Cancer Imaging (2010) **10,** 198–201
DOI: 10.1102/1470-7330.2010.0027

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CASE REPORT

Primary hepatoid carcinoma of the biliary tree: a radiologic mimicker of Klatskin-type tumor

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Date accepted for publication 17 July 2010

Abstract

Hepatoid carcinomas are a group of neoplasms with features resembling hepatocellular carcinomas. Although extremely rare, more cases have been noted to arise from various organs within the last decade. Differentiating these tumors when located in the biliary tree from cholangiocarcinoma is not only a radiologic challenge but also critical, because treatment modalities and operative strategies are dependent on the exact nature of the tumor. We report a unique case in the literature of a 67-year-old Caucasian female who presented with obstructive jaundice due to an obstructing mass seen at the common hepatic duct on imaging with no preceding history of cirrhosis and increased serum α-fetoprotein (AFP), in whom a differential diagnosis from cholangiocarcinoma in a non-cirrhotic liver was particularly difficult given the combination of tumor location and solitary nature. The radiologist may include ectopic hepatoid adenocarcinomas in the differential consideration of an obstructing tumor in the biliary tree especially in patients with increased serum AFP levels.

Keywords: *Hepatoid carcinoma; bile ducts; CT; cholangiocarcinoma; MRCP.*

Introduction

Hepatoid carcinoma was first described as a specific type of primary gastric carcinoma by Ishikura *et al*.[1] with the most frequent site of this carcinoma being the stomach. Hepatoid carcinoma is a variant of adenocarcinoma associated with hepatic differentiation. It is generally composed of adenocarcinomatous and hepatocellular carcinoma (HCC)-like foci and the latter component has the full spectrum of the morphologic and functional features of HCC. It is rare, with incidence accounting for 0.38% of all gastric cancers and much less in other organs. Hepatoid adenocarcinoma is an aggressive carcinoma carrying a poor prognosis compared with the other common tumors in these organs[1]. Rare cases of hepatoid carcinoma have been described in a variety of organs including the esophagus, lung, gallbladder, ovary, cecum, and adrenal cortex[2,3].

Radiologic mimics of cholangiocarcinoma described previously include a heterogeneous group of entities that includes benign conditions as well as malignant tumors such as HCC, metastases, melanoma, lymphoma, leukemia, and carcinoid tumors. The imaging findings of these benign and malignant entities may be indistinguishable from those of cholangiocarcinoma[4,5]. In most cases, a definitive diagnosis can be established only with histopathologic examination[6]. A small case series of ectopic hepatoid carcinoma has been described previously in non-biliary locations[7]. We described yet another differential possibility, although rare, but which in the proper clinical setting must be included in the differential consideration of cholangiocarcinoma.

In reporting this case, we would like to emphasize the role of imaging as a problem-solving tool for analysis of tumors of the biliary tree, including hepatoid carcinoma of the biliary tree.

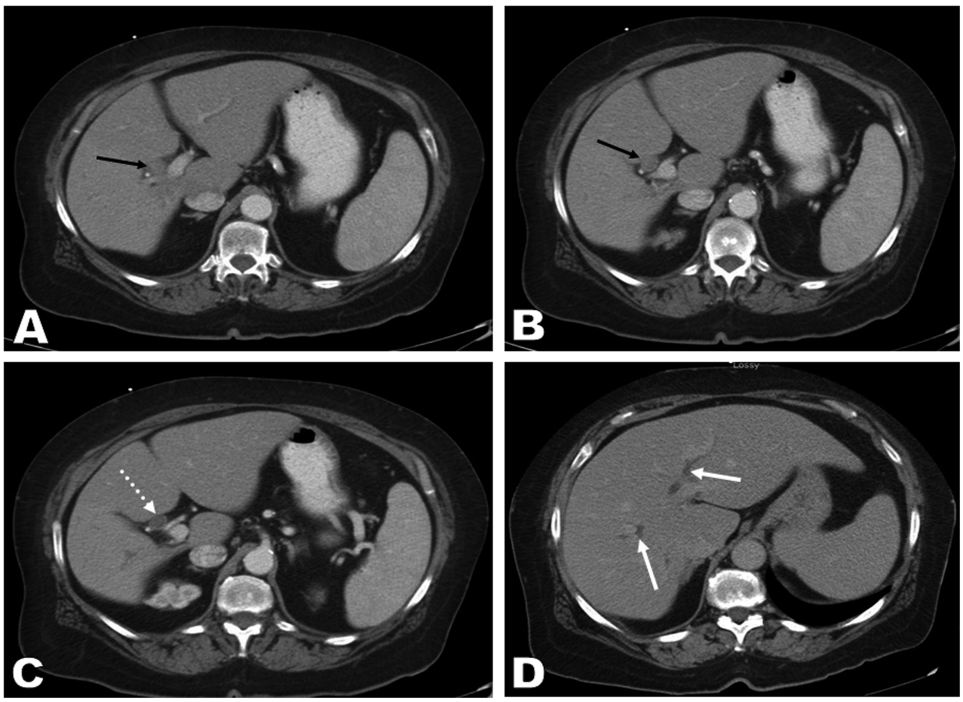

Figure 1 **(A,B) Axial contrast-enhanced CT images demonstrating a subtle soft tissue density mass (black arrows) at the bifurcation region of the common hepatic duct. (C) Axial contrast-enhanced CT image slightly inferior to the common hepatic duct bifurcation shows normal low density bile (dashed white arrow) in the common hepatic duct further confirming the presence of a mass superiorly. (D) Post-contrast axial CT image showing mild dilatation of the right and left hepatic ducts (solid white arrows).**

Case report

A 67-year-old Caucasian female presented with painless jaundice and a history of weight loss and generalized fatigue. Physical examination was within limits of normal. Laboratory analysis revealed an alkaline phosphatase level of 689 IU/L. Alanine aminotransferase and aspartate aminotransferase levels were 209 IU/L and 285 IU/L, respectively. Total bilirubin levels were 8.2 mg/dL with direct bilirubin levels of 6.0mg/dL and indirect bilirubin levels of 2.2 mg/dL. Alpha fetoprotein (AFP) levels were increased at 2478.0 μg/L (normal; 0–8 μg/L). The hepatitis panel was negative for hepatitis B or hepatitis C. The patient denied a history of alcohol abuse. Past medical history was significant for diabetes, hypertension, hyperlipidemia, and coronary artery disease. Past surgical history was significant for appendectomy and cholecystectomy.

Initial sonographic imaging showed mild dilatation of the intra- and extrahepatic bile ducts. Color and pulsed Doppler imaging demonstrated hepatopedal flow in the portal vein and no abnormal hepatic masses were seen on gray-scale imaging. A subsequent computed tomography (CT) examination incidentally showed a large duodenal diverticulum which was thought to be arising from the second portion of the duodenum. A subtle soft tissue density was seen at the junction of the right and left hepatic ducts at the porta hepatis with mild dilatation of the intrahepatic bile ducts above the obstruction (Fig. 1). No CT evidence for cirrhosis such as serrated liver borders, enlarged portal vein, and venous collaterals was observed. Further imaging with magnetic resonance (MR) imaging with magnetic resonance cholangiopancreatography (MRCP) was recommended.

Dynamic MR imaging showed no evidence of an intrahepatic mass in early or delayed phases. Dedicated MRCP images, on both the source and the reconstruction images, showed an irregular filling defect in the region of the right hepatic duct, just before the junction with the left hepatic duct to form the common hepatic duct, which did not have the smooth appearance of a stone. The intrahepatic biliary ducts were mildly dilated above the obstructing mass (Fig. 2A).

Endoscopic retrograde cholangiopancreatography (ERCP) workup was performed and brushings from the region of the obstructing lesion were obtained. Subsequent histopathologic analysis showed hepatoid epithelial malignancy composed of large cells with rounded nuclei, prominent nucleoli, and moderate to large amount of eosinophilic cytoplasm (Fig. 3A). The neoplastic cells formed irregularly shaped nests and cords with occasional canalicular structures containing bile. Mitotic division figures were prominent. The tumor cells were positive for low molecular weight cytokeratin (Cam 5.2), Hepar-1, and demonstrated a canalicular staining pattern (Fig. 3B). CD34 analysis

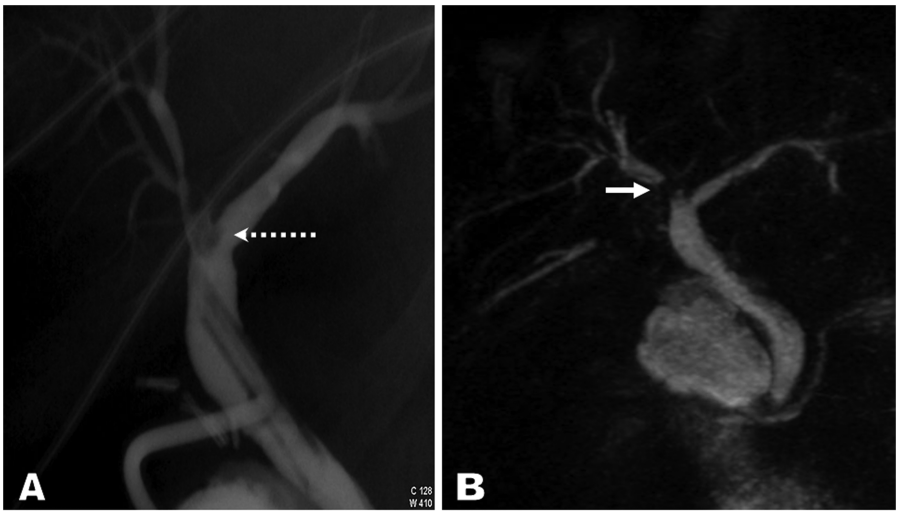

Figure 2 **(A) T-tube percutaneous cholangiogram image depicting an irregular intraluminal filling defect at the confluence of the right and left hepatic ducts (dashed white arrow) suggestive of tumor growth since MRCP examination. (B) Thick slab MRCP image demonstrates a smaller filling defect mainly located in the right hepatic duct.**

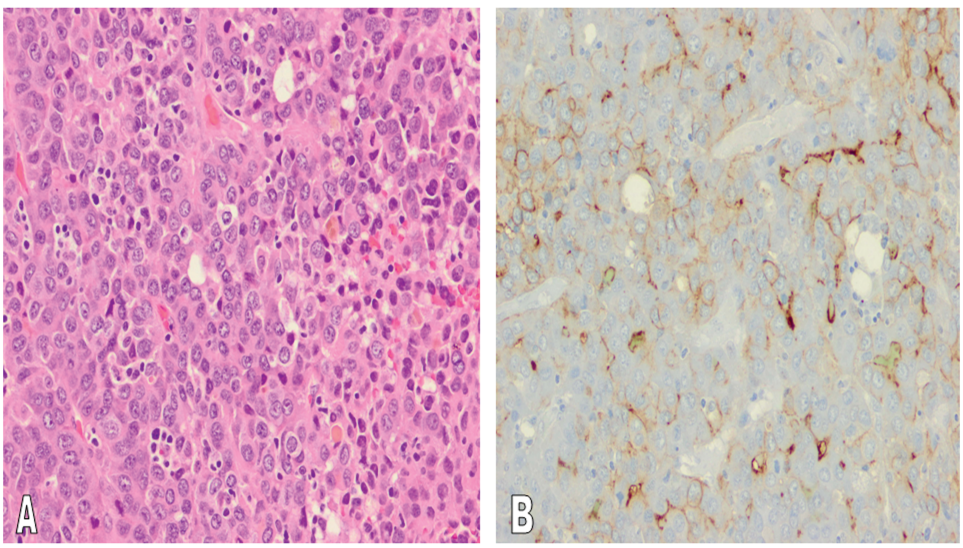

Figure 3 **(A) Routine hematoxylin and eosin histology demonstrating a neoplasm composed of medium-sized cells with eosinophilic cytoplasm and vague organoid architecture. (B) Immunohistochemistry stain for HepPar1 demonstrates a positive canalicular staining pattern and a positive cytoplasmic pattern. All photos were taken at 20× magnification.**

demonstrated a sinusoidal staining pattern surrounding the tumor cells. The tumor was negative for CK7 and CK20. The ectopic hepatoid carcinoma may have arisen from ectopic hepatic tissue in the biliary tree. At this point the patient was thought to have a histologically proven tumor at the bifurcation of the right and left hepatic ducts with increased AFP levels. An internal-external biliary drainage catheter was placed.

On percutaneous T-tube cholangiogram performed after one cycle of chemotherapy, there was an irregular polypoid filling defect at the bifurcation of the left and right hepatic ducts, which was thought to be causing partial obstruction of the right hepatic duct and delayed filling, suspicious for interval growth of the tumor infiltrating the duct in a region more typical for a Klatskin-type tumor (Fig. 2B).

The patient underwent four rounds of chemotherapy and refused a fifth and opted for hospice treatment.

Discussion

Hepatoid carcinoma is a primary neoplasm exhibiting features of HCC in terms of morphology,

immunohistochemistry, and behavior. Hepatoid carcinoma is confirmed by its histomorphologic similarity to hepatocellular carcinoma (HCC), with markedly increased levels of serum AFP. Since the bile ducts and the liver originate from the same endodermal tissue, biliary epithelium has an ability to differentiate into hepatic cells, resulting in a tendency for AFP production[8]. A prompt and accurate diagnosis of hepatoid carcinoma is important because the prognosis is very poor compared with that of common types of adenocarcinoma.

Ectopic hepatoid carcinoma of the biliary tree can be confused with extrahepatic spread of HCC although the latter have advanced intrahepatic tumor and rarely metastasize to the biliary tree. A few cases of small HCCs measuring less than 3 cm with tumor thrombi in the biliary tree have been described previously in the literature[9]. However, on imaging studies these cases showed a small associated hepatic mass. Our case did not demonstrate any evidence of a hepatic mass on CT or MR imaging studies. Furthermore, the intrabiliary mass seen on CT, T-tube cholangiogram, and MRCP did not demonstrate extrabiliary invasion.

The rare hepatoid carcinoma of the biliary tree may mimic Klatskin-type cholangiocarcinoma with its shared clinical features such as old age, anatomic location, and aggressive behavior. A particular polypoid variant of cholangiocarcinoma is infrequently found in both the intra- and extrahepatic ducts. The histologic type of this tumor is mostly papillary adenocarcinoma with intraluminal growth. The tumor is depicted as an intraluminal polypoid mass at both ultrasound and CT and as a polypoid filling defect at cholangiography[10]. Whether ectopic hepatoid carcinoma can resemble other morphologic forms of cholangiocarcinoma described by Lim *et al.*[11] such as periductal infiltrating and mass-forming cholangiocarcinoma is unclear; however, it can mimic the polypoid form of cholangiocarcinoma in radiologic appearance and tumor location as seen in our case. On CT imaging, periductal infiltrating cholangiocarcinoma may show a concentrically thickened common duct wall with enhancement, whereas our case showed no evidence of biliary duct wall enhancement on CT (Fig. 1).

Intraluminal polypoid tumors of the intra- and/or extrahepatic bile ducts are generally associated with partial obstruction and dilatation of the bile ducts[11] similar to the observations in our case. However, the polypoid form of cholangiocarcinoma may have avid mucin secretion in the biliary tree and normal serum AFP levels in contrast to hepatoid carcinoma, which has increased AFP levels and is a non-mucin secreting tumor as demonstrated in our case on ERCP examination[11].

The differentiation between these different pathologic entities is important because no effective adjuvant therapy exists for cholangiocarcinoma, and unless clear indications of nonresectability exist, most patients should be considered for surgical exploration. On the other hand, hepatoid carcinoma, although also aggressive in biologic behavior, can be treated with chemotherapy. In conclusion, although the final diagnosis is confirmed with clinicopathologic findings similar to other benign and malignant entities of the biliary tree that can mimic cholangiocarcinoma, radiologists may include ectopic hepatoid carcinomas in the differential consideration of an obstructing tumor in the biliary tree especially in patients with increased AFP levels. Furthermore, imaging can help differentiate the primary ectopic hepatoid carcinoma of the biliary tree from small HCC with bile duct tumor thrombus even before a histopathologic diagnosis is confirmed.

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