Synchronous Cancers of Hepatic Angiosarcoma and Gallbladder Adenocarcinoma, Mimicking Gallbladder Cancer with Hepatic Invasion: a Case Report

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Synchronous primary cancers in the liver and gallbladder have been rarely reported. We report a case of synchronous cancers of hepatic angiosarcoma and gallbladder adenocarcinoma, mimicking gallbladder cancer with hepatic invasion. Additionally, the clinical implications, the radiologic features, and the diagnostic difficulties are further discussed.

Keywords: Liver; Gallbladder; Multiple primary neoplasms; Angiosarcoma; Adenocarcinoma

INTRODUCTION

To begin with, synchronous double primary malignant neoplasms are secondary malignancies which are typically found occurring simultaneously, or within 6 months after the first malignancy. Generally speaking, synchronous primary cancers in the liver and gallbladder have been rarely reported (1, 2). In this study, we report a case of synchronous double primary cancers of hepatic angiosarcoma and gallbladder adenocarcinoma, which was initially misdiagnosed as gallbladder cancer with hepatic invasion.

CASE REPORT

In this case, a 67-year-old man was admitted to our hospital with symptoms of abdominal discomfort and the passage of dark urine for a week. Laboratory tests demonstrated elevated liver enzyme levels (aspartate aminotransferase: 146 IU/L and alkaline phosphatase: 185 IU/L) and hyperbilirubinemia (total bilirubin: 20.31 mg/dL). The carbohydrate antigen 19-9 level was also shown to be markedly elevated (21,139
U/mL). It was noted that the serum alpha-fetoprotein level was found to be within normal range. In line with these results, the patient had no history of extrahepatic malignant neoplasm nor exposure to any carcinogens.

In this context, the initial contrast-enhanced computed tomography (CT) demonstrated a distal common bile duct stone with dilatation of the upstream biliary tree, suggesting an acute calculous cholangitis. Simultaneously, a 2.5 cm sized hepatic mass and focal irregular thickening of the wall were detected in the liver bed and gallbladder, respectively. Evidently, the two lesions were inseparable from each other (Fig. 1a). In the three-phase contrast-enhanced CT, the hepatic mass revealed a central low attenuation on all three-phase images and thin peripheral enhancement on the portal-venous phase images. For this reason, our initial diagnosis for these lesions was gallbladder cancer with hepatic invasion. The lesions in the liver and gallbladder were further evaluated by magnetic resonance imaging (MRI) for establishing the differential diagnosis. At that time, the liver lesion showed heterogeneous hyperintensity with hypointense areas on T2-weighted images (Fig. 1b) and hypointensity with central hyperintense focus on T1-weighted images (Fig. 1c), indicating the condition of a hemorrhagic necrosis. Additionally, the peripheral area of the hepatic mass and focal thickening in the wall of the gallbladder showed a delayed enhancement on the gadolinium-enhanced MRI (Fig. 1d). Based on the MRI findings, our suggested differential diagnosis was hepatic angiosarcoma and gallbladder adenocarcinoma.
diagnosis was gallbladder cancer with hepatic invasion. Later an ultrasound-guided biopsy of the hepatic lesion was performed, which suggested the presence of a malignant mesenchymal tumor.

The endoscopic retrograde cholangiopancreatography and extraction of stones with administration of antibiotics were performed for the cholangitis, and the review of follow-up laboratory investigations showed normal results. In a follow-up pre-operative CT performed 20 days after hospitalization, the size of the hepatic mass had increased and the focal thickening in the wall of the gallbladder had also progressed. Here it was noted that the hyper-enhanced portions within the hepatic mass were a novel finding on arterial-phase images, indicating a centripetal enhancement on the portal-venous phase images (Fig. 1e).

In addition, several low-attenuation satellite nodules had appeared in the right lobe of the liver. Moreover, a few indeterminate enlarged lymph nodes were also detected in the hepatoduodenal ligament.

As a result of these findings, the patient underwent extended right hepatectomy with cholecystectomy. A later pathological examination of the sample revealed that the hepatic mass was hemorrhagic, partially necrotic, friable, and surrounded by a dense fibrotic rim. Notably, the lumen of the gallbladder contained an intraluminally protruding polypoid solid mass. Additionally, it was noted that the gallbladder mass was adhered tightly to the liver mass. Finally, the hepatic lesion was diagnosed as angiosarcoma and the lesion in the gallbladder was identified as poorly differentiated adenocarcinoma, which presented with

![Fig. 1. (d) Axial postcontrast T1-weighted images using gadoterate meglumine (Uniray®) shows peripheral enhancement of hepatic mass (arrows) and delayed enhancement of the focal wall thickening of the gallbladder (arrowheads). (e) In a follow-up CT performed 20 days after hospitalization, the arterial- and delayed-phase contrast-enhanced images show a newly developed hypervascular area (arrows) within the hepatic mass with persistent enhancement. Note the progression of the focal thickening in the wall of the gallbladder (arrowhead on coronal image).]
the lesions invading each other. Further review and an evaluation of the microscopic findings revealed that the invasion was evident at the borders of the two lesions. Here, it was noted that one of the 12 enlarged lymph nodes was shown to be positive for metastasis, in which metastatic adenocarcinoma and angiosarcoma were found to have coexisted (Fig. 1f). Likewise, the rest of the portion in the resected liver showed the presence of multiple metastasis of angiosarcoma.

In a follow-up CT performed 2 months after surgery, it was identified that multiple hepatic metastasis of angiosarcoma appeared in the remnant portion of the liver (Fig. 1g). At that time, the patient was treated with adjuvant chemotherapy, but later died due to the progression of the angiosarcoma, which was noted within the timeframe of 4 months after the initial diagnosis.

**DISCUSSION**

Synchronous double primary malignant neoplasms are secondary malignancies occurring simultaneously or within 6 months after the first malignancy (1). Generally speaking, multiple primary malignant tumors in a single patient are relatively rare, with an incidence between 0.73% and 11.7% (3). In particular, it is noted that the synchronous primary cancers in the liver and gallbladder have been rarely reported, and there are only eight cases found in the literature review (1, 2, 4). To the best of our knowledge, this is the first case report of synchronous primary cancers of hepatic angiosarcoma and gallbladder adenocarcinoma.

Such cancers are difficult to differentiate from hepatic metastasis of gallbladder adenocarcinoma, because of the rare occurrence and lack of apparent radiological features.
Even in this case, the initial diagnosis was of a gallbladder cancer with hepatic invasion, because the two lesions were inseparable from each other and the hepatic mass showed hypoattenuation. However, in the retrospective review of the image findings, the hypervascular portions within the hepatic mass had appeared on a follow-up CT which was performed 20 days after the first CT. Of course, this result differed from the typical image findings of gallbladder carcinoma, which are typically hypo- or isoattenuation with occasional low-attenuation areas of necrosis (5). This brings an understanding that these findings can help in establishing a definitive diagnosis in these cases.

In a general sense, primary hepatic angiosarcoma is uncommon and accounts for only 2% of the primary hepatic tumors found in patients. It commonly affects patients aged 60–70 years and shows a favoring towards male preponderance. It is known to be associated with environmental or occupational exposure to carcinogens such as with exposure to thorium dioxide, vinyl chloride, arsenic, and radiation. However, most hepatic angiosarcomas encountered in the clinical practice emerge without any such risk factor being involved in the patient’s past history. It is observed that the common radiologic findings of angiosarcoma are of a multinodular lesion or a large solitary mass. This result can show a similar enhancement pattern to hemangioma on the dynamic contrast-enhanced CT image, but is slightly different from that of a typical hemangioma in that it usually presents with a more heterogeneous enhancement, or with showing bizarre areas of the ring enhancement (6). In this case, it was difficult to consider the possibility of angiosarcoma on initial the CT and MRI evaluation, because the mass showed evidence of necrosis except for in some peripheral areas. In the follow-up CT scan, hyper-enhanced portions within the primary mass and several other lesions with progressive enhancement had appeared, which were the suggestive findings of an angiosarcoma.

In conclusion, we report a rare case of synchronous cancers of hepatic angiosarcoma and gallbladder adenocarcinoma, mimicking gallbladder cancer with hepatic invasion. It is difficult to suspect a synchronous tumor only by the review of imaging studies, because the presence of two different cell types can lead to perplexing imaging findings. Although rare, it is important to recognize these entities due to the impact of the diagnosis on management options and prognosis for the patient.

REFERENCES