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CASE REPORT

Gastric adenocarcinoma with hepatoid adenocarcinoma: A case report and literature review

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Abstract

Objective Hepatoid adenocarcinoma of the stomach is exceedingly rare. Only a few cases have been reported worldwide. In this report, we describe our pathological findings along with a review of the literature to improve our understanding of the disease and prevent misdiagnosis, as well as to provide evidence for its treatment and prognosis.

Methods A 68-year-old male patient was admitted to our hospital (Dalian Municipal Central Hospital, Dalian, China) complaining of upper abdominal pain. Physical examination and regular laboratory blood tests showed no obvious abnormalities. A contrast-enhanced computed tomography scan displayed a 3.0 cm × 3.0 cm mass in the gastric antrum, but no metastasis was found in the adjacent organs.

Results A radical gastrectomy was performed and postoperative histopathology showed a moderately differentiated adenocarcinoma with partial hepatoid adenocarcinoma.

Conclusion Hepatoid adenocarcinoma of the stomach is a rare malignant neoplasm. The diagnostic criteria for hepatoid adenocarcinoma of the stomach depends mainly on the clinical, radiographic, and histopathological findings. Pathomorphology and immunohistochemical staining can be utilized to confirm the diagnosis.

Key words: gastric cancer; adenocarcinoma; hepatoid; immunohistochemistry

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Hepatoid adenocarcinoma of the stomach (HAS) is a subtype of gastric tumors with hepatoid features that frequently produces serum alpha fetoprotein (AFP) [1]. Although the pathogenesis and molecular biology of HAS is thought to be due to cellular trans-differentiation from glandular to hepatoid type, the underlying mechanism remains unknown. As its clinical diagnosis is rare and the tumor is difficult to diagnose with gastroscopic biopsy, this disease is often misdiagnosed. Herein, we present a case from our hospital (Dalian Municipal Central Hospital, Dalian, China) to help improve our understanding of HAS and provide evidence for its treatment and prognosis.

Case report

A 68-year-old man was admitted to our hospital with the chief complaint of upper abdominal pain that had begun one month prior. The pain accompanied with abdominal distension was more severe at night, but without nausea and vomiting. As the patient did not experience any relief from the pain, he visited our hospital on April 17, 2017. Physical examination of the patient on admission revealed a pale appearance, his superficial lymph nodes were impalpable, his abdomen was soft to the touch, no palpable mass, rebound tenderness, muscle tension, or ascites; his liver and spleen did not extend beyond the ribs; and normal bowel sounds were observed. The results of regular laboratory blood tests (red blood cell count, hemoglobin, hematocrit, and electrolytes) were normal; the patient's AFP, carcinoembryonic antigen (CEA), and cancer antigen (CA) 19-9 levels were 9.1 ng/mL, 1.5 μg/L, and 3.0 kU/L, respectively. Additionally, he tested negative for hepatitis B surface antigen and antibody, and hepatitis C antibody. Chest computed tomography (CT) showed no abnormalities. Contrast-enhanced CT displayed a 3.0 cm × 3.0 cm mass in the gastric antrum, but no abnormalities

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were found in the liver, gallbladder, pancreas, spleen, or abdominal lymph nodes. The gastroscopy showed a protruded lesion (3.0 cm × 3.0 cm) on the posterior wall of the gastric antrum that was subsequently confirmed as an adenocarcinoma following pathological assessment of the biopsy sample (Fig. 1).

A radical gastrectomy was performed successfully on April 22, 2017. Postoperative histopathology showed a moderately differentiated adenocarcinoma with a partial hepatoid adenocarcinoma (Fig. 2) that had invaded the serous layer. Cancer cells were not visible within the vasculature, and no invasive cells were noted at the upper and lower cutting edges. Six of the eight regional lymph nodes checked were metastatic. Vascular congestion, interstitial edema, and cancer invasion into the omentum were not detected. Immunohistochemically, the tumor cells were positive for cytokeratin (CK) 7 (+), CK19 (+), Ki67 (+70%), villin (partial +), AFP (partial +), and Gly3 (partial +). Postoperatively, the level of AFP decreased to 3.8 ng/mL within 2 weeks; however, no adjuvant chemotherapy was performed because the patient refused to treatment. To date, the patient has shown favorable recovery and had been free of recurrence for 6 months. Long-term, regular follow-up of the patient is currently ongoing.

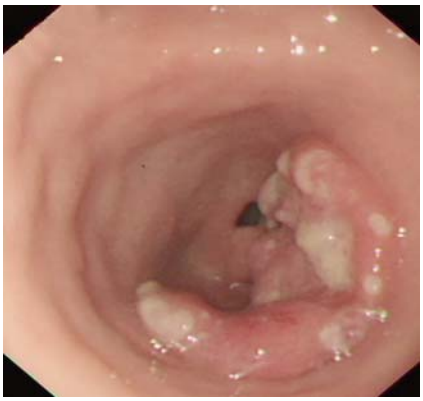

Fig. 1 Gastroscopy showing a protruded lesion (3.0 cm × 3.0 cm) on the posterior wall of the gastric antrum

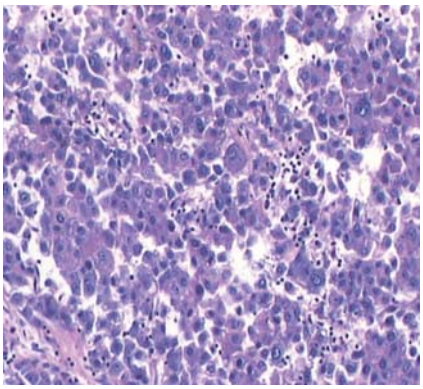

Fig. 2 Histopathology showed a moderately differentiated adenocarcinoma with part of hepatoid adenocarcinoma (deep dyeing with hematoxylin and eosin, × 400)

Discussion

Hepatoid adenocarcinoma (HAC) is a rare type of extrahepatic tumor that is morphologically similar to hepatocellular carcinoma (HCC) [2]. HAC has been reported to develop in a variety of organs, such as the stomach, lungs, gallbladder, urinary bladder, esophagus, pancreas, peritoneum, colon, and rectum. From a histological perspective, the stomach and liver are homologous to the anterior intestine during embryonic development; thus, abnormal differentiation of gastric cancer cells could result in their differentiating into hepatocytes to form HAS [3–4]. Clinically, the age of patients ranges from 44 to 87 years, and the ratio between men and women is 2.3 to 1. The main symptoms include epigastric pain and general fatigue due to anemia. Majority of the cases present at an advanced stage, with elevated serum AFP ranging from < 1.0 ng/mL to 700 000 ng/mL. Frequently, metastasis occurs to the lymph nodes and to the liver [5]. Approximately 70%–80% of patients with HAS have increased AFP levels, which generally declines within 1 to 2 weeks following surgery, and is restored to normal two months post-surgery [6]. Our patient was an elderly man who demonstrated elevated levels of AFP prior surgery.

As originally described by Ishikura *et al* [7], the typical differentiation of HAS is comprises both adenocarcinomatous and hepatocellular regions. The two areas are often intermingled with one another, and extensive venous involvement of the tumor cells was noted. Most adenocarcinoma cells are papillary or tubular. In HCC-like areas, cancer cells are present in cord- or nest-like arrangements, along with interstitial capillary-rich connective tissue and blood sinuses. Moreover, the tumor cells contain various serum proteins, including AFP, alpha-1 antitrypsin (AAT), albumin, and prealbumin in their cytoplasm, which can be confirmed via immunohistochemical staining. Therefore, positive expression of AFP, Gly3, and CK19 are often detected in majority of the tumor cells in the hepatocellular differentiation regions [8].

Endoscopic biopsies are superficial and limited in scope, whereas hepatocellular differentiation regions are often located deep within the tumor tissues; thus, preoperative diagnosis of HAS is particularly difficult because most patients can only be diagnosed by relying on postoperative pathology and immunohistochemical analysis. However, irrespective of whether the levels of AFP are elevated, the appearance of hepatocellular

differentiation regions in adenocarcinoma tissues can considered as a gold standard for diagnosing HAS. Additionally, if a patient with HAS also demonstrates from liver metastasis, we need to distinguish between the former and primary liver cancer. In general, the latter often requires a history of hepatitis and cirrhosis, and it is more common to find a single nodule; while metastasis to the stomach is extremely rare, with the first invasion layer being the serous membrane of the stomach. In addition, the disease should be distinguished from other tumors, such as germ cell tumors, which are also accompanied by elevated levels of AFP.

A standard treatment approach for HAS has yet to be established. Radical surgery is extremely crucial when feasible. Similarly, adjuvant therapy such as chemotherapy, immunotherapy, and radiotherapy are also important in prolonging survival and improving patients' quality of life postoperatively. According to previous reports, 5-fluorouracil (5-FU) and mitomycin C (MMC)-based chemotherapy are the most recommended treatment regimens, although their efficacies still warrant further research [9–10]. The prognosis of HAS is extremely poor, and has a high tendency to metastasize and relapse, with a median overall survival period of 10 to 18 months. AFP expression and tumor-node-metastasis (TNM) stage are closely related to its prognosis [11]. In our case, AFP expression was positive, the tumor stage was considered to be T4N2M0, and no recurrence or metastasis were observed despite chemotherapy not being administered postoperatively.

In conclusion, HAS is a rare malignant neoplasm observed in clinics and is prone to misdiagnosis. There have only been a few cases of HAS reported previous in the literature; hence we present a case of HAS from our hospital to enhance our understanding of this disease in an effort to decrease its misdiagnosis.

Conflicts of interest

The authors indicated no potential conflicts of interest.

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