

Ciliated hepatic foregut cyst with high intra-cystic carbohydrate antigen 19-9 level

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Abstract

A ciliated hepatic foregut cyst (CHFC) is a rare foregut developmental malformation usually diagnosed in adulthood. Five percent of reported cases of CHFC transform into squamous cell carcinoma. We report the presentation, evaluation, and surgical management of a symptomatic 45-year-old male found to have a 6.2 cm CHFC. Contrast tomography-guided fine-needle aspiration

demonstrated columnar, ciliated epithelium consistent with the histologic diagnosis of CHFC. The intracystic levels of carbohydrate antigen (CA) 19-9 and carcinoembryonic antigen (CEA) were extremely high (978118 U/mL and 973 µg/L, respectively). Histologically, the wall of the cyst showed characteristic pseudopapillae lined with a ciliated stratified columnar epithelium, underlying smooth muscle, an outer fibrous layer and no atypia. Immunohistochemistry for CA19-9 and CEA was positive. This is the first case report of a CHFC in which levels of CA 19-9 and CEA were measured. Our findings suggest that a large sized multilocular cyst and elevated cyst CA19-9 and CEA levels do not exclude a CHFC from consideration in the diagnosis. CHFCs should be included in the differential diagnosis of hepatic lesions. Accurate diagnosis of a CHFC is necessary given its potential for malignant transformation, and surgical excision is recommended.

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Key words: Ciliated hepatic foregut cyst; Carbohydrate antigen 19-9; Carcinoembryonic antigen; Computed tomography-guided fine-needle aspiration; Magnetic resonance imaging; Squamous cell carcinoma

Core tip: A ciliated hepatic foregut cyst (CHFC) is a rare foregut developmental malformation usually diagnosed in adulthood. Five percent of reported CHFC cases transform into squamous cell carcinoma. We report the evaluation and surgical management of a symptomatic 45-year-old male found to have a 6.2 cm CHFC diagnosed by an intracystic columnar, ciliated epithelium. We report for the first time extremely high intracystic level of carbohydrate antigen (CA) 19-9 and no atypia. A large sized multilocular cyst and elevated cyst CA19-9 do not exclude CHFCs from diagnostic consideration. Given its potential for malignant transformation, surgical excision is recommended.

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INTRODUCTION

Ciliated hepatic foregut cysts (CHFCs) are extremely rare congenital, benign, most often solitary and unilocular cystic lesions that arise from the embryonic foregut^[1]. The developmental origin may account for the specific histologic features of a pseudostratified, ciliated, mucin-secreting, columnar epithelium^[1]. Ciliated hepatic foregut cysts were first described by Friedrich in 1857, and approximately 100 cases of CHFCs have been reported so far^[2-8]. Most CHFCs are located in the fourth segment of the liver. Malignant transformation to squamous cell carcinoma (SCC) has been reported, and although this is rare, the survival rate after progression to malignancy is poor^[9]. In addition, it is often difficult to distinguish, clinically and radiographically, CHFC from neoplastic cysts such as hepatobiliary cystadenoma and cystadenocarcinoma. While nonneoplastic cysts are characteristically small, unilocular (simple), asymptomatic, and are without malignant potential, neoplastic cysts are large, multilocular, symptomatic, and must be completely excised because of their malignant metastatic potential^[10-12]. Therefore, early and accurate diagnosis is important, and a CHFC should be included in the differential diagnosis of hepatic cysts. We present a case of an unusual CHFC in a 45-year-old male that was large, bilocular, and associated with extremely high cyst levels of carbohydrate antigen (CA) 19-9 and carcinoembryonic antigen (CEA), which is described for the first time.

CASE REPORT

A 45-year-old male complained of a 1-year history of intermittent peri-umbilical pain associated with 13 kg weight loss. There was no associated jaundice or rigors. In his physical examination, fullness was palpated over his epigastrium. Liver function tests were unremarkable. An abdominal ultrasound scan reported a 45 mm diameter complicated, heterogeneous, avascular, cystic lesion in segment 4, with no intrahepatic or extra biliary dilatation or gallstones. Computed triple-phase contrast tomography (CT) and magnetic resonance imaging (MRI) (Figure 1) confirmed a large, solitary 45 mm diameter multilocular cystic mass in segment 4. There were no other mass lesions. The cyst was hypoechoic in ultrasound, hypoattenuating in unenhanced CT, and did not enhance on administration of contrast in CT or MRI. The serological levels of α -fetoprotein, CA19-9 and CEA were within normal limits. Six months later, a

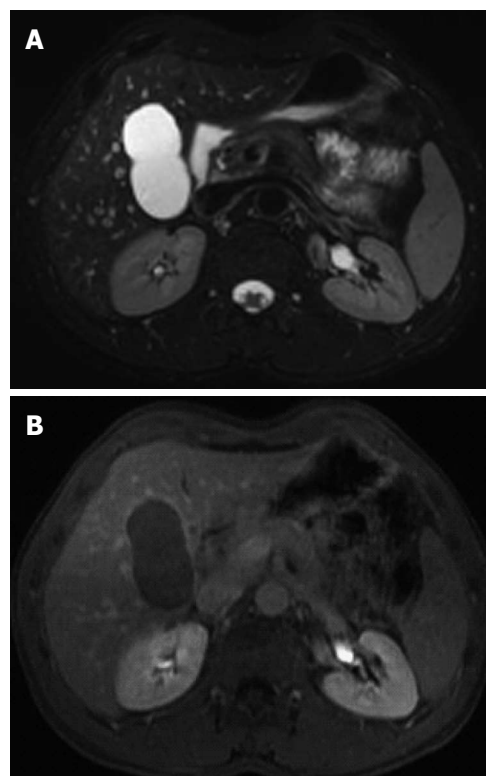


Figure 1 Magnetic resonance imaging. A: With contrast; B: Without contrast. Magnetic resonance imaging demonstrates a 6.2 cm multilocular cystic lesion in segment 4. The cyst content was heterogeneous and avascular and included proteinaceous material. No wall enhancement was detected.

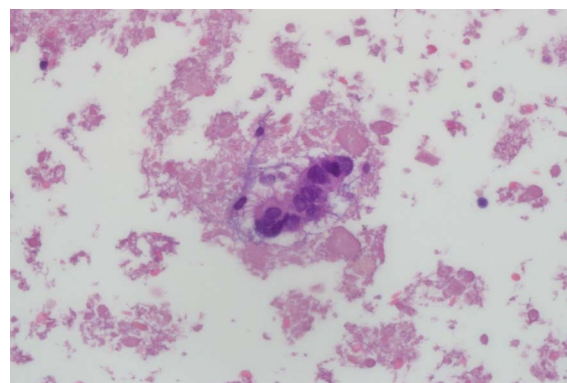


Figure 2 A computed tomography-guided diagnostic fine-needle aspiration revealed ciliated epithelial cells with no atypia.

repeat MRI demonstrated that the diameter of the cystic lesion had increased in size to 6.2 cm and that the cyst content was heterogeneous and avascular and included proteinaceous material. No wall enhancement was detected. CT-guided diagnostic fine-needle aspiration revealed ciliated epithelial cells with no atypia consistent with the diagnosis of CHFC (Figure 2). The intracystic levels of CA19-9 and CEA were extremely high (978118 U/mL and 973 μ g/L, respectively). There was no evidence of malignancy. Magnetic resonance cholangiopancreatography did not disclose a communication between the cyst and the biliary system. In view of the diagnostic

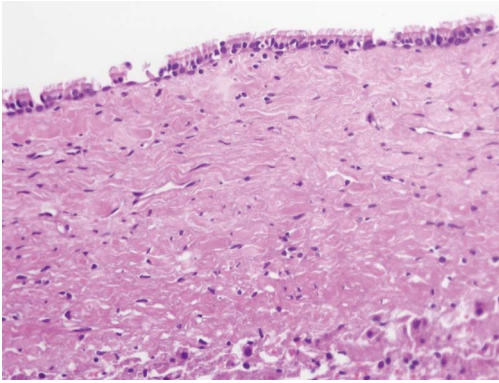


Figure 3 Wall of the cyst. Histologically, the wall of the cyst showed characteristic pseudopapillae lined by ciliated stratified columnar epithelium, loose subepithelial connective tissue, underlying smooth muscle and an outer fibrous layer and no atypia, compatible with diagnosis of a ciliated hepatic foregut cyst.

uncertainty, the cyst was excised. Grossly, the cyst was multilocular, 6 cm in greatest diameter, and contained viscous fluid. Histologically, the wall of the cyst showed characteristic pseudopapillae lined with ciliated stratified columnar epithelium, loose subepithelial connective tissue, underlying smooth muscle, an outer fibrous layer and no atypia, compatible with a diagnosis of a CHFC (Figure 3). Immunohistochemistry for CA19-9 (Figure 4A) and CEA (Figure 4B) was positive.

DISCUSSION

A CHFC is a rare, congenital hepatic lesion characterized by its ciliated columnar epithelial lining. Because of the asymptomatic nature of CHFC, the majority of cases are found incidentally during imaging studies, autopsy, or surgery^[2]. Most cysts are not detected until the fourth decade of life, while some patients may present with right upper abdominal pain, obstructive jaundice, or portal hypertension^[2]. Increased use of abdominal imaging techniques has improved detection rates of CHFC, thus explaining why over 85% of cases have been reported in the past 20 years^[2,6]. The cyst diameter size, at 6.2 cm, was larger than the mean diameter of all previously reported cases of CHFC (> 4 cm)^[2]. In addition, the cyst was multilocular, which is a rare presentation in adult cases of CHFC compared with a previous reported study where over 90% of adult cases of CHFC were unilocular^[2]. However, the cyst was histologically similar to those in the cases previously described.

While the typical clinical course of CHFC is benign, 5 previously reported adult patients had malignant transformation to SCC^[2,9], comprising approximately 5% of all reported CHFCs. This frequency, taken together with the aggressive disease course and poor prognosis, suggests that a CHFC must not be presumed benign and should be regarded with clinical suspicion^[9]. Accurate diagnosis of a CHFC is mandatory given its potential for malignant transformation, and surgical excision is recommended.

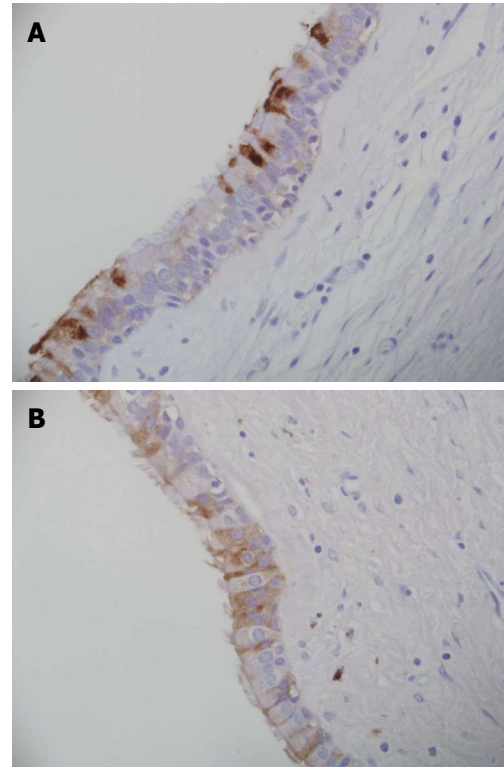


Figure 4 Immunohistochemistry. A: Carbohydrate antigen (CA) 19-9: Some cells, including ciliated ones show apical staining for CA19-9; B: Carcinoembryonic antigen (CEA): Few cells show weak positivity for CEA.

Hepatic biliary cystadenoma and cystadenocarcinoma are often difficult to distinguish clinically and radiographically from CHFCs. Cystadenoma and cystadenocarcinoma are mostly large, multilocular, and symptomatic and include mural nodules and papillary projections, calcifications and wall enhancements^[13]. Aspiration of biliary cystadenoma often demonstrates bile-tinged mucin that can allow differentiation from a CHFC, apart from the obvious ciliated epithelial cells detected in CHFCs. With adequate tissue sampling, cytology can reveal malignant glandular cells and mucin, suggesting biliary cystadenocarcinoma, although these cells are rarely identified^[13]. The role of cyst fluid CEA, CA19-9, and serum tumor markers remains controversial. Although many providers may measure CA19-9, the sensitivity and specificity are not high enough to differentiate a cystadenoma from cystadenocarcinoma^[13]. Fuks *et al*^[14] have recently assessed the ability of intracystic tumor marker concentrations to differentiate hepatic simple cysts from malignant or premalignant mucinous cystic lesions such as biliary cystadenomas. Unlike CEA and CA19-9, a tumor-associated glycoprotein 72 level of more than 25 units/mL differentiated hepatic simple cysts from mucinous cysts, with a sensitivity and a specificity of 0.79 and 0.97, respectively^[14]. We have detected for the first time in our case of CHFC, extremely high levels of cystic fluid CEA and CA19-9. We assume that the epithelial cells lining the cyst can produce mucin, and we have demonstrated that they are also immunoreactive to cytokeratins

CA19-9 and CEA.

Thus, we have presented an unusual case of CHFC that was large, multilocular, and associated with high cystic levels of CA19-9 and CEA. These findings clearly indicate that large size, multilocularity, and elevated CA19-9 do not exclude a CHFC from consideration in the diagnosis. More studies are required to elucidate the role of cyst CA19-9 and CEA levels in the diagnosis of CHFCs. Accurate diagnosis of a CHFC is necessary given its potential for malignant transformation, and surgical excision is recommended.

COMMENTS

Case characteristics

A 45-year-old male with a 1-year history of intermittent peri-umbilical pain.

Clinical diagnosis

Fullness was palpated over the epigastrium.

Laboratory diagnosis

Unremarkable liver function tests; serum levels of α -fetoprotein, carbohydrate antigen (CA) 19-9 and carcinoembryonic antigen (CEA) were within normal limits.

Imaging diagnosis

An abdominal ultrasound scan reported a 45 mm diameter complicated, heterogeneous, avascular, cystic lesion in segment 4. Contrast tomography (CT) and magnetic resonance imaging (MRI) confirmed a large, solitary 6.2 mm diameter multilocular cystic mass in segment 4. The cyst was hypoechoic at ultrasound, hypoattenuating in unenhanced CT, and did not enhance on administration of contrast in CT or MRI.

Pathological diagnosis

CT-guided diagnostic fine-needle aspiration revealed ciliated epithelial cells with no atypia consistent with the diagnosis of a ciliated hepatic foregut cyst (CHFC). The intra-cystic levels of CA19-9 and CEA were extremely high (978118 U/mL and 973 μ g/L, respectively). Histologically, the wall of the cyst showed characteristic pseudopapillae lined by ciliated stratified columnar epithelium compatible with a diagnosis of a CHFC. Immunohistochemistry for CA19-9 and CEA was positive.

Related reports

A CHFC is often difficult to distinguish clinically and radiographically from neoplastic cysts such as hepatobiliary cystadenoma and cystadenocarcinoma. Physicians do not have predictive biomarkers that indicate when a particular patient lesion is malignant.

Term explanation

A ciliated hepatic foregut cyst is an extremely rare congenital, benign, most often solitary and unilocular cystic lesion that arises from the embryonic foregut.

Experiences and lessons

A large size multilocular cyst and elevated cyst CA19-9 and CEA levels should not exclude a CHFC from diagnostic consideration. CHFCs should be included in the differential diagnosis of hepatic lesions. Accurate diagnosis of a CHFC is necessary given its potential for malignant transformation, and surgical excision is recommended.

Peer review

This article reports on an unusual case of ciliated hepatic foregut cyst that was

large, multilocular, and associated with a high intra-cystic levels of CA19-9 and CEA and not malignant.

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