Case Report

Unusual Morphologic Features of Small Duct Intrahepatic Cholangiocarcinoma with Ductal Plate Malformation

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Abstract

We present a case of small duct intrahepatic cholangiocarcinoma with a ductal plate malformation (iCCA with DPM) showing unusual pathologic features. iCCA with DPM is an uncommon subtype of small duct iCCA. This uncommon neoplasm has unique clinicopathological characteristics. Pathological evaluation is necessary for diagnosing correctly.

Keywords: Ductal plate malformation, Intrahepatic cholangiocarcinoma, Combined hepatocellular-cholangiocarcinoma

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Introduction

Intrahepatic cholangiocarcinoma (iCCA) is a moderately differentiated adeno-carcinoma with tubular or micropapillary structure with a desmoplastic stroma, accounting for 5 - 15% of the cases of primary liver cancer. The etiology of iCCA is associated with biliary tract inflammation and infection, biliary tract formation, and viral infection.[1] The incidence of this malignant neoplasm is highest in Southeast Asia, particularly in Thailand. According to the most recent World Health Organization (WHO) classification, iCCA is classified as large duct and small duct subtypes based on histomorphology.[2] iCCA can be further categorized into several histological variants. iCCA with a predominant ductal plate malformation (DPM) pattern was initially proposed in a Japanese literature as a new subtype of iCCA originating from small ducts.[3] Due to its rarity, data on iCCA with DPM is limited. At the time of writing, there is an uncertainty whether iCCA with DPM represents a subtype of iCCA or arises from a pre-existing DPM. We reported a case of resected iCCA with a DPM pattern at Thammasat University Hospital.

Case presentation

A 76-year-old woman with a known history of hepatitis B cirrhosis came to the hospital for routine surveillance. Ultrasonography revealed a 4 × 3 cm mass in the liver. Computed tomography of the abdomen showed an ill-defined heterogeneous hypovascular mass at hepatic segment VIII/V, measuring 5.4 × 4.2 cm. The mass displayed diffuse heterogeneous enhancement on the arterial phase with centrally progressive enhancement on delayed phase images. Such radiologic findings could be compatible with either mass-forming iCCA or combined hepatocellular-cholangiocarcinoma. Right hepatectomy was performed. The specimen was submitted for pathological evaluation.

Grossly, a lobulated, inhomogeneous light brown mass in a cirrhotic liver was noted on the cut section (Figure 1). Microscopically, the majority of tumors (approximately 70% of total tumor volume) had a vague multinodular appearance with intervening fibrous bands (Figure 2a). Such a histomorphologic feature was also known as a DPM pattern. Typical small duct iCCA was occasionally noted (Figure 2b). The tumor cells were small, oval,

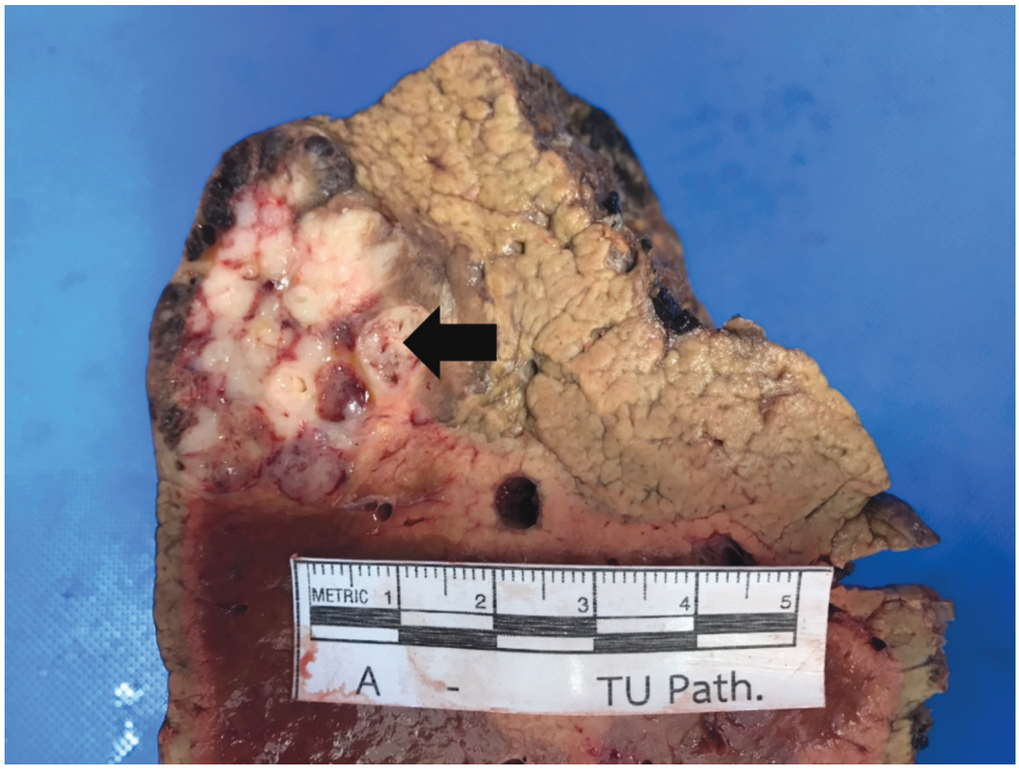

Figure 1 Gross appearance of resected small duct iCCA with DPM. An infiltrative, lobulated, inhomogeneous light brown mass is observed. The non-neoplastic liver parenchyma shows macronodular and micronodular cirrhosis.

and possessed mildly pleomorphic nuclei. Some of these cells were arranged in a solid pattern (Figure 2c), reminiscent of hepatocellular carcinoma. Portal tracts were entrapped within the mass, suggesting a replacing growth pattern. Both lymphovascular invasion and perineural invasion were absent. Neither biliary intraepithelial neoplasia nor parasitic infestation was observed. The cancer cells were highlighted by CK7 (Figure 3a) and were occasionally reactive with arginase1 (Figure 3b). Neither immunoreactivity with CK19 nor HepPar1 was observed. The cancer cells were weakly reactive with AFP. The apical domain of tumor cells was highlighted by EMA (Figure 3c). The Ki-67 labeling index was approximately 30% in the small duct iCCA component and 5% in a DPM component (Figure 3d). No nuclear immunoreactivity with p53 was observed. The pathological diagnosis was iCCA with a DPM pattern. The patient had recurrence-free survival at eleven months following the surgery.

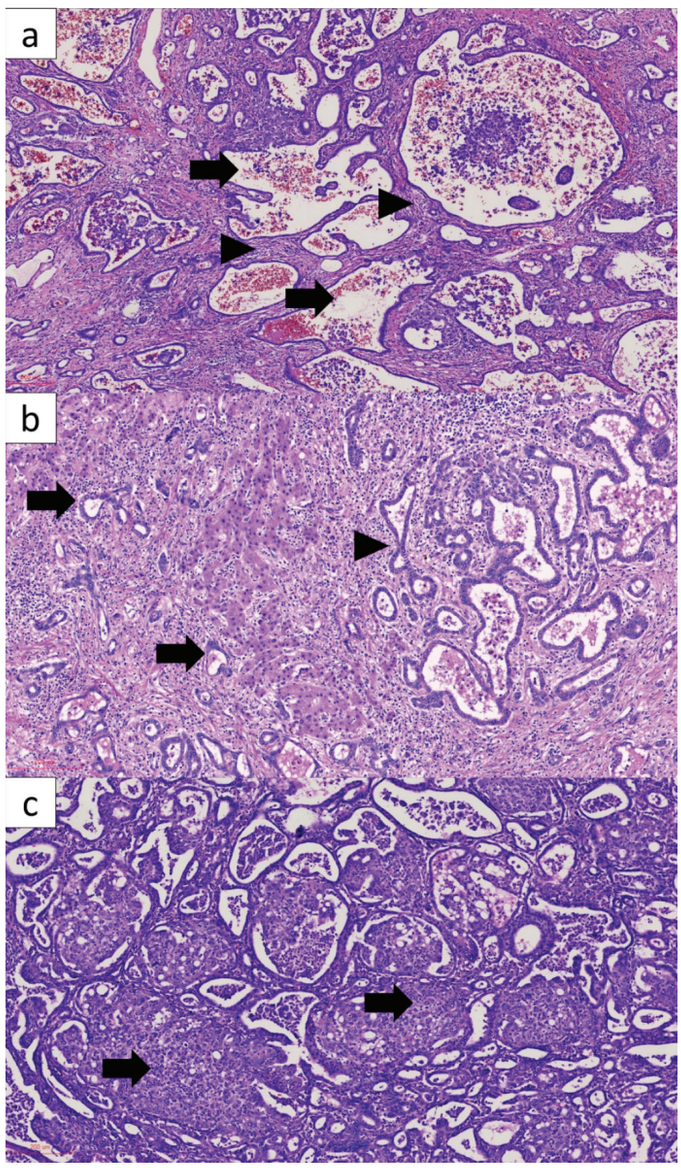

Figure 2 Histomorphology of resected small duct iCCA with DPM. (a) Microscopically, the tumor has a DPM pattern, characterized by a vague multinodular appearance composed of mildly pleomorphic, cuboidal to low columnar neoplastic cells arranged in a glandular pattern (arrows) with intervening fibrous bands (arrowheads). (b) The typical small duct iCCA (arrows) is intermixed with DPM (arrowhead). (c) Some tumor cells are arranged in a solid pattern (arrows), reminiscent of that of hepatocellular carcinoma.

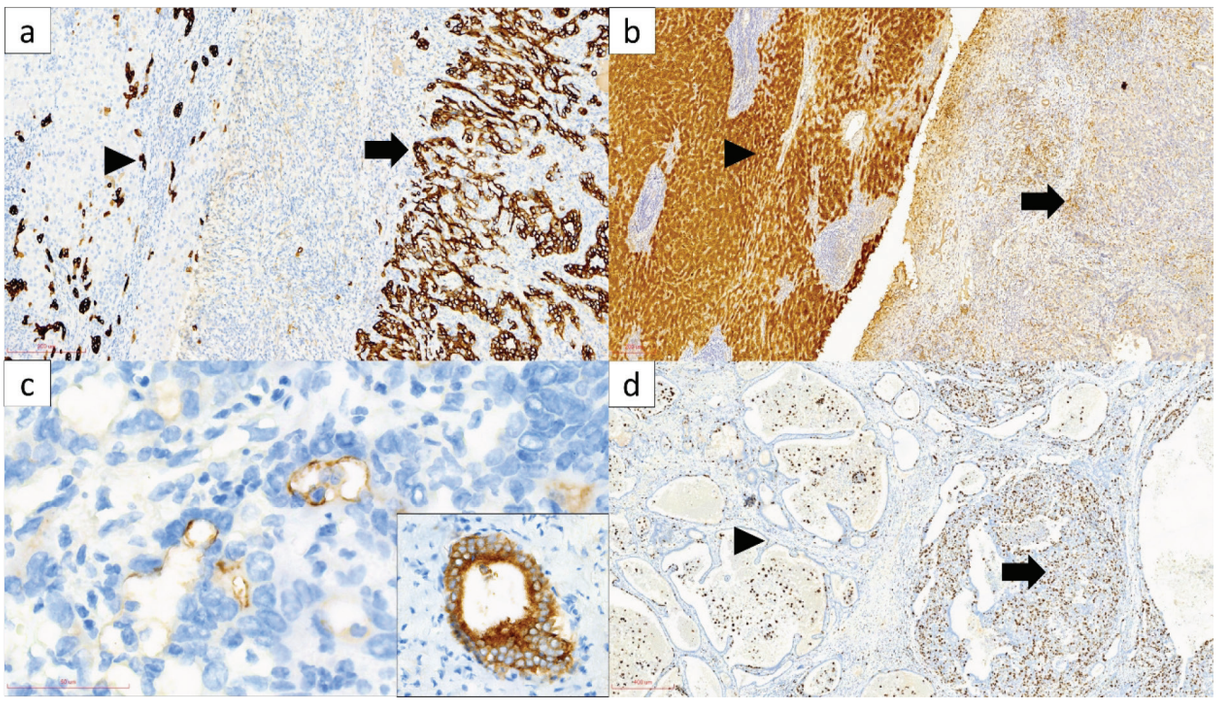

Figure 3 Immunophenotype of small duct iCCA with DPM. (a) CK7 highlights the cancer cells (arrow). Non-neoplastic bile ducts serve as an internal control (arrowhead). (b) The tumor cells show focal immunoreactivity with arginase1 (arrow). Non-neoplastic hepatocytes serve as an internal control (arrowhead). (c) EMA highlights the apical domain of neoplastic cells. Of note, such an immunostain highlights both apical and basolateral domains of large bile ducts (inset). (d) The Ki-67 labeling index is approximately 30% in small duct iCCA component (arrow) and 5% in a DPM component (arrowhead).

Discussion

iCCA with a predominant DPM pattern was initially proposed by Nakanuma et al. in Japanese literature as a new subtype of iCCA.[3] Most reported cases were older adults from East Asia.[3-5] This uncommon subtype accounted for 2.9% of iCCA in one reported series.[5] Most of the cases were associated with chronic liver diseases.[3-5] Some of them might coexist with von Meyenburg complex, congenital biliary atresia, or polycystic liver disease.[4] Magnetic resonance imaging (MRI) findings of the majority of cases demonstrated at least one major feature of LI-RADS (i.e., non-rim arterial hyperenhancement, enhancing capsule, and non-peripheral washout in portal phase), which favored HCC.[5] Tumors were variable in size. All of the cases were histologically small-duct type. DPM features include irregularly shaped and variably dilated glands covered by a low columnar or cuboidal biliary epithelium, bulging or irregular protrusions covered by biliary epithelium into the dilated lumen bridge-like structures covered by biliary epithelium in the dilated lumen.[3] A spectrum of transition from benign DPM-like features to malignant epithelium with different degrees of dysplasia could be identified in some cases.[4] No lymphovascular invasion, perineural invasion, or parasitic infestation was identified in all cases.[4-6]

The neoplastic cells in iCCA with DPM were highlighted by both CK7 and CK19.[3-4] Apart from histomorphology, an expression of EMA on the luminal side of the neoplastic glands in carcinomas with a DPM pattern was the other evidence that iCCA with a DPM pattern originated from small ducts.[3] The cancer cells were not reactive with markers of hepatocytic differentiation, including HepPar1 and AFP.[3,4] To the best of our knowledge, no study has evaluated the immunoreactivity of iCCA with DPM with arginase1.

iCCA with DPM is likely to progress from definitely benign to biliary intraepithelial neoplasia, then finally to intrahepatic cholangiocarcinoma as

opposed to from DPM. Immunohistochemistry of previously reported cases showed a transition phase with increased expression of Ki-67 and p53. The mechanism remains an issue to be studied further.[4] Small duct iCCA with a DPM pattern may be characterized by ARID1A alterations, and ARID1A immunohistochemistry can be used as a diagnostic immunohistochemical marker for such a rare tumor.[6]

Due to its rarity, iCCA with a DPM pattern can be easily misdiagnosed as combined hepatocellular-cholangiocarcinoma (cHCC-CCA). According to the present case, the tumor cells show an admixture of glandular and solid patterns with CK7+/Arginase1+ immunophenotype. Several primary liver cancers (PLCs) can have a pathologic resemblance to cHCC-CCA; therefore, cHCC-CCA may be overdiagnosed.[7] However, the diagnosis of cHCC-CCA must be based on an unequivocal presence of both hepatocellular carcinoma (HCC) and iCCA components using immunohistochemistry as an adjunct.[8] Although neoplastic cells in the present case reveal immunoreactivity with both hepatocytic and cholangiocytic markers, the presence of a solid pattern does not qualify as a morphologic feature of HCC. Therefore, this tumor should not be diagnosed as cHCC-CCA.

We presented a case of small duct iCCA with a DPM pattern showing unusual pathologic features. iCCA with DPM is an uncommon subtype of small duct iCCA in which most cases were reported from Asian countries. Small duct iCCA with DPM has unique clinicopathological, radiological, and molecular characteristics. Provisional radiological diagnoses are usually inaccurate. A careful pathological evaluation is needed to arrive at the correct diagnosis.

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Conflicts of interest: None declared.

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