

Cistoadenocarcinoma biliar

Biliary cystadenocarcinoma

INTRODUCTION

Biliary cystadenocarcinoma is an uncommon cystic tumor occurring in less than 5% of all hepatic tumors (1). Up till 1998, there have only been 113 cases reported in the literature (2). This tumor can arise in the liver or in the extrahepatic biliary system, which is less frequent (3). Cystadenocarcinomas are generally multiloculated (1). A palpable mass or hepatomegaly is the usual clinical finding (1). Cystadenocarcinomas normally contain hemorrhagic or chocolate-colored fluid (4, 5). It is postulated that biliary cystadenocarcinomas arise from a preexisting biliary cystadenoma (4). This is a report of a patient with biliary cystadenocarcinoma who was previously treated 1 year before this diagnosis for a biliary cystadenoma.

Unitermos: Biliary Cystadenocarcinoma, Cystic Liver Disease, Biliary Cystadenoma.

CASE REPORT

C.V.M., a 45-year-old white man presented with syncope, abdominal pain in epigastric region, pallor, diaphoresis and a large epigastric palpable mass. The computed tomographic (CT) images revealed a low-density cystic lesion in the liver, with internal septation in segments I, II, III and IV and parts of segments V and VIII (Figure 1). The patient was anemic at presentation. He was treated by partial cyst resection and electrocoagulation of the capsule in contact with the liver parenchyma because of the proximity of the medial hepatic artery. The liquid in the interior of the cyst was noted to be cloudy brownish. At operation, a liver cyst was also seen. The biopsy revealed hepatic adeno-

ma. The cytopathologic examination was negative for malignant cells as well as the culture tests. Other tests that were performed included: glucose, 16; proteins, 4.34; lactate dehydrogenase (DHL), 24.700; pH, 6.76; cholesterol, 71; carcino embryonic antigen (CEA), 17.865; CA 19-9, 329. The patient had an unremarkable postoperative course.

One year after his initial surgery, the patient began complaining of abdominal pain. A fixed, non-pulsating mass was detected in the right hypochondrium during abdominal examination. The laboratory tests were as follows: AST, 11 mU/mL; ALT, 26 mU/mL; alkaline phosphatase, 261 mU/mL; total protein, 7.3 g/dL; albumin, 3.6 g/dL; total bilirubin, 0.4 mg/dL. Abdominal computed tomographic imaging revealed a cystic lesion measuring 4.4 cm arising in previous resection edge until the dermis (Figure 2), enlargement of right abdominal wall and retus abdominal muscle and

AZAMBUJA E – Medical Oncologist, MD; Hospital de Clínicas de Porto Alegre.

BATISTA RG – Medicine Student; Universidade federal do Rio Grande do Sul – Hospital de Clínicas de Porto Alegre.

WAECHTER FL – Hepato-biliary-pancreatic Surgeon, MD; Hospital Moinhos de Vento.

SAMPAIO JA – Hepato-biliary-pancreatic Surgeon, MD; Hospital Moinhos de Vento.

ÁLVARES-DA-SILVA MR – Hepatologist, MD; Hospital Moinhos de Vento.

FLECK JF – Medical Oncologist, MD; PhD; Hospital de Clínicas de Porto Alegre.

Serviço de Oncologia – Hospital de Clínicas de Porto Alegre.

✉ Endereço para correspondência:

Dr. Evandro de Azambuja

Rua Ramiro Barcelos, 2350

90035-003 – Porto Alegre, RS, Brasil

Fone: (55)(51) 3316-8494

☎ (55)(51) 3328-4790

✉ e_brussels@hotmail.com or

evandro.azambuja@bordet.be

a nodular image in subcutaneous tissue measuring 3.0 cm (figure B).

On August 2002, he underwent a segmentectomy (V and VIII segments), resection of regenerated hepatic tissue, hepatic linfoadenectomy, abdominal wall and diaphragm resections. Microscopic examination showed a well differentiated biliary cystadenocarcinoma with adequate surgical margins

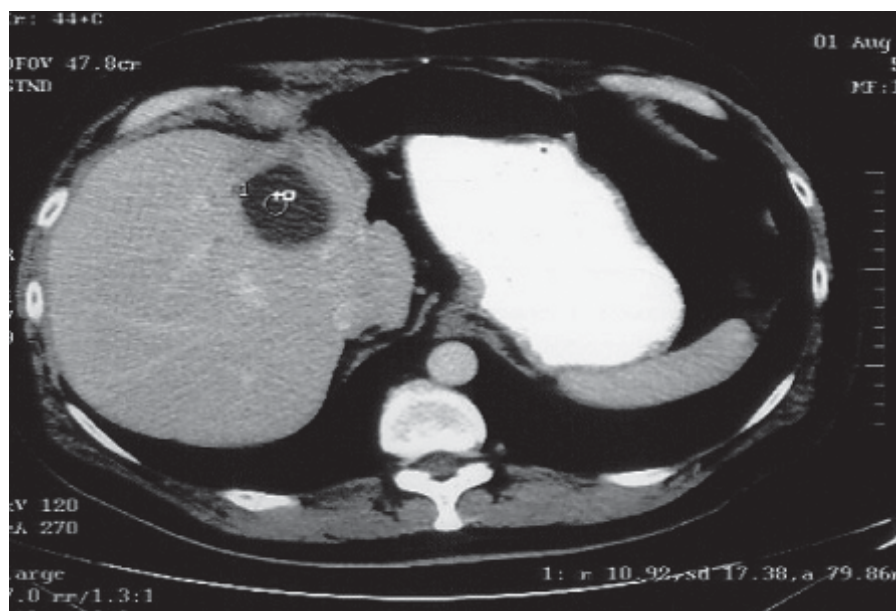


Figure 1 – cystic low-density lesion with internal septation.

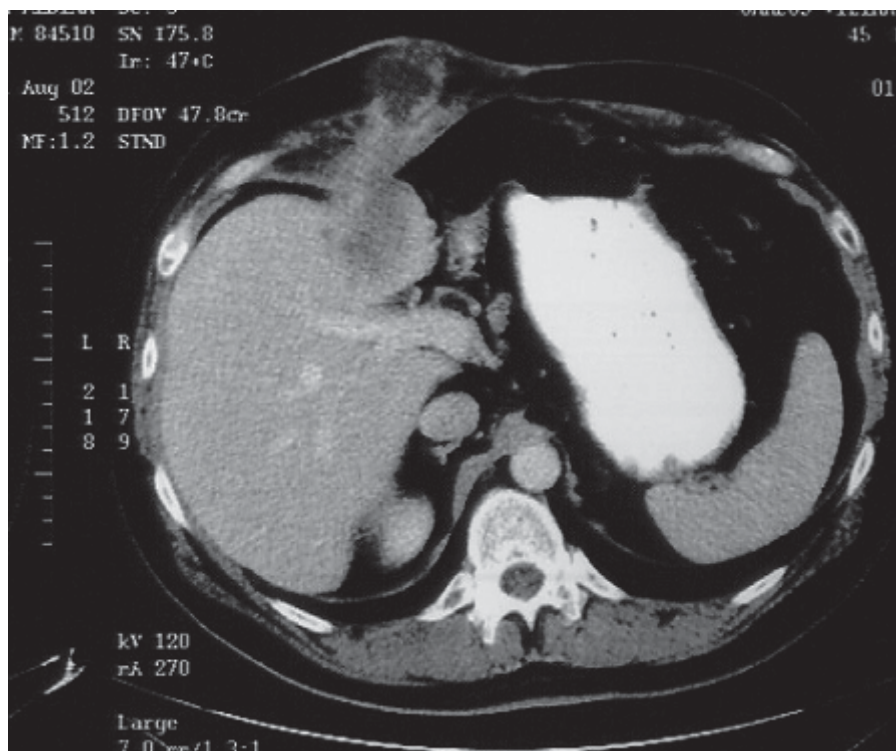


Figure 2 – cystic lesion measuring 4.4 cm arising in previous resection edge until the dermis.

(Figure 3). Postoperative laboratory tests were as follows: AST, 24 mU/mL; ALT, 76 mU/mL; alkaline phosphatase, 93 mU/mL; total protein, 5.3 g/dL; albumin, 3.3 g/dL; total bilirubin 0.55 mg/dL; gama GT, 57; DHL, 276; protorombine time, 58%; CEA, 1; CA 19-9, < 1. He was discharged 2 weeks later and after one month, he had recovered completely enough to returne to work. One year later he remains symptoms free.

DISCUSSION

Biliary cystadenocarcinoma is a rare malignant epithelial tumor of the hepatic tissue. Takayasu et al (6,7) reported an incidence of 0.41% among all hepatic malignant epithelial tumors. This tumor usually occurs in middle-aged women, having a less favorable prognosis in men (6). Approximately 85% of these tumors are intrahepatic and 15% are extrahepatic, localized in the biliary ducts or the gallbladder (8). A palpable mass or hepatomegaly is the

usual clinical finding, followed by abdominal pain or discomfort and elevated liver function tests (1,9). Non-specific clinical manifestations are variable and include upper abdominal mass, local pain, jaundice, ascites and weight loss (2,4,10). The most common symptom is obstructive jaundice when the tumor is located in extrahepatic region. Distant metastases are infrequent (3). Takayasu et al reported bone metastases in 1 patient and Cheung et al reported pulmonary metastases (7,11). Mucobilia (9), fibropolycystic disease (12), duodenal perforation or invasion (6, 13), peritoneal carcinomatosis (14), nausea (5) and recurrent jaundice (5) are uncommon manifestations of biliary cystadenocarcinoma.

Biliary cystadenocarcinoma has been described to arise from a congenital liver cyst, bile duct or biliary cystadenoma (15,16). Other proposed theory is that it develops from ectopic remnants of primitive foregut sequestered within the liver or from rests of embryonic gallbladder tissue. Because

90% of the biliary cystadenocarcinoma are composed of benign epithelium, it has been postulated that this tumor could arise from a previously benign cystadenoma (2).

These tumors can have a good prognosis if ovarian stroma is present. It occurs only in women. The subgroup of biliary cystadenocarcinomas tumors that are associated with a pre-existing cystadenoma is thought to have a particularly poor prognosis. This subgroup occurs in both men and women, has a more aggressive phenotype and a reported mortality of up to 50% (8). Is not clear if changes of atypia or dysplasia in the epithelium have the worst prognosis (8). Some parts of the tumor can display poor differentiation presenting anaplastic or sarcomatous transformation. It is possible that anaplastic alteration is associated with less aggressive invasion of the tumor (17). However compared with other primary malignancies of the liver, biliary cystadenocarcinomas has generally have more indolent disease, and are associated with a more favorable prognosis (2,18).

Histologically, biliary cystadenocarcinoma differs from biliary cystadenoma, because it presents with cellular pleomorphism, anaplasia and infiltration of the underlying fibrostroma. The malignant epithelium is typically multi-layered with numerous papillary projections, which breaks or erodes the basement membrane. Benign columnar epithelium is observed in 91% of the cases (9). The walls of the biliary cystadenocarcinoma are generally collagenous and hyalinized or relatively acellular (1). It could be due to this feature that a benign diagnosis was iniatially made in our patient. Sometimes an unusual case of biliary cystadenocarcinoma with oncocytic differentiation can occur (19). Biliary cystadenocarcinoma can be categorized as “noninvasive type” when the tumor is confined to the cyst wall without any invasion into the liver parenchyma or adjacents organs and “invasive type” for tumors extending through the diaphragm or surrounding liver tissue (17).

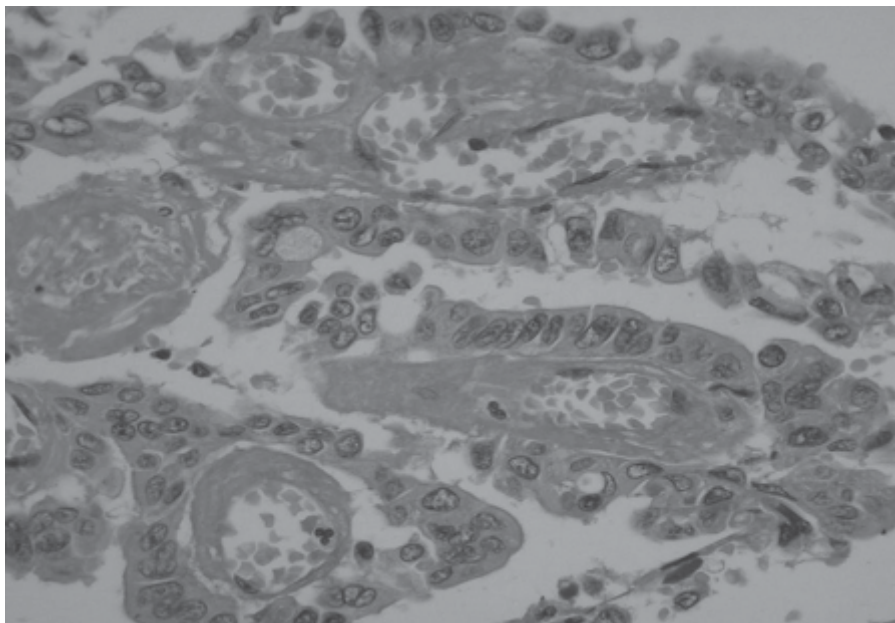


Figure 3 – a well differentiated biliary cystadenocarcinoma with no tumor in the surgical limits.

Immunohistochemical studies in cystadenocarcinoma show positive reactions with carcinoembryonic antigen (CEA), tissue polypeptide antigen, carbohydrate 19-9, and Dupan-2 (17). High levels of serum and cystic CEA and CA 19-9 seem to help in the diagnosis of cystadenoma but not cystadenocarcinoma. Histological evaluation is the only method to discriminate malignant from benign cysts (20).

Biliary cystadenocarcinoma can appear as an isolated unilocular cystic mass or as a multilocular cystic mass with multiple satellite tumors. The most characteristic manifestation are isolated multilocular cystic mass. On computed tomography (CT), these lesions are low-density, intrahepatic lesions with internal septa and mural nodules. These tumors contain mucinous, serous, bile-tinged or brownish cloudy fluid without cells (21). Irregular, papillary growths and mural nodules along the internal septa and wall are seen in biliary cystadenocarcinoma (21). Calcification is uncommon finding, however calcific foci in the septa and wall are rarely detected on CT and if the calcification is present, it indicates a more likely diagnosis of biliary cystadenocarcinoma (10, 22). In

this case, the patient presented with cystic lesion irregular walls, few septations, and no calcification seen on initial CT scan at the first surgery and cystic lesion with irregular walls. Drip infusion cholangiographic-CT, a simple and noninvasive examination may be the most useful for differentiating biliary cystadenoma/cystadenocarcinoma from other intrahepatic cystic lesions (23). Magnetic resonance imaging (MRI), because of increased contrast and spatial resolution, may be a more specific imaging modality in the detection of biliary cystic neoplasms (24).

Using hepatic angiography, biliary cystadenocarcinomas are seen as abnormal clusters of vessels within the walls and on delayed images, accumulation of contrast material within the wall of septa (21). Stretching of the thin hepatic arteries and irregular calibres of the peripheral arteries in the arterial phase and stains in the parenchymal phase are also demonstrated (7). On sonograms they appear as ovoid, cystic mass with multiple septa and papillary excrescences or fluid-fluid levels (21). Ultrasonography can show internal septa more accurately than CT (22).

In a study by Seo et al (25) using cholangioscopic findings to detect bile duct tumors, 2 patients (1.8%) were diagnosed as biliary cystadenocarcinoma among 111 patients being investigated for biliary masses. It was noted that laparoscopically the malignant lesions had larger cystic spaces and mucosal masses resembling “coral reef” compared with the benign-tumors.

The differential diagnoses that need to be considered in the investigation of a biliary tumor are that of an abscess, hydatid disease of the liver (8, 21), hematomas, echinococcal cyst, undifferentiated embryonal sarcoma and cystic metastasis (21).

With regards to establishing a diagnosis, fine needle aspiration biopsy is often avoided due to its potential to disseminate the tumor into the peritoneum (9, 13, 7). According to Iemoto et al (2, 14), aspiration or drainage should be performed carefully to avoid complications as peritoneal pseudomyxoma or carcinomatosis. Surgical excision is the treatment of choice for both benign and malignant lesions if there are no contraindications (6, 8, 9, 13).

In cystadenocarcinoma, total resection is the preferred treatment. In case of insufficient remaining liver tissue or location of the tumor near important arteries, crioterapy, micro-wave coagulation, or interstitial thermotherapy by laser are possible options. Radiofrequency ablation (RFA) of hepatic malignancies is a safe and promising technique for unresectable tumors and can be performed percutaneously, laparoscopically or during an open surgical procedure with low rates of morbidity, mortality and local recurrence. RFA can be combined safely with partial hepatic resection of large lesions (26).

No further treatment is usually required if the tumor is confined to the liver (2). At present there is no evidence to suggest that postoperative chemotherapy or radiotherapy are of benefit. In patients with metastatic disease, chemotherapy and / or radiotherapy have been used. Doxorubicin and 5-fluorouracil containing regimens have been previously reported in the literature with varying degrees of response (2).

The prognosis for the patients who have the tumor completely resected is good (12). The overall 5-year survival for patients with biliary cystadenocarcinoma who had been treated by surgical resection is 65-71%. If a complete surgical resection with negative histologic margins is achieved, a 5-year survival rate of 100% and a recurrence rate of 13% have been described (9).

REFERENCES

- ISHAK KG, WILLIS GW, CUMMINS SD, et al. Biliary cystadenoma and cystadenocarcinoma: report of 14 cases and review of the literature. *Cancer* 1977; 38: 322-338.
- LÄUFFER JM, BAER HU, MAURER CA, et al. Biliary cystadenocarcinoma of the liver: the need for complete resection. *Eur J Cancer* 1998; 34: 1845-1851.
- KIMURA H, KAGAWA K, DEGUCHI T, et al. Extrahepatic biliary cystadenocarcinoma arising from the left hepatic duct. *J Gastroenterol* 1998; 33: 895-898.
- WOODS GL. Biliary cystadenocarcinoma: case report of hepatic malignancy originating in benign cystadenoma. *Cancer* 1981; 47: 2936-2940.
- KANAMORI H, KAWAHARA H, OH S, et al. A case of biliary cystadenocarcinoma with recurrent jaundice. *Cancer* 1985; 55: 2722-2724.
- BACHER H, CERWENKA H, WERKGARTNER G, et al. Primary biliary cystadenocarcinoma perforating the duodenum and left intrahepatic biliary tree – mimicking a hydatid cyst. *Liver* 1999; 19: 39-41.
- TAKAYASU K, MURAMATSU Y, MORIYAMA N, et al. Imaging diagnosis of bile duct cystadenocarcinoma. *Cancer* 1988; 61: 941-946.
- BUETOW PC, BUCK JL, PANTON-GRAG-BROWN L, et al. Biliary cystadenoma and cystadenocarcinoma: clinical-imaging-pathologic correlation with emphasis on the importance of ovarian stroma. *Radiology* 1995; 196: 805-810.
- CHAMBERLAIN R, BLUMGART LH. Mucobilia in association with a biliary cystadenocarcinoma of caudate duct: a rare cause of malignant biliary obstruction. *HPB Surg* 2000; 11: 345-351.
- KINOSHITA H, TANIMURA H, ONISHI H, et al. Clinical features and imaging diagnosis of biliary cystadenocarcinoma of the liver. *Hepatogastroenterology*. 2001; 48: 250-252.
- CHEUNG YK, CHAN FL, LEONG LLY, et al. Biliary cystadenoma and cystadenocarcinoma: some unusual features. *Clin Radio*. 1991; 43: 183-185.
- THEISE ND, MILLER F, WORMAN HJ, et al. Biliary cystadenocarcinoma arising in a liver with fibropolycystic disease. *Arc Pathol Lab Med* 1993; 117: 163-165.
- STACHER R, SZOLAR DH, BACHER H, et al. Mucinous biliary cystadenocarcinoma containing gas bubbles secondary to duodenal invasion. *Br J Radiol* 1998; 71: 683-685.
- IEMOTO Y, KONDO Y, FUKAMACHI S. Biliary cystadenocarcinoma with peritoneal carcinomatosis. *Cancer* 1981; 48: 1664-1667.
- TOMIMATSU M, OKUDA H, SAITO A, et al. A case of biliary cystadenocarcinoma with morphologic and histochemical features of hepatocytes. *Cancer* 1989; 64: 1323-1328.
- KUBOTA E, KATSUMI K, IIDA M, et al. Biliary cystadenocarcinoma followed up as benign cystadenoma for 10 years. *J Gastroenterol*. 2003; 38: 278-282.
- NAKAJIMA T, SUGANO I, MATSUZAKI O, et al. Biliary cystadenocarcinoma of the liver. *Cancer* 1992; 69: 2426-2432.
- GOURLEY WK, KUMAR D, BOUTON MS, et al. Cystadenoma and cystadenocarcinoma with mesenchymal stroma of the liver. *Arch Pathol Lab Med* 1992; 116: 1047-1050.
- BARDIN RL, TRUPIANO JK, HOWERTON RM, et al. Oncocytic biliary cystadenocarcinoma: a case report and review of the literature. *Arch Pathol Lab Med*. 2004; 128: 25-28
- TRESALLET C, JORDI-GALAIS P, NGUYEN-THANH Q, et al. Cystadenoma of the liver with high levels of ACE and CA 19-9 in the cyst. *Gastroenterol Clin Biol* 2003; 27: 413-415.
- CHOI BI, LIM JH, HAN MC, et al. Biliary cystadenoma and cystadenocarcinoma: CT and sonographic findings. *Radiology* 1989; 171: 57-61.
- KOROBKIN M, STEPHENS DH, LEE JKT, et al. Biliary cystadenoma and cystadenocarcinoma: CT and sonographic findings. *Am J Roentgen* 1989; 153: 507-511.
- MATSUMOTO J, KONDO S, OKUSHIBA S, et al. DIC-CT findings of biliary cystadenocarcinoma communicating with the bile duct: a case report. *Hepatogastroenterology*. 2001; 48:1005-1006.
- WILLIAMS DM, VITELLAS KM, SHEAFOR D. Biliary cystadenocarcinoma: seven year follow up and the role of MRI and MRCP. *Magn Reson Imaging*. 2001; 19: 1203-1208.
- SEO DW, LEE SK, YOO KS, et al. Cholangioscopic findings in bile duct tumors. *Gastrointest Endosc* 2000; 52: 630-634.
- CURLEY SA. Radiofrequency ablation management of liver tumors. *Ann Surg Oncol* 2003; 10: 338-347.