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Case Report
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Hepatoid Adenocarcinoma of Gallbladder: A Case Report

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Abstract

Hepatoid Adenocarcinoma (HAC) is a specific extrahepatic cancer presenting Hepatocellular Carcinoma (HCC) characteristics. Diagnosis of HAC is difficult since clinical manifestations and examination results are highly similar to HCC. HAC has been rarely reported in case reports, and most frequently occurs in stomach. Here we reported a 42-year-old man who presented with right upper abdomen pain and occasionally nausea. He was firstly diagnosed as gallbladder cancer based on the imaging and laboratory results. Radical gallbladder cancer resection was preformed, however, the pathology demonstrated moderately-poorly differentiated gallbladder adenocarcinoma, with hepatoid adenocarcinoma differentiation.

Finally, he was diagnosed as HAC of gallbladder.

Introduction

Hepatoid Adenocarcinoma (HAC) was first described in 1970 as an α-Fetoprotein (AFP) producing carcinoma of gastric [1]. Usually, HAC is related with high serum AFP level since highly comparable in biological and morphological features with HCC. HAC may arise in different organs including stomach, gallbladder, lung, esophagus, urinary bladder, etc. [2]. Stomach represents the majority of HAC origin; other organs of HAC are sporadically reported in cases and case series [3]. The prognosis of HAC is quite poor due to its rarity and no consensus is reached in therapy. Most HAC was detected through immunohistochemical methods. Surgery still remains the most effective measure followed by chemotherapy and radiotherapy [4]. Hence, early and accurate diagnosis appears to be fundamental.

Case Presentation

A 43-yeat-old male presented was admitted with right upper abdomen pain and occasionally nausea. Hepatobiliary ultrasound and MRCP showed gallbladder occupation and malignant tumor was suspected. Further testing was performed and the gallbladder tumor enhancement was observed in contrast CT as showed in Figure 1. Laboratory tests revealed abnormal liver function, specifically, ALT 168 U/L, and AST 258 U/L. Other results were within normal limits, including serum AFP, CEA and CA199. Hepatitis B virus antigen was positive and the patient had not received any anti-virus therapy.

Cholecystectomy and liver segment IVb, segment V resection along with regional lymph node dissection were performed.

Gross examination showed a 2.1 cm × 1.8 cm × 1.4 cm gray-white solid mass in the gallbladder. Tumor invasion was limited to the gallbladder wall.

Microscopically, no nerve invasion nor vessel carcinoma embolus was observed, all the margins were negative, and all the 9 lymph nodes were without metastasis.

Immunohistochemically, CK7, MSH2, MSH6, MLH1 and PMS2 were positive, with focal hepatocyte and AFP positive. CK20, Her2 and EBER were all negative (Figure 2).

According to the pathology results, the patient was finally diagnosed as HAC of gallbladder.

To our knowledge, there is no standard therapy for gallbladder HAC, especially for adjuvant therapy after surgery. We administered Gemcitabine plus Cisplatin chemotherapy in combination with PD-1 antibody for the patient 1 month after surgery. In particular, 1000 mg/m^2 Gemcitabine and 25 mg/m^2 Cisplatin was delivered on day 1, day 8. 200 mg PD-1 antibody was delivered on

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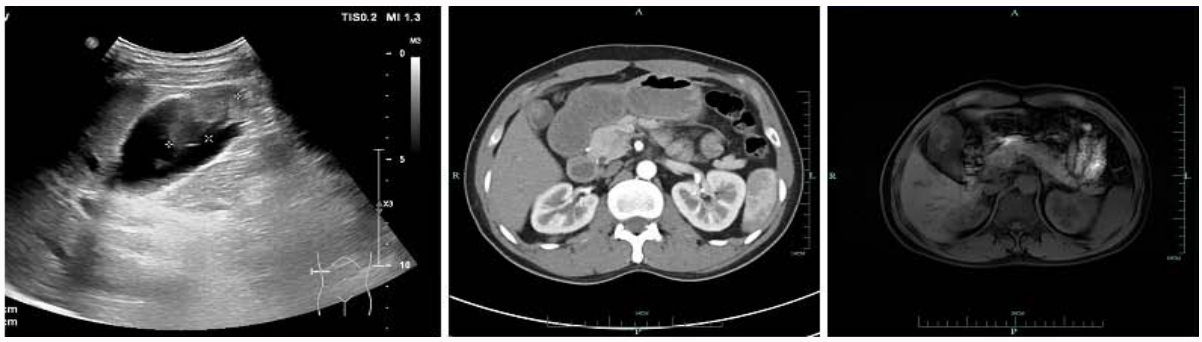

Figure 1: Abdominal ultrasonic and contract CT, MR imaging of the patient.

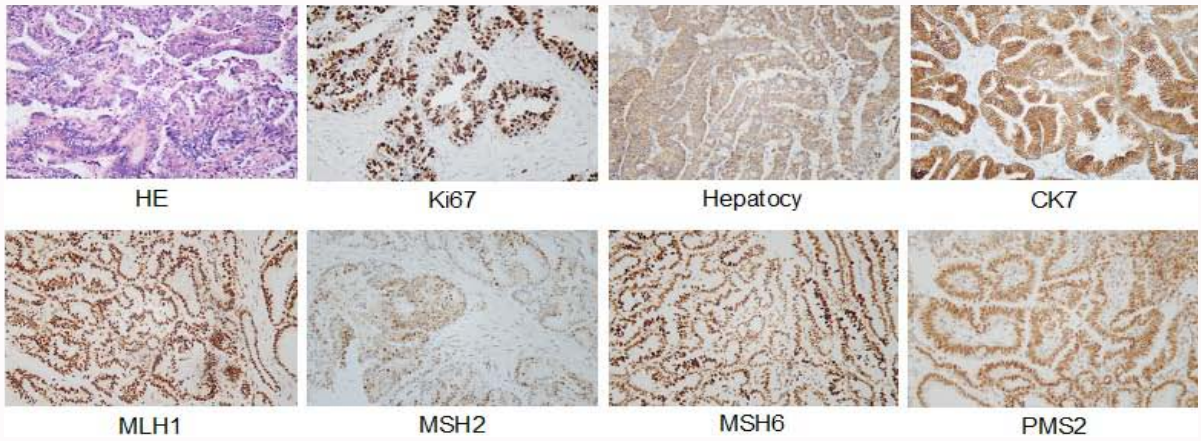

Figure 2: IHC image of the patient.

day 1, every 3 weeks is a treatment cycle. The patient received a total of 6 cycles and was well tolerated. He is still alive without tumor recurrence.

Discussion

Hepatoid Adenocarcinoma (HAC) is a rare and aggressive variety of extrahepatic cancer with hepatocyte differentiation. Gallbladder HAC represents an infrequent origin of HAC. Prompt and accurate diagnosis of the primary tumor site of HAC is critical to improve outcomes.

Nowadays, HAC diagnosis largely relies on pathological Immunohistochemical (IHC). Su et al. [5] summarized clinical and pathological characteristics of HAC reported in literature. Most patients were found AFP positive in IHC stains, and some other specific IHC markers such as Cytokeratin (CK) 19, Hep-Par 1 and Glypican 3 (GPC-3) may also help determine HAC diagnosis. Most patients had high level of serum AFP (84.8%), and metastases were usually found when diagnosed. Surgical resection remains the primary treatment in HAC, followed by adjuvant chemotherapy and radiotherapy. The median survival of all HAC patients is reported to be 12 months.

Treatment for HAC still remains controversial. Simmet et al. [6] first reported two cases of metastatic HAC treated by Cisplatin-etoposide as first-line chemotherapy. The result was encouraging and the authors considered Cisplatin-based regimen to be the most promising option for mHAC. We scheduled a GP plus PD-1 therapy for the patient. After 4 months treatment, the patient kept a fine physical status, and reached a disease-free survival of 20 months till today. His latest examination demonstrates no recurrence. However, genome sequencing may be inspiring to better understand the genotype of the tumor, and acquire a satisfying outcome.

In conclusion, we report a rare case of gallbladder hepatoid adenocarcinoma. The diagnosis of HAC is difficult and prognosis is poor. Treatment for HAC varies and we explored a GP chemotherapy plus PD-1 antibody regimen in this case. The result is promising but need to be verified in more cases.

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