Hepatoid Carcinoma of The Gallbladder


ABSTRACT

Hepatoid carcinoma is a special type of extrahepatic tumor associated with hepatic differentiation, and has the morphological and functional features of hepatocellular carcinoma. Hepatoid carcinoma of the gallbladder is very rarely reported in the literature.

We report a case of hepatoid carcinoma of the gallbladder in a 71-year-old female who presented with abdominal pain and was first diagnosed as cholelithiasis with cholecystitis. The microscopic findings of the gallbladder after cholecystectomy showed an area of tumor with polygonal cells, eosinophilic cytoplasm, distinct cell borders, round vesicular nuclei and prominent nucleoli, arranged in trabecular pattern resembling hepatocellular carcinoma intermingled with areas of adenocarcinoma or cholangiocarcinoma. The specimen from the pancreas also showed the same type of tumor cells. Histochemically, some of tumor cells were positive for Victoria Blue, Stein, and P AS. The immunohistochemistry for alpha-fetoprotein (AFP) showed strong intra cytoplasmic positivity, both in tumor cells with hepatic differentiation and tumor cells with bile duct epithelium differentiation.

Based on these findings, this case was diagnosed as hepatoid carcinoma of the gallbladder with metastasis to the pancreas. This is the first case that has been reported in our department.

Key words: hepatoid carcinoma, gallbladder.

INTRODUCTION

Hepatoid carcinoma is a special type of extrahepatic adenocarcinoma, which has a morphologic and functional similarity to hepatocellular carcinoma. This tumor has been reported in various organs, such as gastrointestinal tract, pancreas, gallbladder, vagina, uterus, ovary, kidney, urinary bladder, and testicle. Hepatoid carcinoma is an aggressive neoplasm with poor prognosis.

Hepatoid carcinoma of the gallbladder is very rarely reported in the literatures, two cases were reported in the English literature, and other two cases were reported in Japan. In our department, no case has been reported.

CASE ILLUSTRATION

A female 71-year-old presented with abdominal pain. The ultrasonography examination showed acute cholecystitis with adhesion to the surrounding tissues, cholelithiasis without biliary obstruction, and fatty liver. The clinical diagnosis was cholelithiasis with cholecystitis. Laparotomy was performed.

At laparatomy, the gallbladder was inflamed. There were stones in the lumen. Some nodules were found at the head of the pancreas. The liver surface was smooth, and no metastatic lesions were seen. Cholecystectomy, and also biopsy of the pancreas and liver were performed.

One month post operatively, the patient returned to the hospital with abdominal enlargement and pain. On physical examination, there was pain on pressure at the right upper quadrant of the abdomen with ascites. The laboratory data showed an anemic condition with haemoglobin 9.3 gr% (12–16 gr%), hematocrit 27% (40–54%), leucocytes 11600/mm³ (5000–10000/mm³), platelets 316.000/mm³ (200–400.000/mm³). Serum potassium level is high (6.11 meq/L), serum albumin level is low (2.6 gr%). Chest x-ray showed right pleural effusion with suspected metastatic lesion. The patient died after 2 days of treatment, because of acute renal failure and terminal state of the disease.

Gross Findings

The gallbladder measured 80 x 30 x 20 mm. Sectioning revealed white tumor mass with firm consistency protruding into the lumen.
The other specimen consisted of biopsies of the pancreas and the liver. The pancreas specimen was white, firm, measuring about 5 mm in diameter. The liver specimen measured about 5 mm in diameter, with firm consistency.

Microscopic Findings

The microscopic examination of the gallbladder showed a tumor mass with a papillary epithelial growth consistent with cholangiocarcinoma. In other part, there was growth into the lumen intermingled with areas of solid growth pattern invading the muscular and serosa layers. In the area with solid growth pattern, the tumor cells were arranged in a trabecular pattern, and consisted of polygonal cells with eosinophilic cytoplasm, distinct cell border, and round vesicular nuclei with prominent nucleoli. Bile pigment in some tumor cells was found. Many vascular emboli were also detected.

The specimen from the pancreas also showed the same tumor cells with solid growth pattern.

The liver only showed a mild fatty change and perivascular necrosis. No neoplastic cells were found.
Hepatoid carcinoma is a special type of extrahepatic adenocarcinoma associated with hepatic differentiation. Akiyama et al defined that hepatoid carcinoma is an extrahepatic tumor characterized by both the histological structures of ‘hepatoid differentiation’ and excessive production of alpha-fetoprotein (AFP). Wee mentioned that hepatoid carcinoma whether AFP producing or not, tend to fare worse than other AFP producing carcinomas. Hepatoid carcinoma is as an aggressive neoplasm with poor prognosis.

There are two theories of the histogenesis of hepatoid carcinoma. One is that adenocarcinoma acquires hepatic differentiation during progression of the tumor, and another is that bipotential cells differentiate into cells with glandular and hepatoid features.

Hepatoid carcinoma usually presents in middle to elderly aged males and females. In our case, the tumor occurred in a 71-year-old female. In two cases that had been reported in Japan, Sakamoto et al reported a case of hepatoid carcinoma of the gallbladder in a 72-year-old male, and Nakashima et al also reported this tumor in a 77-year-old male.

Hepatoid carcinoma was first proposed as a specific subtype of primary gastric cancer with poor prognosis, but recently has been reported in various organs, such as the gastrointestinal tract, pancreas, uterus, ovary, vagina, kidney, urinary bladder and testicle. The most frequent site of this carcinoma is the stomach.

Hepatoid carcinoma of the gallbladder is very rarely reported in the literature. In English literature only two cases have been reported. In Japan, two cases have been reported. In our department, this is the first case.
Microscopically, tumor cells have abundant eosinophilic cytoplasm with round to oval nuclei and the typical structure of the lesion is a sinusoidal or trabecular pattern, resembling hepatocellular carcinoma.\(^2,3,4\)

In our case, the tumor cells in the gallbladder also showed polygonal cells with eosinophilic cytoplasm, distinct cell border, and round nuclei in a trabecular pattern resembling hepatoplastic carcinoma, intermingled with component of cholangiocarcinoma.

Sakamoto et al\(^2\), reported a case of hepatoid adenocarcinoma of the gallbladder in a 72-year-old male, in which the microscopic examination showed the areas of well differentiated adenocarcinoma in the mucosa of the gallbladder adjacent to the area of carcinoma with hepatoid features. In our case, the components of adenocarcinoma/cholangiocarcinoma were intermingled with the hepatoid features.

Immunohistochemistry of tumor cells in hepatoid carcinoma might show liver specific proteins such as alpha-fetoprotein (AFP), albumin, transferrin, PIVKA and alpha-1 antitrypsin. Hep Par 1 is a marker for hepatic differentiation, and has been reported positive in many cases of hepatoid carcinoma.\(^1,2,3,7,8\) In some studies, the tumor cells were immunoreactive for CK 8 and 19, but negative for CK 7. This suggests that hepatoid carcinoma has an intermittent immunohistochemical profile between hepatocellular carcinoma (positive for CK 8 but negative for CK 7 and 19) and adenocarcinoma of bile duct (positive for all CK 7, 8 and 19).\(^2\)

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<th>Table 1. Immunohistochemistry for Hepatoid Carcinoma, Hepatocellular Carcinoma and Cholangiocarcinoma</th>
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<td>Tumor type</td>
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<td>Hepatocellular carcinoma</td>
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<td>Hepatoid carcinoma</td>
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Tumor cells are usually positive for alpha-fetoprotein (AFP), and serum AFP level although not always is also elevated in many cases.\(^2,5,7\) Akiyama et al\(^3\) defined hepatoid carcinoma as an extrahepatic tumor characterized by both the histological structures of ‘hepatoid differentiation’ and excessive production of AFP. However, others mentioned that specificity for AFP is not necessarily diagnostic for hepatoid carcinoma because not all hepatoid carcinomas are associated with AFP overproduction, so the diagnosis of hepatoid carcinoma could be made essentially by histologic features of the tumor.\(^2\) Hepatoid carcinoma whether AFP producing or not, tends to fare worse than other AFP producing carcinomas.\(^4\)

In our case immunohistochemical staining for alpha-fetoprotein (AFP) was positive. The histochemical staining for Victoria blue, stein, and PAS was also positive in the cytoplasm of some tumor cells. These results contribute to the finding for true entity and the differentiation of the tumor toward liver cell neoplasm.

**CONCLUSION**

Hepatoid carcinoma of the gallbladder is a very rare and aggressive tumor. We report the case in a 71-year-old female with hepatoid carcinoma of the gallbladder with metastasis to pancreas. Microscopic examination showed polygonal tumor cells with eosinophilic cytoplasm, distinct cell border, and round nuclei in a trabecular pattern resembling hepatoplastic carcinoma, which were intermingled with the components of cholangiocarcinoma. Immunohistochemical staining for AFP and histochemical staining for Victoria blue, stein and PAS were positive. Serum AFP level of this patient was not examined.

**REFERENCES**