

Computed tomography of biliary cystadenoma and biliary cystadenocarcinoma

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ABSTRACT

Introduction: Biliary cystadenoma (BCA) and biliary cystadenocarcinoma (BCAC) are rare biliary ductal neoplasms of the liver. This study aims to describe the computed tomography (CT) findings of these neoplasms and to distinguish between both entities.

Methods: We retrospectively reviewed the CT findings of five patients with proven BCA and seven patients with proven BCAC at our institution from July 2000 to August 2006. The CT parameters were analysed, including number, size, location, and characteristics of the cystic lesion: presence and number of internal septation, calcifications and enhanced mural nodule.

Results: All 12 patients had a solitary, large well-defined intrahepatic cystic lesion. Lesions in all five patients with proven BCA (100 percent) and six patients with proven BCAC (86 percent) had a multilocular appearance. The remaining patient with proven BCAC had a unilocular lesion. Smooth, thin septa and walls were found in five patients with BCA (100 percent). The enhanced mural nodule at the septum or wall was identified in seven patients with BCAC (100 percent) but was not found in the BCA patients (p-value is less than 0.001). The other parameters including size, location and number of septa had no statistically significant differences between BCA and BCAC.

Conclusion: BCA and BCAC should be considered in the differential diagnosis, when a solitary large well-defined multilocular intrahepatic cystic lesion is detected in a middle-aged woman. The presence of an enhanced mural nodule is the most important finding to suggest BCAC.

Keywords: biliary cystadenocarcinoma, biliary cystadenoma, biliary ductal tumour, computed

tomography, liver neoplasm

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INTRODUCTION

Biliary cystadenoma (BCA) and biliary cystadenocarcinoma (BCAC) are rare biliary ductal neoplasms and account for less than 5% of intrahepatic cystic lesions of biliary origin. BCA is considered a benign lesion with malignant potential, whereas BCAC is a malignant lesion.⁽¹⁻⁶⁾ The treatment of choice for these neoplasms is surgical. However, the surgical procedure for treatment of BCAC is more aggressive than that of BCA; the former should be totally excised with a wide margin of normal liver tissue.⁽⁷⁻⁹⁾ It is important to differentiate these neoplasms from other more common hepatic cystic lesions, such as simple cysts, abscesses, hydatid cysts and metastases, which have different treatments. Preoperative radiological imaging, particularly computed tomography (CT), plays an important role in recognising and characterising the lesion. Radiological features of these neoplasms are difficult to distinguish accurately from other hepatic cystic lesions. Familiarity with the characteristic radiological features may provide enough information to arouse suspicion of BCA and BCAC, and to prevent delayed treatment. This study aims to describe common CT findings in BCA and BCAC. We also evaluate the role of CT in distinguishing BCA from BCAC, and review the literature.

METHODS

This study was approved by our institutional review board. We retrospectively reviewed the clinical histories and radiological features of five patients with pathologically proven BCA, six patients with BCAC, and one patient with BCAC and squamous cell carcinoma, at our institution from July 2000 to August 2006. All 12 patients were proven by surgery, with right hepatectomy in five patients, left hepatectomy in four patients, cyst enucleation in two patients and marsupialisation in one patient. The demographical and clinical findings were taken from medical records. CT was obtained for all 12

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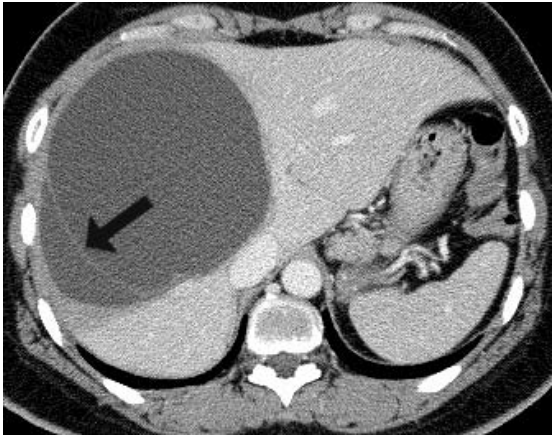


Fig. 1 A 42-year-old woman with BCA in the right lobe of the liver. Enhanced CT image shows a large cystic mass with a single smooth, thin internal septation (arrow) in the anterior segment of the right hepatic lobe. A smooth thin wall is seen without internal mural nodules.

patients, with a 16-slice multidetector (16-MDCT) scanner (Aquilion 16, Toshiba, Tochigi-Ken, Japan) in six patients and a conventional scanner (Cytec 3000i, General Electric Medical Systems, Milwaukee, WI, USA) in six patients. The CT protocols for each patient varied, depending on the CT machines. For the 16-MDCT, unenhanced CT study of the liver was performed. Dynamic study consisted of a total volume of 100 ml of ionic or nonionic intravenous contrast material (350 mg I/ml) administered at a rate of 2–3 ml/sec, with a scanning delay of 25 seconds for the hepatic arterial phase and 65 seconds for the portal venous phase. The examinations were performed using spiral technique. The images were retrospectively reviewed on thick 7-mm reconstruction thickness and thin 2-mm reconstruction thickness. For the conventional CT machine, unenhanced and portovenous phase-enhanced CT were performed with 10-mm reconstruction thickness and interval.

The following imaging parameters were evaluated: number, size, location, characteristics of cystic lesion including presence and number of internal septations, presence of enhanced mural nodule at wall or septum, wall or internal septal calcification, and bile duct communication. We classified the number of septations into three groups. The unilocular lesion was defined as no septum within the cystic lesion. A few septations were defined as the presence of up to three septum. Multiple septations were defined as more than three septa within the cyst. The CT findings were analysed by consensus review of two abdominal radiologists. The significant statistical difference of each parameter between BCA and BCAC were analysed using Fisher's exact test and Mann-Whitney test.

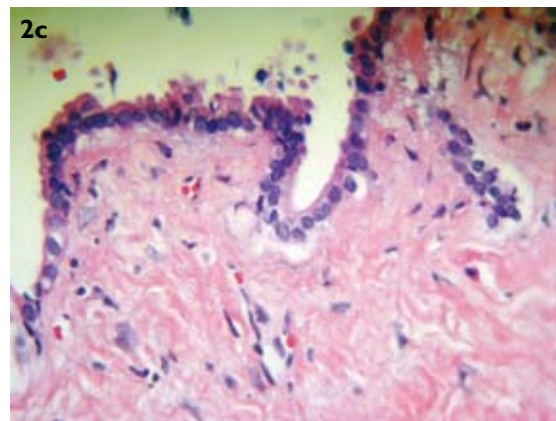
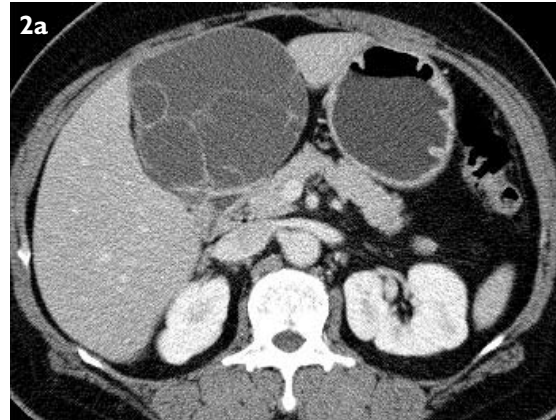


Fig. 2 A 51-year-old woman with BCA in the medial segment of the left lobe of the liver. (a) Enhanced CT image shows a well-defined cystic mass with multiple smooth, thin internal septations and smooth, thin wall without enhanced mural nodule. (b) Gross photograph of the resected cystic mass shows a large, opened cystic locule and several small cystic lesions containing viscous green content. The cyst wall is smooth and glistening. (c) Photomicrograph of the epithelial lining on the cystic wall shows tall columnar cells with bland-looking round nuclei (Haematoxylin & eosin, x 40).

RESULTS

All five patients with proven BCA were female with a mean age of 40.6 (range 30–51) years. For the seven patients with BCAC, five were female and two were male, with a mean age of 51.3 (range 41–63) years. All 12 lesions appeared as well-defined, solitary cystic lesions

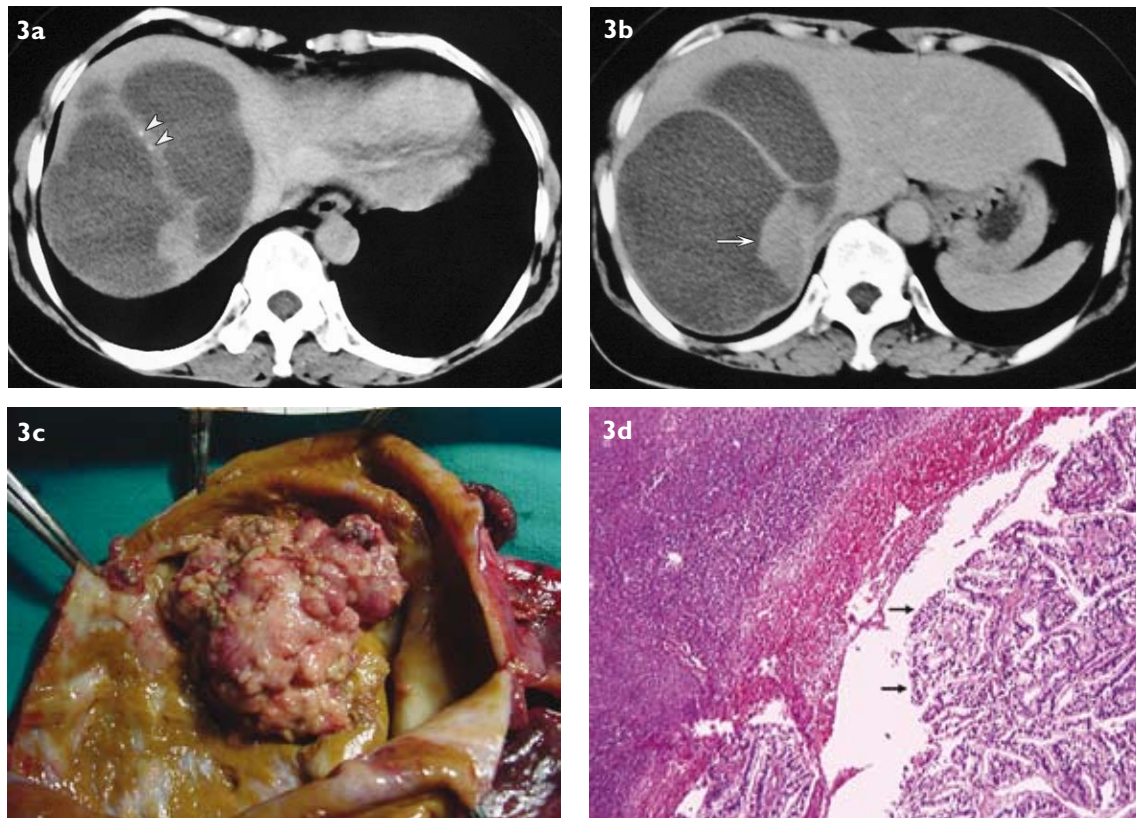


Fig. 3 A 52-year-old woman with BCAC in the right lobe of the liver. (a-b) Enhanced CT images show a large cystic mass with a few irregular, thick internal septations. Faint punctate calcification at internal septation is noted (arrowheads). An enhanced mural nodule is also seen (arrow). (c) Photograph of the opened cystic lesion shows a thick fibrous capsule together with a large solid growth with irregular surface attached to the inner surface. There are retained bile pigments on the cystic wall. (d) Photomicrograph of the attached tumour mass on the haemorrhagic cyst wall shows a tumour mass formed as polypoid growth (arrows) consisting of tall columnar cells bearing bizarre hyperchromatic nuclei. Papillary growth pattern with thin fibrovascular cores is prominent (Haematoxylin & eosin, x 10).

Table I. The CT features of five patients with BCA and seven patients with BCAC.

CT parameters	BCA (n = 5)	BCAC (n = 7)	p-value
Mean size (range) (cm)	12 (8–18)	11.9 (8–20)	1.0
No. (%) septate			
Unilocular	0 (0)	1 (14.3)	0.454
A few ≤ 3 septa	3 (60)	2 (28.6)	
Multiple > 3 septa	2 (40)	4 (57.1)	
No. (%) all or septate calcification	0 (0)	2 (28.6)	0.470
No. (%) enhanced mural nodule at wall and septum	0 (0)	7 (100)	0.001

in the liver. The mean size of BCA was 12.0 (range 8–18) cm, and the mean size of BCAC was 11.9 (range 8–20) cm. Of the 12 lesions, seven lesions were located in the right lobe (58.3%), four in the left lobe (33.3%) and one in both lobes (8.3%). All five patients with BCA (100%) (Figs. 1 & 2) and six of seven patients with BCAC (86%) (Figs. 3 & 4) had a multilocular appearance on CT. The remaining patient had a large, unilocular cystic lesion with

enhanced, irregular mural nodules along the wall. This patient had pathologically-proven BCAC with squamous cell carcinoma (Fig. 5). The CT findings of 12 patients are shown in Table I. No communication between bile duct and cystic neoplasm was identified in any of the 12 patients. Of these morphological parameters, the only statistically significant difference between both neoplasms was the presence of an enhanced mural nodule at the wall or septum, which was identified in all seven patients with BCAC (100%), but was not found in any of the five patients with BCA (0%) ($p < 0.001$). Tumour size, location, number of septations and presence of calcification were not statistically significant parameters between both neoplasms (Table I).

DISCUSSION

BCA and BCAC are rare cystic neoplasms arising from the hepatobiliary epithelium.⁽¹⁻³⁾ However, these cystic neoplasms are being discovered more frequently because of technological advances in abdominal imaging and an increased awareness of these entities. Although they may occur in any portion of the biliary tree, they are most commonly located intrahepatically, accounting for

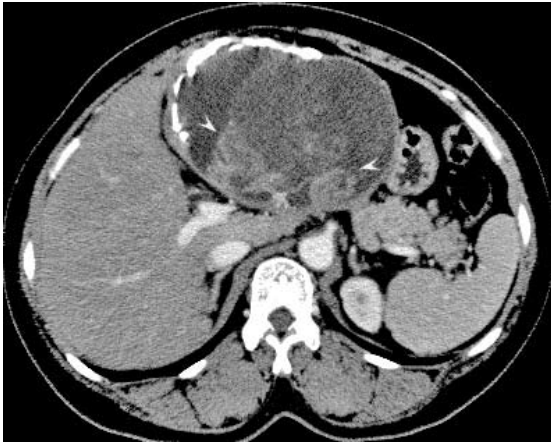


Fig. 4 A 52-year-old woman with BCAC in the lateral segment of the left lobe of the liver. Enhanced CT image shows a large cystic mass with irregular, thick calcified wall and a large enhanced mural nodule (arrowheads) within the larger locule.

83% of cases. Of the remainder, 13% are located in the extrahepatic bile duct and 0.02% are in the gallbladder. Among intrahepatic lesions, 55% occur in the right lobe, 29% occur in the left lobe and 16% occur in both lobes.^(5,6)

The clinical manifestations of these neoplasms are variable and nonspecific. More than 80% of BCA and 63% of BCAC occur in women, and more than 80% are seen in patients older than 30 years of age.⁽¹⁾ In our study, 100% of BCA and 71.4% of BCAC occurred in women, with a mean age of 51.3 years. The diagnosis of these neoplasms is difficult preoperatively. Even though these neoplasms arise from the hepatobiliary epithelium, the serum carbohydrate antigen (CA) 19-9 and carcinoembryonic antigen are usually within the normal range. A recent study from surgery proposed cyst fluid analysis for CA 19-9 preoperatively to help diagnosis, but there is the possibility of carcinomatosis following cyst aspiration or biopsy.^(10,11) Therefore, preoperative radiological imaging, particularly CT, plays a key role to recognise and suggest BCA and BCAC, prior to definite surgical resection.^(7,8,11,12)

The characteristic radiological features of BCA and BCAC are usually a solitary, large, well-defined multilocular cystic lesion. The thick fibrous capsule and internal septations are often visible and help distinguish these lesions from a simple cyst. Finding smooth and thin internal septa are indicative of BCA. The presence of septation with nodularity or mural nodule is suggestive of BCAC, although these mural nodules are seen in both BCA and BCAC, but more commonly in BCAC. Calcifications along the wall and internal septum are uncommon and are variable in appearances, including fine, punctate, curvilinear, or coarse.⁽¹³⁻¹⁵⁾ The presence of coarse calcifications is suggestive of BCAC.^(7,14) In our study, although calcification was uncommon (28.6%), it

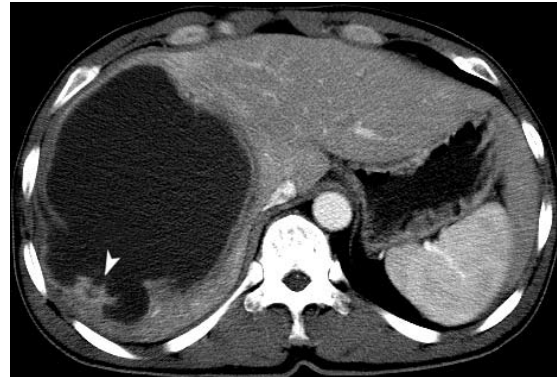


Fig. 5 A 47-year-old man with mixed BCAC and squamous cell carcinoma in the right lobe of the liver. Enhanced CT image of liver shows a large, unilocular cystic mass with enhanced thickened wall and irregular mural nodules (arrowhead) along the posterior wall.

was identified only in BCAC. Unilocular lesion has been reported, and is often incorrectly diagnosed as a simple cyst, which results in inadequate therapy.^(1,13-15) However, a unilocular lesion in our study had been diagnosed as BCAC preoperatively, because of the presence of enhanced mural nodules along the wall on preoperative CT. This patient had pathologically-proven BCAC and squamous cell carcinoma. Bile duct dilatation in BCA and BCAC may be present, which commonly results from extrinsic compression and less commonly from intraductal protrusion. Communication to biliary tree has been reported, but was not found in our study.^(13,15,16)

Regarding which parameters help distinguish BCAC from BCA, our results were similar to those of previous studies, which noted that the presence of internal septations with enhanced mural nodules were suggestive of BCAC.⁽¹³⁻¹⁵⁾ The distinction of BCA and BCAC preoperatively is important for surgical planning. The treatment of BCAC is at least complete excision, which means complete tumour resection with a wide margin of normal liver tissue or a typical lobectomy.⁽⁷⁻⁹⁾ In contrast, the effective treatment of BCA includes complete cyst enucleation, which means total removal of the cystic tumour by dissecting the cyst wall from normal liver tissue, and more aggressive complete excision, depending on patient status, tumour size and location, and sometimes, the inability to conclusively distinguish radiologically the BCA from BCAC.^(1,7,8) The two disorders most likely to be confused with these neoplasms are liver abscess and hydatid cyst of the liver. The combination of clinical and laboratory findings, including serological tests, should point to an infectious cause of these cases. The cystic dilatation of the intrahepatic bile duct from mucin hypersecreting intraductal papillary tumour of the bile duct is the one neoplasm to differentiate from BCA and BCAC as the tumour does not have bile duct communication and

the mucin content is confined only in the cyst.⁽¹⁷⁻¹⁹⁾

Limitations of our study were the retrospective study design and the small number of patients. Only surgical cases with histological proof were included in our study. Some cases with benign-appearing cystic lesions on radiological images might not have been excised, and therefore, were not included in this study. This might have been the reason for the small number of BCA patients in our study. In conclusion, we suggest adding BCA and BCAC to the differential diagnosis when a solitary large well-defined multilocular intrahepatic cystic lesion is detected in a middle-aged woman. The presence of an enhanced mural nodule is the most important finding to suggest BCAC.

REFERENCES

- Ishak KG, Willis GW, Cummins SD, Bullock AA. Biliary cystadenoma and cystadenocarcinoma: report of 14 cases and review of the literature. *Cancer* 1977; 39:322-38.
- Mortel  KJ, Ros PR. Cystic focal liver lesions in the adult: differential CT and MR imaging features. *Radiographics* 2001; 21:895-910.
- Woods GL. Biliary cystadenocarcinoma: Case report of hepatic malignancy originating in benign cystadenoma. *Cancer* 1981; 47:2936-40.
- Matsuoka Y, Hayashi K, Yano M. Case report: malignant transformation of biliary cystadenoma with mesenchymal stroma: documentation by CT. *Clin Radiol* 1997; 52:318-21.
- Devaney K, Goodman ZD, Ishak KG. Hepatobiliary cystadenoma and cystadenocarcinoma. A light microscopic and immunohistochemical study of 70 patients. *Am J Surg Pathol* 1994; 18:1078-91.
- Palacios E, Shannon M, Solomon C, Guzman M. Biliary cystadenoma: ultrasound, CT, and MRI. *Gastrointest Radiol* 1990; 15:313-6.
- L uffer JM, Baer HU, Maurer CA, et al. Biliary cystadenocarcinoma of the liver: the need for complete resection. *Eur J Cancer* 1998; 34:1845-51.
- Thomas KT, Welch D, Trueblood A, et al. Effective treatment of biliary cystadenoma. *Ann Surg* 2005; 241:769-73.
- Dixon E, Sutherland FR, Mitchell P, McKinnon G, Nayak V. Cystadenomas of the liver: a spectrum of disease. *Can J Surg* 2001; 44:371-6.
- Iemoto Y, Kondo Y, Fukamachi S. Biliary cystadenocarcinoma with peritoneal carcinomatosis. *Cancer* 1981; 48:1664-7.
- Koffron A, Rao S, Ferrario M, Abecassis M. Intrahepatic biliary cystadenoma: role of cyst fluid analysis and surgical management in the laparoscopic era. *Surgery* 2004; 136:926-36.
- Kim K, Choi J, Park Y, Lee W, Kim B. Biliary cystadenoma of the liver. *J Hepatobiliary Pancreat Surg* 1998; 5:348-52.
- Choi BI, Lim JH, Han MC, et al. Biliary cystadenoma and cystadenocarcinoma: CT and sonographic findings. *Radiology* 1989; 171:57-61.
- Buetow PC, Buck JL, Pantongrag-Brown L, et al. Biliary cystadenoma and cystadenocarcinoma: clinical-imaging-pathologic correlations with emphasis on the importance of ovarian stroma. *Radiology* 1995; 196:805-10.
- Korobkin M, Stephens DH, Lee JK, et al. Biliary cystadenoma and cystadenocarcinoma: CT and sonographic findings. *Am J Roentgenol* 1989; 153:507-11.
- Sato M, Watanabe Y, Tokui K, et al. Hepatobiliary cystadenocarcinoma connected to the hepatic duct: a case report and review of the literature. *Hepatogastroenterology* 2003; 50:1621-4.
- Kokubo T, Itai Y, Ohtomo K, et al. Mucin-hypersecreting intrahepatic biliary neoplasms. *Radiology* 1988; 168:609-14.
- Lim JH, Ko YT, Lee DH, Hong KS. Oriental cholangiohepatitis: sonographic findings in 48 cases. *Am J Roentgenol* 1990; 155:511-4.
- Zen Y, Fujii T, Itatsu K, et al. Biliary cystic tumors with bile duct communication: a cystic variant of intraductal papillary neoplasm of the bile duct. *Mod Pathol* 2006; 19:1243-54.