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Case Report

A case of surgical resection for well-differentiated squamous cell carcinoma arising in a ciliated hepatic foregut cyst

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Ciliated hepatic foregut cysts (CHFC) are extremely rare, and most are benign cysts of the liver arising from remnants of the embryonic foregut. CHFC is usually found incidentally and as mostly asymptomatic cysts. We report squamous cell carcinoma (SCC) arising in a CHFC in a 50-year-old Japanese woman. She consulted our hospital for upper abdominal pain. A computed tomography and an ultrasound showed a cystic region including calcification and a solid mass in segment 4 of the liver. Left hepatectomy, B6 bile duct resection, and biliary-jejunal anastomosis were performed. Microscopic examination revealed that part of the cyst was lined by a characteristic ciliated pseudostratified columnar epithelium surrounding a connective tissue, a slightly thick fibrotic smooth muscle stromal layer, and an outer fibrous capsule. The cyst wall contained a low-papillary mural nodule showing atypical squamous hyperplasia with high-grade dysplasia. Stromal invasion was identified at the base of the nodule, leading to the diagnosis of well-differentiated SCC arising from a CHFC. We recommend careful clinical follow-up for patients with relatively large CHFCs as potentially malignant lesions and excision if they show any clinical manifestation.

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Key words: Ciliated hepatic foregut cysts; Liver; Squamous cell carcinoma

Background

First reported by Friedreich in 1857, ciliated hepatic foregut cyst (CHFC) is an extremely rare, mostly benign, solitary unilocular, rarely multilocular cyst of the liver arising from remnants of the embryonic foregut[1]. A hallmark of CHFC is the presence of pseudostratified columnar epithelium, and the cyst is usually surrounded by a subepithelial connective tissue layer, a smooth muscle bundle, and an outer fibrous capsule[2]. In 1984, when Wheeler and Edmondson first described such a lesion sharing a common morphologic pattern with a bronchogenic cyst, they therefore used the term "ciliated hepatic foregut cyst"[2]. Though this kind of lesion had always been considered benign in nature, in 1999 Vick et al. was the first to report a case of malignant transformation[3]. We report a case of extremely rare malignant transformation of CHFC that we surgically resected[3-7].

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Case

A 50-year-old Japanese woman with no remarkable medical history consulted our hospital for upper abdominal pain that she had been experiencing for a few days after the onset of cold symptoms. Physical examination revealed deep tenderness in the upper abdomen. Laboratory studies revealed a slight elevation of white blood cells (91.00 cells/mm^3), elevation of alkaline phosphate (ALP) 500 U/ml, γ-glutamyl transferase (γ-GTP) 139 U/ml, C-reactive protein (CRP) 2.64 mg/dl, and CA19-9 397.7 U/ml. Aspartate transaminase (AST), alanine aminotransferase (ALT), total bilirubin, and other serological markers (AFP, PIVKA-2, CEA) were within normal limits. Computed tomography (CT) showed a 4cm indeterminate cystic region including calcification and mural nodule in segment 4 of the liver (Figure 1). An endoscopic retrograde cholangiography (ERC) showed stenosis of the B6-posterior biliary branch by compression of the cystic lesion, and there was no evidence of communication between the cystic lesion and the bile duct radiologically (Figure 2). Due to the preoperative diagnosis of mucinous cyst neoplasm, the patient underwent left hepatectomy. To complete the tumor resection, the B6-posterior biliary branch involved by the cystic tumor was resected and B6-posterior biliaryjejunal anastomosis was performed. Gross examination showed a liver cystic tumor 4 cm in diameter with a mural nodule displaying a smooth white inner surface (Figure 3). Microscopic observation revealed that part of the cyst was lined by a characteristic ciliated pseudostratified columnar epithelium surrounding the connective tissue, a slightly thick fibrotic smooth muscle stromal layer, and an outer fibrous capsule, compatible with a diagnosis of CHFC (Figure 4A, B). Most of the inner surface was lined by metaplastic squamous epithelium. In and around the mural nodule area, an atypical squamous hyperplasia with hyperkeratosis and anisonucleosis, numerous nuclear divisions, and disordered nuclear polarity were observed. Stromal invasion was observed at the base of the mural nodule. Immunohistochemically, p53 was found to be overexpressed in dysplastic squamous cells. The high-grade dysplasia and the stromal invasion led to a diagnosis of well-differentiated SCC arising from CHFC (Figure 5A, B). No vascular invasion was identified. The resection margins were negative for malignancy. There was evidence of communication between the cystic lesion and the B6-posterior biliary branch microscopically. At 12 months of follow-up, a recurrent lesion was detected in segment 5 of the liver. The patient underwent partial hepatectomy. At 18 months of follow-up, surveillance CT

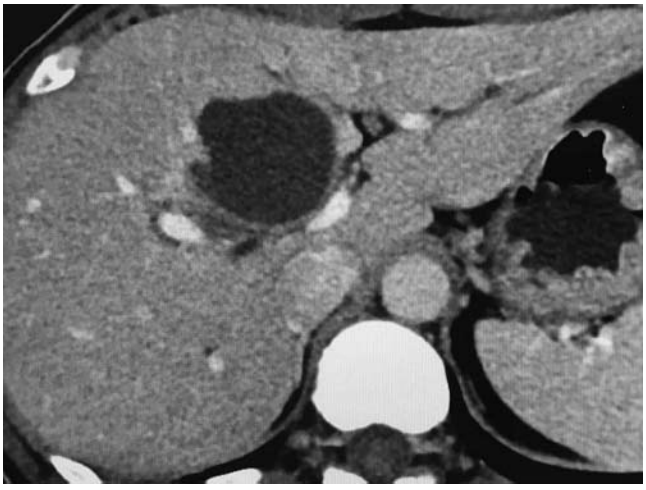

Figure 1. A computed tomography scan of the abdomen showed a cystic region including calcification and solid mass in segment 4 of the liver.

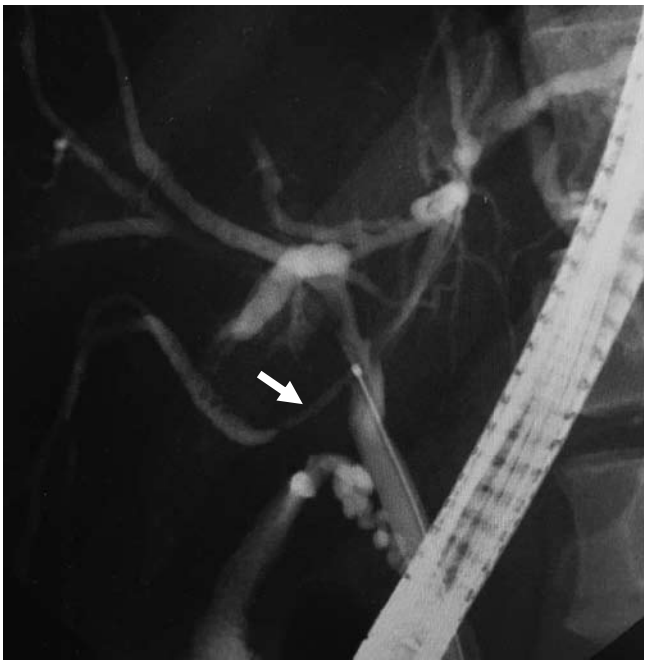

Figure 2. An endoscopic retrograde cholangiography showed stenosis of the B6-posterior biliary branch by compression of the cystic lesion. There was no evidence of communication between the cystic lesion and the bile duct. Arrow indicates the stenosis of the B6-posterior biliary branch.

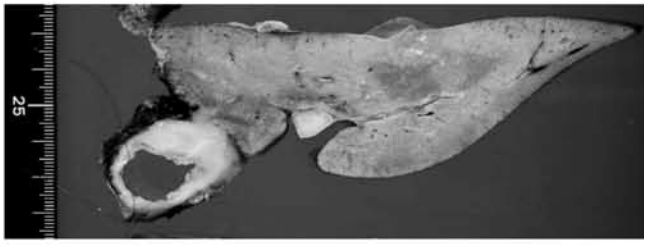

Figure 3. Gross examination showed a liver cystic tumor with a mural nodule displaying a smooth white inner surface.

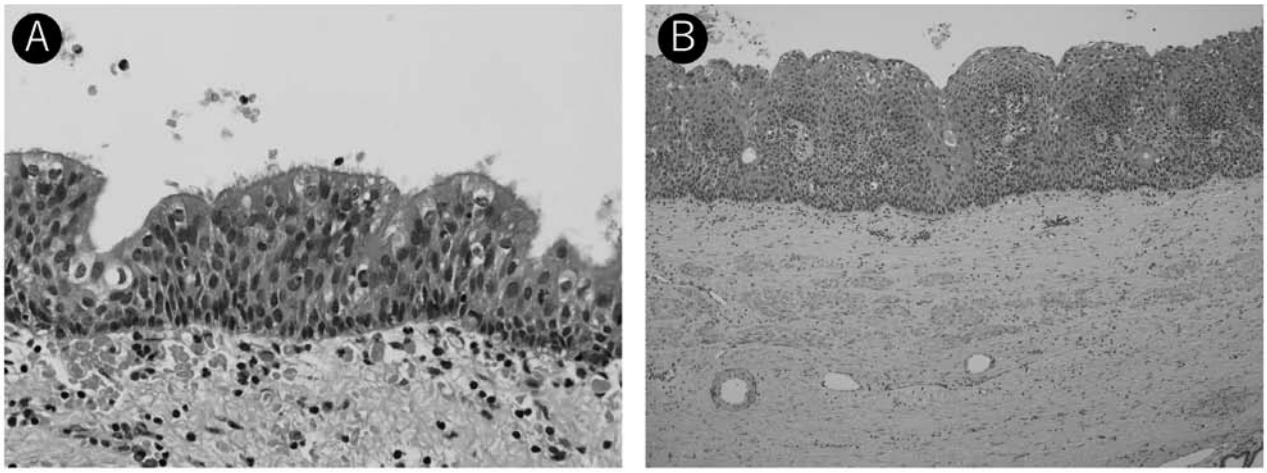

Figure 4. (A) Part of the cyst was lined by a characteristic ciliated pseudostratified columnar epithelium. (B) Most of the inner surface was lined by a metaplastic squamous epithelium surrounding connective tissue, a slightly thick fibrotic smooth muscle stromal layer, and an outer fibrous capsule.

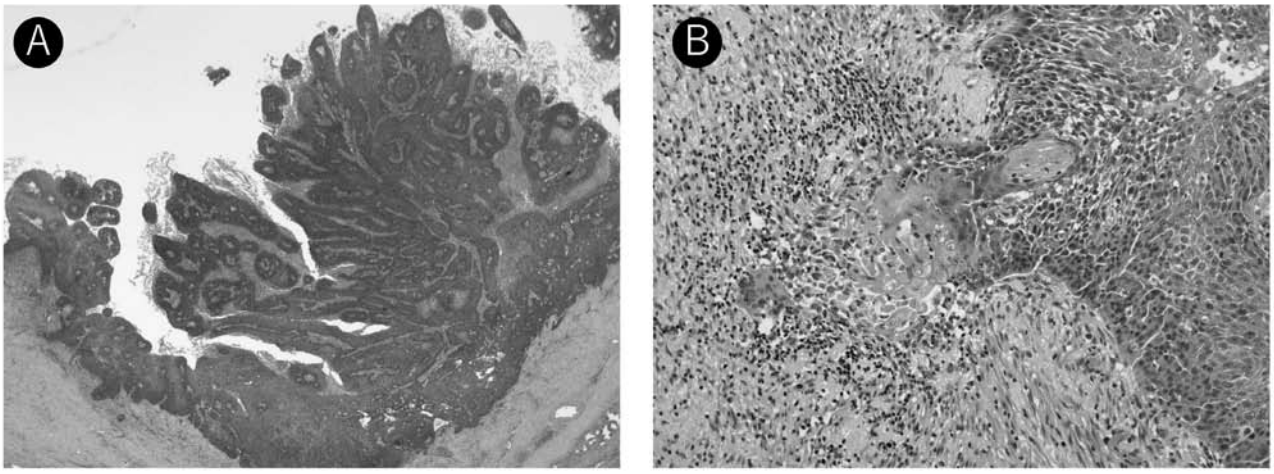

Figure 5. (A) In and around the papillary mural nodule, atypical squamous hyperplasia with mild hyperkeratosis was observed. (B) High-grade dysplasia with anisonucleosis, mitotic figures, and disordered nuclear polarity were observed. At the base of the nodule, the basement membrane was destroyed, and tumor cell invasion into the connective tissue was found to be associated with inflammatory cell infiltration.

demonstrated evidence of extrahepatic recurrence as peritoneal dissemination. At 30 months of follow-up, the patient is currently receiving systemic chemotherapy using docetaxel.

Discussion

CHFC is rare lesion believed to arise during embryonic development. The foregut extends from the oropharynx to the hepatic diverticulum. The oropharynx, esophagus, stomach, duodenum, liver, gallbladder, pancreas, tracheobronchic tree, and lungs develop as a consequence of the branching of the foregut. At 4 weeks, the embryo liver appears as a diverticulum from the ventral part of the last area of the foregut. CHFC may occur as either an anomalous, detached primordium of the hepatic diverticulum or an independent bud from the nearby enteric foregut[5,8]. CHFC usually presents as incidental and mostly asymptomatic findings at autopsy, during surgery, or on imaging studies. To our knowledge, only 5 other cases of carcinomatous degeneration of CHFC have been published in the English literature[3-7]. As our case shows, neoplastic transformation of CHFC would arise from squamous dysplasia. The observation of gradually increasing expression of p53 supports this hypothesis. While our patient is alive with recurrence after 30 months of follow-up, 3 of the 5 cases in the literature died or relapsed within a year[3,4,7]. Since there is no evidence of available chemotherapy, surgical resection is the only therapeutic approach thus far. However,

our case and the 5 other reports suggest that primary SCC of the liver arising from a CHFC is an aggressive malignancy with a poor prognosis. Therefore, accurate diagnosis and sufficient treatment are crucial. Unfortunately, it is often difficult to distinguish a malignant transformation of CHFC from a neoplastic cyst radiographically. Interestingly, while most benign CHFC rarely exceed 4 cm in diameter and average approximately 3.0 cm^9, malignant transformation has resulted in diameters larger than 4 cm, and our case is the smallest of the reported SCC cases. And the fact that all SCC cases had any symptoms such as vague fullness or pain of the right upper quadrant, fever, or weight loss. We detected a communication between the cystic lesion and B6-posterior biliary branch; imaging easily showed the resultant inflammation and expansion. This, in turn, would cause the cyst to become symptomatic and to grow. Chronic inflammation of the epithelium of the cyst may occur in a malignant tumor. Given the previous and present findings, if we could detect a relatively large CHFC by chance, then careful clinical follow-up of potentially malignant lesions should be performed, and such lesions should be excised if they show any clinical manifestation[10].

Conclusions

We reported a case of surgical resection for well-differentiated SCC arising in a CHFC. Neoplastic transformation would arise from squamous dysplasia. Surgical excision is strongly recommended for SCCs that are larger than 4 cm in diameter or that show any clinical manifestation.

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