INTRODUCTION

Hepatoid adenocarcinoma is a special type of extrahepatic adenocarcinoma that morphologically mimics hepatocellular carcinoma (HCC). Clinical and immunohistochemical features of hepatoid adenocarcinoma are similar to those of HCC, such as elevated serum alpha-fetoprotein (AFP) level, immunoreactivity with AFP, polyclonal carcinoembryonic antigen (CEA), and alpha-1 antitrypsin.1 Because of these clinical and pathological features, it is difficult to differentiate hepatic metastasis of hepatoid adenocarcinoma from HCC. Moreover, the imaging findings of hepatoid adenocarcinoma are not well known. Therefore, we report a case of hepatic metastases from hepatoid adenocarcinoma of stomach mimicking HCC with image findings and a review of the literature.

CASE

A 65-year-old man was admitted to our hospital for evaluation of a huge hepatic tumor that was incidentally detected during an abdominal sonographic screening examination. He complained of mild abdominal discomfort. He had a medical history of hypertension and a social history of alcohol for several decades. The laboratory tests at the time of admission showed an aspartate aminotransferase (AST) level of 90 IU/L, alanine aminotransferase level (ALT) of 17 IU/L, total bilirubin level of 0.9 mg/dL, alkaline phosphatase level of 67 IU/L. The serum level of AFP (5,714 IU/mL) and protein induced by vitamin K absence or antagonist-II (PIVKA-II; 1,005 mAU/mL) were markedly elevated. The CEA level was within normal limits. His serum was positive for hepatitis B surface antibody, but negative for hepatitis B surface antigen and anti-HCV.

The ultrasonographic images showed a 9 cm sized hyperechoic mass with internal anechoic portion in right hepatic lobe with adjacent small hypoechoic nodules (Fig. 1A). We then performed contrast-enhanced multidetector-row CT. The contrast-enhanced dynamic CT images revealed a 9.5×7 cm sized mass in the liver, comprised of a central necrotic portion and a peripheral solid enhancing portion. Liver cirrhotic changes were not observed on CT or ultrasonographic images. After contrast enhancement, the peripheral solid portion of the huge hepatic mass showed heterogeneous enhancement on arterial phase image and washout of contrast enhancement on delayed phase image. The tumor thrombus was visualized in adjacent right portal vein and a 1.3 cm sized mass was observed in inferior aspect of huge hepatic mass. The tumor thrombi were observed in proximal main portal vein...
to superior mesenteric vein. The multiple enlarged, conglomerate lymph nodes were observed along the left gastric artery, gastroduodenal artery and right gastroepiploic artery. The CT images also revealed irregular wall thickening of gastric antrum (arrows) and tumor thrombus (arrowheads) in the main portal vein. On the lower section image (C) shows multiple conglomerate enlarged lymph nodes (arrows) along gastroduodenal artery and right gastroepiploic artery. Also tumor thrombus (arrowheads) is shown in superior mesenteric vein. (D-F) Gadoxetic acid-enhanced MR images show huge central necrotic hepatic mass (arrows) and small hepatic mass (arrowhead), with heterogeneous early enhancement on arterial phase (D), low signal intensity on late dynamic phase (E) and hepatobiliary phase (F).

Figure 1. Hepatic metastases from gastric hepatoid adenocarcinoma in 65-year-old man. (A) Abdominal ultrasonography shows hyperechoic mass (arrows) with internal anechoic portion in right hepatic lobe, without evidence of liver cirrhosis. Also abdominal ultrasonography shows small hypoechoic mass (arrowhead) around main huge hepatic mass. (B, C) An enhanced abdomen CT image (B) shows irregular wall thickening of gastric antrum (arrows) and tumor thrombus (arrowheads) in the main portal vein. On the lower section image (C) shows multiple conglomerate enlarged lymph nodes (arrows) along gastroduodenal artery and right gastroepiploic artery. Also tumor thrombus (arrowheads) is shown in superior mesenteric vein. (D-F) Gadoxetic acid-enhanced MR images show huge central necrotic hepatic mass (arrows) and small hepatic mass (arrowhead), with heterogeneous early enhancement on arterial phase (D), low signal intensity on late dynamic phase (E) and hepatobiliary phase (F).

For evaluation of gastric abnormality, an endoscopic biopsy was performed. An infiltrative mass with ulceration at the gastric antrum was detected on the endoscopic image and endoscopic specimens were obtained in the gastric lesion. The specimen was pathologically confirmed as poorly differentiated adenocarcinoma. For further evaluation of the hepatic tumors, contrast enhanced liver magnetic resonance imaging (MRI) using gadoxetic-acid was performed. The huge hepatic mass consisted of a central necrotic portion and a peripheral solid portion. The peripheral solid portion showed low signal intensity on T1WI and high signal intensity on T2WI. After contrast enhancement, the peripheral solid portion of the huge hepatic mass showed heterogeneous enhancement on arterial phase image, low signal intensity on portal venous, late dynamic and hepatobiliary phase images (Fig. 1D, 1E, 1F). Dynamic MRI revealed several small nodules that were unclear on abdominal CT. These lesions showed typical enhancement pattern of HCC such as early enhancement on arterial phase and delayed washout on late dynamic and hepatobiliary phases.

Based on laboratory tests showing marked elevated AFP and PIVKA-II, existence of pathologic proven gastric adenocarcinoma, and typical enhancement pattern of HCC of huge and small hepatic tumors on CT and MRI, we thought two possible diagnoses; the one was double primary malignancy as primary advanced gastric malignancy and primary HCC in the liver. The other was AFP producing gastric malignancy and its hepatic metastases. The ultrasonography-guided biopsy of the hepatic tumors was performed. Microscopic examination revealed that the histology of the hepatic tumor was similar to that of specimens from the gastric cancer. The results of immunohistochemical stains were positive for AFP, Glypican-3, Glutamine synthase, Cytokeratin, and
CK8/18. But CK20, CK7, and human serum albumin were negative. These histologic features resulted in the diagnosis of this case as a gastric hepatoid adenocarcinoma with hepatic metastases. He had eight cycles of chemotherapy with FOLFOX and he remains alive for five months after diagnosis.

DISCUSSION

Hepatoid adenocarcinoma is an AFP producing adenocarcinoma, which has a histological similarity to HCC. It was first described by Ishikura et al.⁷ Since its first description in the stomach, which is the most common location, it had been found in a variety of organs such as lung, pancreas, esophagus, colon, urinary bladder, renal pelvis, ovaries, uterus, cervix and ampulla of Vater. Hepatoid adenocarcinoma is reported to comprise 0.38 % of all gastric cancer. Clinically, the neoplasm is characterized by older age, a high serum AFP level, aggressive behavior and the presence of a hepatic tumor in the absence of the risk factors of HCC. Its poor prognosis is due to a strong tendency toward liver and lymph node metastases and venous invasion.³–⁵

Lee et al.⁶ reported four cases of hepatic metastases from gastric hepatoid carcinoma. In their cases, hepatic metastases had two patterns. One was multiple hepatic metastases of a similar size without portal venous thrombosis, and the other was hepatic metastases that appeared as a dominant bulky mass with adjacent portal venous thrombosis. They reported that the pattern of a dominant bulky mass was more common. In our case, hepatic metastases appeared in a pattern of a dominant bulky mass similar to previous studies, with several small masses. The abdominal CT and liver MRI showed that the enhancement pattern of hepatic masses, especially small hepatic masses, is similar to that of HCC. Given these imaging findings, it is hard to differentiate hepatic metastases from gastric hepatoid adenocarcinoma and HCC only by imaging finding of the hepatic mass, without knowing of the primary malignancy.

Generally, tumor thrombus in the portal venous system originating from gastric cancer is rare.⁶ However, tumor thrombus in the portal venous system is more frequently found in gastric hepatoid carcinoma than other gastric adenocarcinoma.¹, ³ Also, tumor thrombus by hepatoid adenocarcinoma appeared in two patterns. One pattern is tumor thrombus around a hepatic mass, caused by invasion of metastatic cancer. The other is tumor thrombus remote from or without a hepatic mass, caused by invasion of a primary hepatoid carcinoma.⁶, ⁷ In our case, tumor thrombi were found in both patterns. The pattern of tumor thrombi remote from the hepatic mass was helpful for differential diagnosis.

In conclusion, metastatic carcinoma from hepatoid adenocarcinoma should be included in the differential diagnosis in older patients with elevated serum AFP level and hepatic masses with imaging features of HCC in the absence of risk factors of HCC. In that situation, concomitant primary gastric cancer and tumor thrombus remote from the hepatic mass are helpful in differential diagnosis of metastatic carcinoma from hepatoid adenocarcinoma and HCC. When a metastatic carcinoma from hepatoid carcinoma is highly suspected, gastroscopy should be performed even if a primary gastric cancer is not clearly demonstrated on imaging studies.

SUMMARY

Hepatoid adenocarcinoma is a special type of extrahepatic adenocarcinoma that mimics hepatocellular carcinoma morphologically. The stomach is one of the most common sites of hepatoid adenocarcinoma. Hepatoid adenocarcinoma is characterized histologically by hepatoid differentiation and production of large amounts of AFP. It is not easy to differentiate hepatic metastases from hepatoid adenocarcinoma and hepatocellular carcinoma when hepatic tumor is incidentally detected. Furthermore, imaging findings of hepatoid adenocarcinoma are rarely described. Therefore, we report a case of hepatic metastases from hepatoid adenocarcinoma of stomach mimicking hepatocellular carcinoma with image findings and a review of the literature.

Conflicts of Interest

The authors have no conflicts to disclose.

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