a rare and aggressive tumor exhibiting rapid growth and a high recurrence rate following resection. To date, there have been no reports of primary liver SC occurring simultaneously with hepatocellular carcinoma (HCC). This is the case report of a 54-year-old man with liver cirrhosis due to hepatitis B virus (HBV) infection and alcoholic hepatitis. The abdominal computed tomography and magnetic resonance imaging revealed two distinct hepatic masses in a background of hepatic cirrhosis and esophageal varices. Following a clinical diagnosis of two HCCs, a right hepatic lobectomy was performed. Grossly, two distinct lesions were identified: the larger mass was gray to white and well-demarcated, sized 2.5x2.0 cm, located in S5-6, whereas the other was a gray to whitish nodule, sized 1.3x1.0 cm, located in S8. The microscopic analysis revealed that the larger mass was a primary liver SC, which was immunoreactive for cytokeratin (CK) and vimentin (VMT) and negative for hepatocyte-specific antigen (HSA). The other nodule was histologically diagnosed as HCC, which was positive for HSA and CK and negative for HSA, VMT, CK7 and CK19. There was no transition or intermingling lesion between the two tumors. To the best of our knowledge, this is the first case report of double primary liver cancer comprising an SC and a HCC.

Introduction

Primary liver cancer (PLC) is the fifth most common malignancy worldwide (1) and hepatocellular carcinoma (HCC) is the most common histological type of PLC (2). HCC commonly develops in patients with carcinogenetic backgrounds of chronic viral infection, such as hepatitis B virus (HBV) or hepatitis C virus, or alcoholic liver injury. Primary liver sarcomatoid carcinoma (SC) is a rare tumor that may be associated with HCC and cholangiocarcinoma (2). Primary liver SC may also arise as a pure sarcomatous carcinoma, which is associated with a poor prognosis due to rapid growth and high recurrence rate following resection (3). This is the case report of a patient with combined HCC and primary liver SC, in a background of HBV chronic viral hepatitis with cirrhosis and alcoholic liver injury. To the best of our knowledge, this is the first case report of combined HCC and primary liver SC.

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Case report

A 54-year-old man, who had been routinely checked for chronic hepatitis associated with HBV infection, liver cirhosis and alcoholic liver injury, complained of fatigue and general weakness. The biochemical indices of liver function were unremarkable. Abdominal ultrasonography revealed mild hepatic shrinkage and coarse nodular echoes. There was a small enhancing nodule in S5-S6 and a small hypoechoic nodule in the right lobe of the liver. Abdominal computed tomography (CT) and magnetic resonance imaging (MRI) revealed two masses in the right robe of the liver, one in S5-S6, sized 2 cm (Fig. 1b) and the other in S8, sized 1.3 cm (Fig. 1c). Right lobectomy was performed upon a clinical diagnosis of double HCC. Grossly, the surgical specimen displayed two distinct masses, in a background of typical multinodular cirrhotic changes. The larger mass was well-demarcated, measuring 2.5x2.0 cm, of gray to white color and exhibiting central hemorrhage (Fig. 1a, labeled as 'A'). Microscopically, the tumor was composed of pleomorphic cells of round to oval and spindle shape, haphazardly arranged, with frequent atypical mitotic figures. The microscopic characteristics were not suggestive of HCC (Fig. 2a). The tumor cells were immunoreactive for cytokeratin (CK) (Fig. 2b) and vimentin (VMT) (Fig. 2c), but negative for hepatocyte-specific antigen (HSA) (Fig. 2d), CK19, CK20 and CD68. The other mass was a white to gray nodule, sized 1.3x1.0 cm, with small satellite lesions (Fig. 1a, labeled as 'B'). Microscopically, variable characteristics of HCC were observed, with a pseudoglandular and trabecular appearance (Fig. 3a and b). The tumor cells were positive for HSA (Fig. 3c) and CK, but negative for CK7, CK19 and VMT (Fig. 3d). There was no transition or intermingling of cells between the two tumors. The final diagnosis was double primary tumor of the liver (primary liver SC and HCC). At

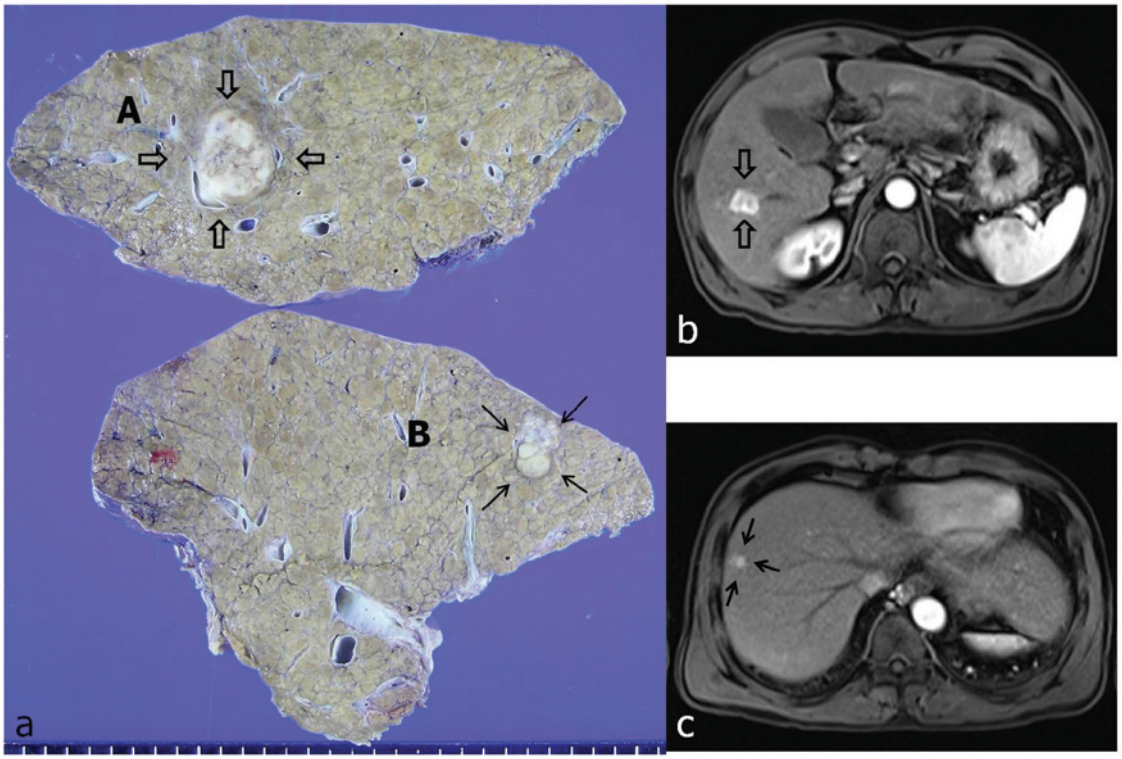

Figure 1. Radiological and macroscopic characteristics of the two lesions. (a) Macroscopic resected specimen: A, round mass with central hemorrhage (block arrows) sized 2.5x2.0 cm; and B, white to gray mass (line arrows), sized 1.3x1.0 cm, with small satellite lesions, in a background of typical multinodular cirrhotic change. (b and c) Radiological findings. Magnetic resonance imaging revealed two enhancing nodules in S5-S6 (b, block arrows) and S8 of the liver (c, line arrows).

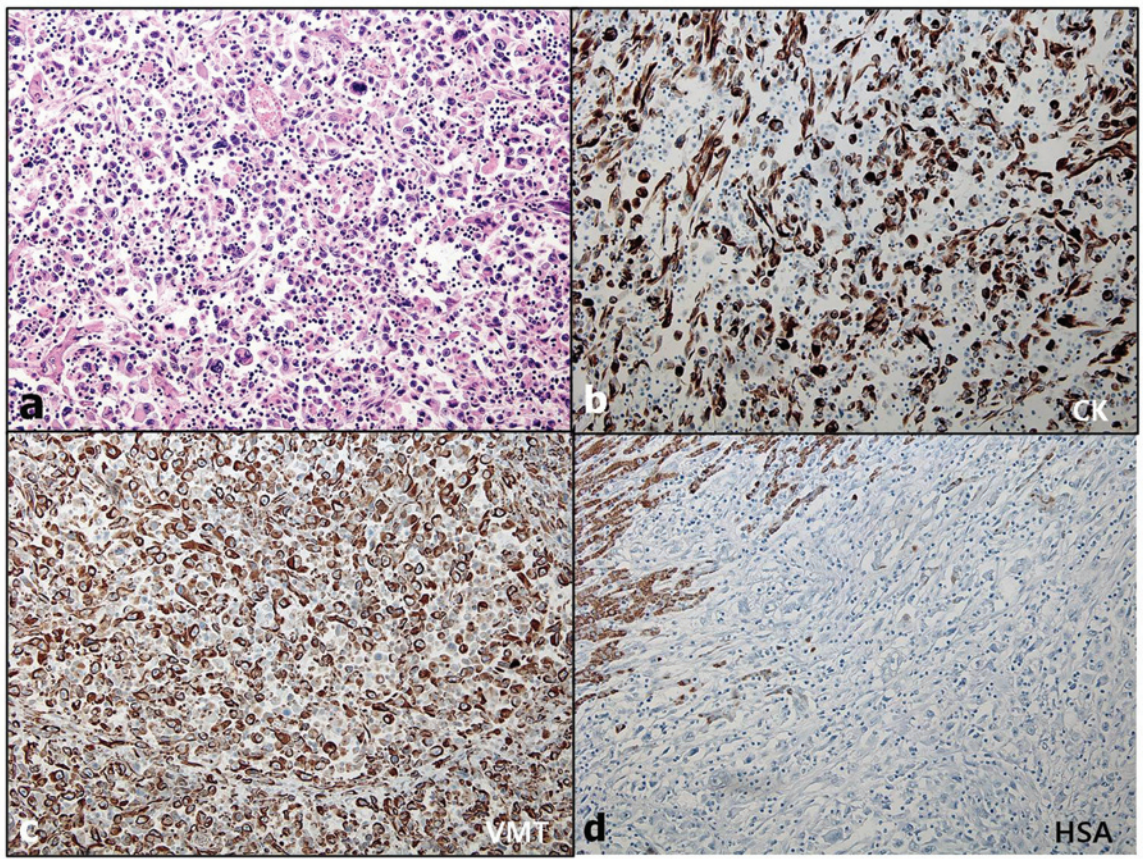

Figure 2. Histopathological findings of tumor 'A' (Fig. 1). (a) With hematoxylin-eosin staining, pleomorphic tumor cells of round to oval and spindle shape are haphazardly arranged, with frequent atypical mitotic figures. The tumor cells were immunoreactive for (b) cytokeratin (CK) and (c) vimentin (VMT), but negative for (d) hepatocyte-specific antigen (HSA).

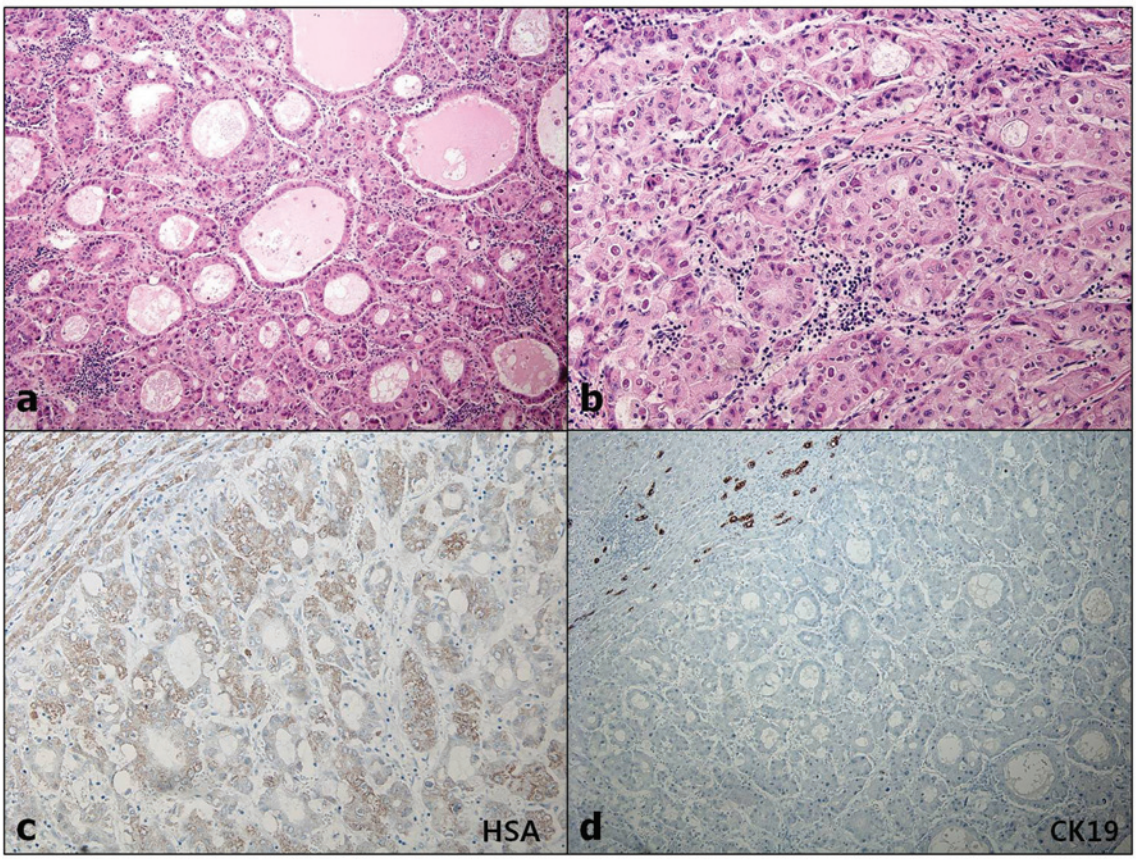

Figure 3. Histopathological findings of tumor 'B' (Fig. 1). With hematoxylin-eosin staining, variable characteristics of hepatocellular carcinoma were identified, with (a) pseudoglandular and (b) trabecular appearance. The tumor cells were positive for (c) hepatocyte-specific antigen (HSA), but negative for (d) cytokeratin 19 (CK19).

4 months after resection, the patient developed uncontrolled ascites and succumbed to peritoneal cancer seeding.

Discussion

Primary liver SC and carcinosarcoma (CS) of the liver comprise a mixture of carcinomatous and sarcomatous elements and are very rare worldwide, with only a few such cases reported in the English literature (4). CS is defined by the World Health Organization (WHO) as a malignant tumor that consists of an intimate mixture of carcinomatous (either HCC or cholangiocellular carcinoma) and sarcomatous elements (5). If the sarcomatous areas with malignant epithelial components were composed of variable malignant mesenchymal components, the tumor would be considered to be a CS. However, if the sarcomatous areas were composed of only malignant spindle cells and were shown to display epithelial characteristics based on immunohistochemical and electron microscopic findings, the tumor would be diagnosed as SC or spindle cell carcinoma (6). The sarcomatous elements of CS lack epithelial markers and the tumor is considered a true heterogonous sarcoma, whereas the sarcomatous element of SC retains the expression of epithelial markers (4). In the present case, the morphological characteristics of the tumor were similar to those of undifferentiated sarcoma. The microscopic examination of hematoxylin-eosin stained specimens revealed a diffuse proliferation of atypical and pleomorphic spindle cells with hyperchromatic nuclei, high nuclear-to-cytoplasmic ratio and poor cellular adhesion. Frequent atypical mitotic figures were also identified. Immunohistochemically, the tumor cells were immunoreactive for epithelial markers (CK).

The pathogenesis of the sarcomatoid component in primary SC and CS of the liver remains unclear. Therefore, knowledge of the histogenesis of sarcomatoid transformation in liver cancer is crucial (4). Murata *et al* (7) reported that genetic and immunohistochemical analyses support the hypothesis that undifferentiated, sarcomatoid HCC and cholangiocarcinoma may be derived from an original HCC, while Fayyazi *et al* hypothesized that this tumor arises from totipotent stem cells that are able to differentiate into both epithelial and mesenchymal cells (8), and other researchers suggested that the carcinomatous components were likely to transform into sarcomatous components through a metaplastic process (9,10). Certain authors reported that the neoplastic cells of conventional HCC may be capable of transforming into multipotent immature cells, which, in turn, redifferentiate into sarcomatous components (9,11-14). In addition, the WHO tumor classification (4th edition) suggests that the sarcomatoid component represents clonal evolution from a differentiated component (HCC or cholangiocarcinoma) (15).

In addition to SC, there was another tumor in this patient, which was diagnosed as HCC with a pseudoglandular and trabecular pattern. To the best of our knowledge, this is the first case report of synchronous development of hepatic SC and

HCC, whereas on preoperative radiological studies (abdominal ultrasound, CT and MRI) these two masses were considered to be HCCs, due to their similar imaging characteristics.

We reported a case of synchronously detected primary liver SC and HCC in a background of HBV chronic viral hepatitis with cirrhosis and alcoholic liver injury. In conclusion, as primary liver SC is an aggressive tumor with a high recurrence rate and a tendency for rapid growth, accurate and prompt diagnosis through thorough tissue sampling and intensive immunohistochemical analysis is crucial.

Acknowledgements

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References

1. Cao J, Huang L, Liu C, *et al*: Double primary hepatic cancer (hepatocellular carcinoma and intrahepatic cholangiocarcinoma) in a single patient: a clinicopathologic study of 35 resected cases. J Gastroenterol Hepatol 28: 1025-1031, 2013.
2. Uemoto J, Hoshi N, Hirabayashi K, *et al*: Collision tumors of hepatocellular carcinoma and malignant peritoneal mesothelioma. Med Mol Morphol 46: 177-183, 2013.
3. Yokomizo J, Cho A, Yamamoto H, *et al*: Sarcomatous hepatocellular carcinoma without previous anticancer therapy. J Hepatobiliary Pancreat Surg 14: 324-327, 2007.
4. Wang QB, Cui BK, Weng JM, Wu QL, Qiu JL and Lin X: Clinicopathological characteristics and outcome of primary sarcomatoid carcinoma and carcinosarcoma of the liver. J Gastrointest Surg 16: 1715-1726, 2012.
5. Nomura K, Aizawa S and Ushigome S: Carcinosarcoma of the liver. Arch Pathol Lab Med 124: 888-890, 2000.
6. Kwon JH, Kang YN and Kang KJ: Carcinosarcoma of the liver: a case report. Korean J Radiol 8: 343-347, 2007.
7. Murata M, Miyoshi Y, Iwao K, *et al*: Combined hepatocellular/cholangiocellular carcinoma with sarcomatoid features: genetic analysis for histogenesis. Hepatol Res 21: 220-227, 2001.
8. Fayyazi A, Nolte W, Oestmann JW, Sattler B, Ramadori G and Radzun HJ: Carcinosarcoma of the liver. Histopathology 32: 385-387, 1998.
9. Kubosawa H, Ishige H, Kondo Y, Konno A, Yamamoto T and Nagao K: Hepatocellular carcinoma with rhabdomyoblastic differentiation. Cancer 62: 781-786, 1988.
10. Rosai J (ed): Rosai and Ackerman's Surgical Pathology. 9th edition. Mosby, Edinburgh, pp 259, 2004.
11. Lao XM, Chen DY, Zhang YQ, Xiang J, Guo RP, Lin XJ and Li JQ: Primary carcinosarcoma of the liver: clinicopathologic features of 5 cases and a review of the literature. Am J Surg Pathol 31: 817-826, 2007.
12. Maeda T, Adachi E, Kajiyama K, Takenaka K, Sugimachi K and Tsuneyoshi M: Spindle cell hepatocellular carcinoma. A clinicopathologic and immunohistochemical analysis of 15 cases. Cancer 77: 51-57, 1996.
13. Wick MR and Swanson PE: Carcinosarcomas: current perspectives and an historical review of nosological concepts. Semin Diagn Pathol 10: 118-127, 1993.
14. Nakajima T, Kubosawa H, Kondo Y, Konno A and Iwama S: Combined hepatocellular-cholangiocarcinoma with variable sarcomatous transformation. Am J Clin Pathol 90: 309-312, 1998.
15. Miettinen M, Fletcher CDM, Kindblom LG, Zimmermann A and Tsui WMS: Mesenchymal tumours of the liver. World Health Organization Classification of Tumours of the Digestive System. FT Bosman, F carneiro, RH Hruban, ND Theise, Fred T and Bosman (eds.). 4th edition. IARC Press, Lyon, p249, 2010.