

Case Report

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ABSTRACT

Hepatic metastasis from hepatoid adenocarcinoma of the stomach (HAS) is a rare malignant tumor with hepatocellular differentiation. For the hepatic tumor in middle-aged and elderly people, the image presence of hepatocellular carcinoma (HCC) and production of large amounts of alpha fetoprotein (AFP) and the presence of stomach tumor, that suggest the diagnosis of hepatic metastasis from HAS. Here, the authors report a case of hepatic metastasis from HAS. The characteristics of the disease were analyzed on the basis of clinical symptoms, MR imaging findings, laboratory examinations and pathological diagnosis results. The imaging features and differential diagnosis methods of the disease were summarized combined with literature review, aiming to improve the understanding and diagnostic ability of the disease.

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Introduction

Hepatoid adenocarcinoma (HAC) is a primary adenocarcinoma characterized by hepatoid differentiation and abundant Alpha fetoprotein (AFP) production. It is a special subtype of extrahepatic adenocarcinoma. This paper analyzed the data of a patient diagnosed with hepatic metastasis from gastric hepatoid adenocarcinoma by histopathological examination, and discussed the characteristics of hepatic metastasis from HAS through literature review.

Case report

A 61-year-old female was admitted with anorexia and fatigue. The patient felt anorexia in the previous 2 months without obvious inducement, nausea, or vomiting, or abdominal pain. No additional disease was found in the patient's medical history.

Laboratory tests revealed total bilirubin: 38.9 μ mol/L (normal, 0-23.0), direct bilirubin: 12.2 μ mol/L (normal, 0-4.0), indirect bilirubin: 26.7 μ mol/L (normal, 0-21.0), alanine aminotransferase: 56U/L (normal, 7-40.0), aspartate aminotransferase: 40U/L (normal, 13.0-35.0), alkaline phos-

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Fig. 1 – (A) Axial CT view reveals a dominant mass, located on the left lobe of the liver. The mass exhibits hemorrhage (white arrow). (B) Axial T1-weighted MRI shows a hypointense mass. (C) Axial T2-weighted MRI shows the hyperintense mass with a clear boundary. (D) Diffusion-weighted imaging shows that the mass is hyperintense. (E) ADC map shows that the mass is hypointense. (F) The arterial phase shows that the mass was initially obviously heterogeneously enhanced (white arrow) after the administration of gadolinium. (G) Both the portal phase and (H and I) delayed-phase images show that the enhancement degree of the lesion was decreased but still visible. The mass exhibits necrosis (H, white arrow) and capsule (I, white arrow). (J) Axial enhanced T1-weighted MRI shows cancer thrombus in the left branch of the portal vein (white arrow). (K) Axial T2-weighted MRI and (L) Diffusion-weighted imaging show the hyperintense mass in the gastric antrum (white arrows).

phatase: 631U/L(normal, 50.0-135.0), γ -glutamyltransferase: 902U/L(normal, 7.0-45.0) and high levels of AFP: >2000 ng/mL (normal, 0-8.78), carbohydrate antigen 125 (CA125): 264.80 U/mL(normal, 0-35.0), nerve-specific enolase (NSE): 79.08 ng/mL(normal, 0-17.0) and CA211 (50.17 ng/mL) (normal, 0-3.3).

Non-contrast computed tomography (CT) scan of the upper abdomen revealed a giant soft-tissue density mass in the left lobe of the liver (Fig. 1A). The mass size was approximately $15.7 \text{cm} \times 10.1 \text{cm} \times 13.3 \text{cm}$ with a well-defined margin. CT value was about 39HU. Multiple patchy high-density shadows can be seen inside the lesion. A small amount of fluid is seen below the liver capsule adjacent to the mass. A mass was found in the antrum of the stomach.

Upper abdominal magnetic resonance imaging (MRI) was performed on a 3.0-T system (Siemens, Erlangen, Germany). MR imaging showed a heterogeneous T1 hypointense and T2 hyperintense giant mass with a well-established capsule in the left lobe of the liver (Fig. B and C). On diffusion-weighted imaging (DWI), the lesion showed high signal intensity, with low apparent diffusion coefficient (ADC) value (Fig. D and E). These findings consistent with restricted diffusion. In addition, in-phase and out-phase images showed no signal decline within the mass, which suggests that the lesion did not contain lipids. On dynamic contrast scanning, the lesion was initially obviously heterogeneous enhancement after the administration of gadolinium, and the enhancement degree of the lesion was decreased but still visible on both portal-phase



Fig. 2 – (A) shows intraoperative view of the mass. (B) The mass is completely excised. (C) The mass is heterogeneous, yellowish, and solid with hemorrhages, necrosis.



Fig. 3 – (A) Hematoxylin and eosin (H&E) stain (magnification, x200) shows areas of hepatoid differentiation and adenocarcinoma. (B) CDX-2 (magnification, x200), (C) AFP (magnification, x200) and (D) SALL4 (magnification, x200) show positive expression.

and the delayed-phase images (Fig. F-I). Cancer thrombus was found in the left branch of the portal vein (Fig. J).

Clinically, the indication of the operation was clear because the patient had a giant tumor, so a left hepatectomy was performed. During the operation, a soft-tissue tumor was confirmed to originate from the left lobe of liver, which was clearly separated from normal liver tissue (Fig. 2). A mass was found and resected in the antrum of the stomach during intraoperative exploration (Fig. K and L).

The pathology report mentioned undifferentiated carcinoma of probable gastric origin (Fig. A). The results of immunohistochemical stains were positive for AFP, generator paralleling controller-3 (GPC-3), Heat shock proteins (HSP70), Villin, Cytokeratin-19 (CK19), Caudal Type Homeobox 2 (CDX-2), Spalt Like Transcription Factor 4 (SALL4) and Cytokeratin-7 (CK7) (Fig. B-D). These histologic features resulted in the diagnosis of this case as a hepatic metastasis from hepatoid adenocarcinoma of the stomach.

Discussion

Stomach tumors producing AFP were first reported by Bourreille et al in 1970 [1]. Ishikura et al. later named it as hepatoid adenocarcinoma of the stomach (HAS) [2]. HAC can occur in the stomach, intestine, pancreas, ovary, lung and other sites, among which the stomach is the most common site [3–7]. HAS accounts for 0.17%-15% of all gastric cancers. HAC is aggressive and has a low survival rate, mainly due to extensive hematogenous liver metastasis and early lymph node metastasis. The molecular mechanism of HAC is still unknown. Histologically, HAC has morphologic and immunohistochemical similarity to hepatocellular carcinoma. It consists of large eosinophils similar in morphology to HCC. They arranged in trabecular shape or solid nested, separated by internal vascular channels, and can be detected by AFP in situ.

The liver is the most common metastatic site for HAS. In enhancement, liver metastases of HAS have obvious enhancement in arterial phase due to rich blood vessels, and contrast agent wash out in portal vein phase or delayed phase, which is similar to HCC [8]. Hemorrhage or necrosis is common in hepatic metastases of HAS and is often not associated with chronic diffuse hepatic disease. Most hepatic metastases of HAS showed tumor necrosis regardless of tumor size. Necrosis can be found even in nodules less than 1cm in diameter, whereas the necrosis rate of HCC is relatively low (10%-40%) [9]. Tumor necrosis is believed to be caused by hypoxia resulting from tumor overgrowth and subsequent necrosis in the tumor center [10]. Hemorrhage is a common feature of hepatic metastasis of HAC and HCC. Tumor hemorrhage was observed in HAC metastases larger than 5 cm. HCC with larger diameter also has a higher bleeding probability [3]. There are 2 types of liver metastases with HAS: large masses with adjacent portal vein cancer thrombus (common, portal vein cancer thrombus 60%-75%); many nodules of similar size that were not accompanied by portal vein cancer thrombus [8]. Large masses are more common. HAC is accompanied by venous cancer thrombus (portal vein, hepatic vein, inferior vena cava and gastroomental vein) in 2 ways: one is the cancer thrombus around the hepatic mass, caused by the invasion of metastatic cancer; the other is the cancer thrombus of portal vein, which is far away from the mass or without the mass [11].

Liver metastases of HAS need to be differentiated from HCC, most of which have a history of hepatitis and cirrhosis. Necrosis occurs in HCC larger than 3cm. Most are not associated with stomach cancer.

Conclusion

In conclusion, CT or MRI enhancement plays an important role in the diagnosis and evaluation of hepatic metastasis from hepatoid adenocarcinoma. Although the final diagnosis of HAC still depends on pathology, for elderly patients with significantly elevated serum AFP, mass with imaging features of HCC and no risk factors for HCC, HAC metastasis should be included in the differential diagnosis. In this case, the presence of portal vein cancer thrombus and necrosis suggest imaging clues for the diagnosis of HAC. For patients with suspected HAC, further gastroscopy is required.

Patient consent

The Institutional Review Board of Shuguang Hospital Affiliated to Shanghai University of Traditional Chinese Medicine has approved this retrospective case report, and we have obtained informed consent from the patient for the publication of this case report.

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