

Successful preoperative diagnosis of biliary cystadenoma with mesenchymal stroma and its characteristic imaging features: Report of two cases

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We report two cases of biliary cystadenoma with mesenchymal stroma, in which we reached a preoperative diagnosis. There are three characteristics in imaging. First, there is no communication between the tumors and biliary ducts. Second, the wall of the tumor is smooth and septa inside the tumor result in a "cysts-in-cyst" appearance. Third, papillary projections that are characteristic of the intraductal papillary mucinous neoplasm of the bile duct are rarely seen. We provide characteristic figures that are remarkably helpful for the preoperative diagnosis.

Key words: Biliary cystadenoma, mesenchymal stroma, cysts-in-cyst appearance, mucinous cystic neoplasm

Mezanşimal stromalı bilier kistadenomun preoperatif başarılı tanısı ve karakteristik radyolojik bulguları: İki olgu sunumu

Mezanşimal stromalı bilier kistadenomu olan ve preoperative tanı koyduğumuz iki olguyu rapor ediyoruz. Radyolojik olarak 3 özelliği vardır. İlki, tümörler ve safra kanalı arasında iletişim yoktur. İkincisi, tümörün duvarı düzgündür ve içerisindeki septa "kistin içinde kist" görünümüne sahiptir. Üçüncüsü ise nadiren görülen safra kanalının intraduktal papiller müsinöz tümörü için karakteristik olan papiller projeksiyonlardır. Preoperatif tanı için belirgin şekilde yardımcı olan karakteristik figürleri sunuyoruz.

Anahtar kelimeler: Bilier kistadenom, mezanşimal stroma, kistin içinde kist görünümü, müsinöz kistik neoplazi

INTRODUCTION

Wheeler et al. (1) first reported biliary cystadenoma with mesenchymal stroma (BCMS) in 1985. BCMS has multilocular cysts with outer capsules and internal septa. The wall of the tumor is smooth and without papillary projections (2,3). Dilatation of the bile duct is rare. Histologically, the epithelium is single-layered cuboid to columnar cells, and under the epithelium lies the mesenchymal stroma (MS), which is a dense proliferation of abundant spindle-shaped cells (1,4,5), immunohistochemically positive for estrogen receptor (ER)

and progesterone receptor (PgR) (3). Although BCMS is basically benign, it has malignant potential. Therefore, the recommended treatment is complete resection (5-7). Preoperative diagnosis is difficult and the final diagnosis is usually achieved by histological examination.

Here, we report two cases in which the preoperative diagnosis of BCMS was made based on the characteristic imaging features. We provide characteristic imaging figures that are remarkably helpful for the preoperative diagnosis.

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Manuscript received: 25.07.2010 **Accepted:** 23.12.2010

Turk J Gastroenterol 2011; 22 (6): 631-635

doi: 10.4318/tjg.2011.0277

CASE REPORTS

Case 1

A 40-year-old woman with an unremarkable past medical history and family history developed epigastralgia. Abdominal ultrasonography (US) performed two years previously at another hospital revealed a multicystic tumor in the liver. She had not received any treatment and her symptoms remained. Because follow-up US revealed a gradual increase in the tumor size, she was referred to our hospital for further examination.

The physical examination was normal, as were laboratory tests including liver function and tumor markers such as carcinoembryonic antigen (CEA) and carbohydrate antigen 19-9 (CA19-9). Hepatitis virus serology was negative. Abdominal US revealed a multilobular cyst in the medial segment of the liver; the mass was 6 cm in diameter, with thin internal septa. No papillary projections were detected (Figure 1). Doppler color US demonstra-



Figure 1. Case 1. US revealed a multilobular cyst in the medial segment of the liver, measuring 6 cm in diameter with internal septa.

ted blood flow in the septa. Magnetic resonance imaging (MRI) showed a 6-cm diameter multilobular cyst with internal septa in the medial segment of the liver. The wall of the cyst was smooth, and neither papillary projections nor solid components were observed within the tumor. The cystic fluid was hypointense on T1-weighted imaging and hyperintense on T2-weighted imaging (Figure 2). It was revealed by endoscopic retrograde cholangiopancreatography (ERCP) that there was no communication between the cyst and the intrahepatic bile duct. There was no filling defect in the bile duct, and it suggested that no mucus was present (Figure 3). Imaging tests accordingly suggested a preoperative diagnosis of BCMS. Partial hepatic resection of segments 4 and 5 was performed without intraoperative complications.

Macroscopically, the resected tumor was a multilobular cystic tumor, 6 cm in diameter, with a thick capsule and septa. The wall of the tumor was smooth, and no papillary projections were seen (Figure 4). The cyst fluid was odorless, yellowish brown and mucinous, and its CA19-9 level was 3,796,000 U/ml. Histological examination revealed a single layer of mucosal epithelial cells without heteroplasia. Underlying the epithelium was MS, a dense proliferation of abundant spindle-shaped

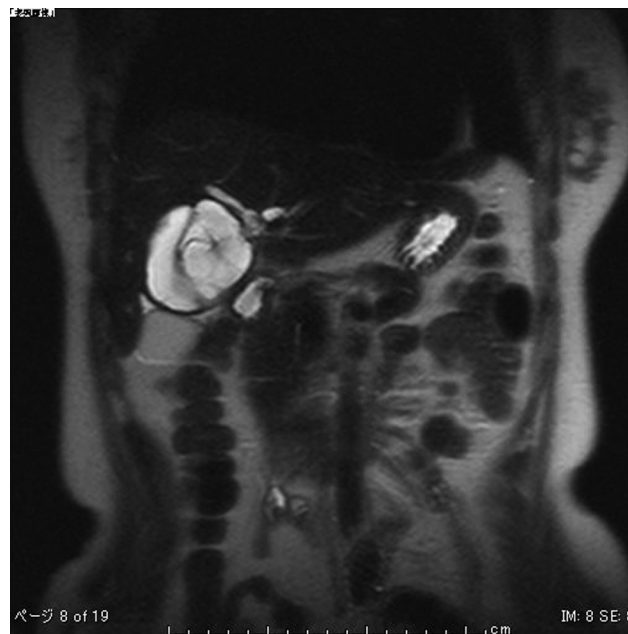


Figure 2. Case 1. MRI showed a 6-cm diameter multilobular cyst with septa in the medial segment of the liver. The wall of the cyst was smooth, and neither papillary projections nor solid components were seen. The cystic fluid was hypointense on T1-weighted imaging and hyperintense on T2-weighted imaging.



Figure 3. Case 1. ERCP revealed no communication between the cyst and the intrahepatic bile duct. There was no filling defect in the bile duct, and it suggested that no mucus was present.

cells (Figure 5). The stroma was immunohistochemically positive for ER and PgR. The final diagnosis was BCMS.

The postoperative course was uneventful and the patient was discharged two weeks after the operation. There was no evidence of recurrence in the three-year period since the operation.

Case 2

A 65-year-old woman had undergone abdominal US as part of an annual medical check-up three years previously. This revealed a multilobular cyst in the left lobe of the liver. As she had no symptoms at that time, she did not receive any treatment. However, three years later she developed right upper quadrant pain and was referred to our hospital for further examination and treatment.

Her past medical history included an appendectomy at age 22. Her sister had been diagnosed with simple hepatic cysts. The physical examination was normal, and laboratory tests were within normal limits, with the exception of elevated serum levels of tumor markers (CA19-9, 8920 U/ml; DUPAN-2, 1447 U/ml). US revealed a multilobular cyst, 10 cm in diameter, in segment 4 of the liver. The cyst had internal septa and it looked as if there were several cysts within a cyst, a “cysts-in-cyst” appearance. Some of the septa showed Doppler color flow. Neither solid areas nor papillary

projections were seen. There were many other simple cysts in both lobes of the liver. MRI showed a 10-cm diameter multilobular cyst with internal septa in segment 4 of the liver. The wall and the septa of the cyst were smooth, and neither papillary projections nor solid components were seen. The interior of the cyst was hypointense on T1-weighted imaging and hyperintense on T2-weighted imaging (Figure 6). ERCP showed that there was no dilatation of the bile duct or the pancreatic duct. There was a slight stenosis of the left hepatic duct, caused by compression from the tumor. No communication between the cyst and the intrahepatic bile duct was observed. There was no fil-



Figure 4. Case 1. The resected tumor was a multilobular cystic structure, 6 cm in diameter, with a thick outer capsule and internal septa. The wall of the tumor was smooth and no papillary projections were seen.

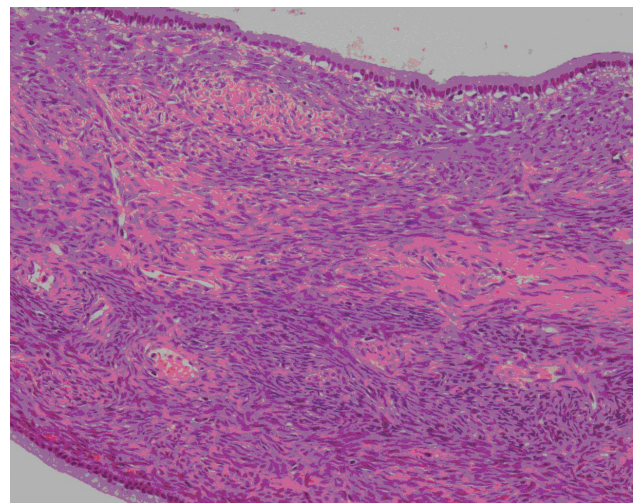


Figure 5. Case 1. Microscopic examination revealed a single layer of mucosal epithelial cells without heteroplasia. Underlying the epithelium was MS, a dense proliferation of abundant spindle-shaped cells.

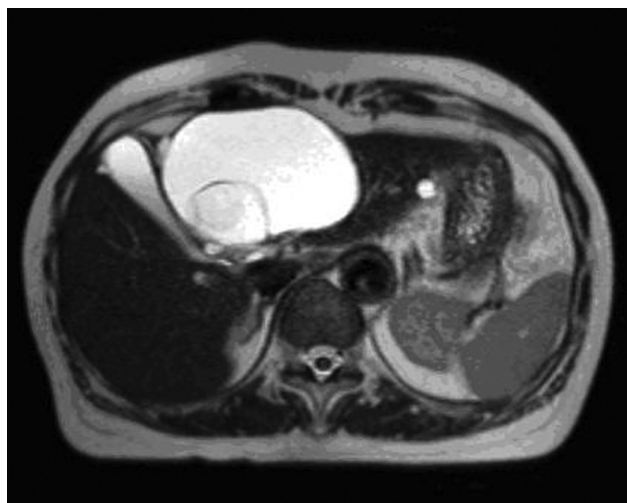


Figure 6. Case 2. MRI showed a 10 cm diameter multilobular cyst with internal septa in segment 4 of the liver. The cystic fluid was hypointense on T1-weighted imaging and hyperintense on T2-weighted imaging.

ling defect in the bile duct. Those studies suggested a preoperative diagnosis of BCMS. Left hepatectomy with cholecystectomy was performed. The resected material contained a 10-cm diameter cyst with internal septa. Neither papillary projections nor solid components were seen. Multiple unilobular cysts, of which the largest was 3 cm in diameter, were also observed in the specimen. The levels of CA19-9 and CEA in the cyst fluid were 26,190,000 U/ml and 4.5 µg/L, respectively.

Histological examination revealed a single layer of cuboid to columnar epithelial cells without papillary or ductal proliferations. No atypia was seen in the epithelium, which was surrounded by MS consisting of dense proliferation of spindle-shaped cells, immunohistochemically positive for ER and PgR. The resected margin was negative. The final diagnosis was BCMS. Serum levels of CA19-9 and DUPAN-2 declined remarkably to 20 U/ml and 123 U/ml, respectively, after the operation.

The patient's postoperative course was uneventful and she was discharged 13 days after the operation. Two years after the operation, no evidence of recurrence was seen.

DISCUSSION

Wheeler *et al.* (1) first reported 17 cases of BCMS in 1985. The entity is characterized by three distinct layers: (1) an epithelial layer of mucin-producing columnar to cuboidal cells lining the cysts; (2) a layer of undifferentiated mesenchymal cells,

usually less than 3 mm in thickness, underlying the epithelial lining; and (3) just outside the stromal band of cells, a dense layer of collagenous connective tissue, usually 2-5 mm in thickness (1).

The histogenesis of BCMS remains unclear, although there are various hypotheses. Devaney *et al.* (4) suggested that the tumor may arise from ectopic ovarian tissue, while Akwari *et al.* (5) and Subramony *et al.* (2) proposed that it may arise from immature endoderm or mesoderm of the liver or biliary duct. There are also reports of BCMS occurring in oral contraceptive users, suggesting that estrogen-containing oral contraceptives may promote these tumors (3).

Biliary cystadenoma with mesenchymal stroma (BCMS) is usually diagnosed as a cystic lesion in the liver before an operation. Then, after it is resected, it is revealed as BCMS histologically. Preoperative diagnosis of BCMS is rare. We experienced two cases of BCMS in which the diagnoses were achieved preoperatively based on the characteristic imaging figures.

The differential diagnosis of BCMS from other cystic diseases of the liver is important. The differential diagnosis includes biliary intraductal papillary mucinous cystic tumors (neoplasm) (IPMN), simple liver cyst, parasitic cyst (particularly hydatid cyst), hematoma, post-traumatic cyst, liver abscess, congenital cyst, and polycystic disease.

Some cases reprinted as cystadenomas of the liver may include both BCMS and biliary IPMN. Although it is difficult to differentiate BCMS from IPMN preoperatively, we insist that these two entities can be differentiated by imaging features.

There are three main characteristics in imaging. First, in BCMS, the wall of the tumor is smooth, and septa inside the tumor result in a cysts-in-cyst appearance. Second, papillary projections that are characteristic of biliary IPMN are rarely seen. Third, there is no communication between tumors and biliary ducts. On the contrary, in biliary IPMN, there are dilated bile ducts caused by large quantities of mucus secreted by the tumor, and communication between the tumor and the intrahepatic bile ducts was also detected (8).

Because BCMS can recur after incomplete resection or drainage and because it has the potential for malignant change, the recommended treatment is complete resection (5-7). A margin of normal liver should be ensured, and in some cases, a lobectomy is recommended.

Although BCMS has malignant potential, those lesions that do show malignant change (cystadenocarcinoma with MS) grow slowly and have better prognosis than other cystadenocarcinomas (without MS) (4,5,7). Most patients with BCMS have symptoms such as abdominal pain, abdominal discomfort, jaundice, and nausea (3,5,9-11).

About 20% of the BCMS patients in the literature were reported to have elevated liver function tests (5). Serum CA19-9 levels are believed to be a valuable marker in the diagnosis and postoperative monitoring of BCMS since they are reported to return to normal after complete resection, as in our Case 2 (2,3). The preoperative serum level of DUPAN-2 was also high, and normalized after resection of the tumor in our Case 2. However, no other reports provide information regarding the utility of DUPAN-2 in BCMS. Elevation of CA19-9 and CEA levels can be observed in cystic fluid of this tumor (3), unlike in simple cysts and polycystic liver disease (2), but there is no evidence as to whether or not the level of these markers is related to malignant potential.

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Shiono et al. (12) reported the concept of extraovarian mesenteric mucinous cystic neoplasms (MCN). Extraovarian MCN includes biliary MCN, and its characteristics are similar to those of BCMS. Although the consensus has not been reached, BCMS may become incorporated into the concept of biliary MCN.

Biliary cystadenoma with mesenchymal stroma (BCMS) (biliary MCN) is a rare entity, and the number of reported cases is as yet very small. Preoperative diagnosis of BCMS has been rare so far, but we strongly insist that it is possible using several images such as US, computed tomography (CT), MRI, and ERCP. Based on characteristic imaging features, more BCMS will be diagnosed preoperatively, and accumulation of the cases can be achieved. It is important to accumulate the cases of BCMS to clarify the nature of the tumor and to construct guidelines for adequate diagnosis and treatment.

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