

# A Mucinous Cystic Neoplasm Originating from the Gallbladder: A Case Report and Literature Review

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## ABSTRACT

**Introduction:** Mucinous cystic neoplasms of the gallbladder are extremely rare, benign, unilocular or multilocular cystic tumors that contain septations. Mucinous cystadenoma, a subtype of mucinous cystic neoplasm, is defined as epithelial cystic proliferations composed of cells that contain intracytoplasmic mucin.

**Case Presentation:** A 70-year-old African American woman was admitted to the hospital because of progressive lower back pain and inability to walk. She was scheduled for a kyphoplasty. However, the day before surgery, she reported severe abdominal pain radiating to her right shoulder. On further workup, results of abdominal ultrasonography revealed a cystic mass in the lumen of the gallbladder. The kyphoplasty was postponed and a laparoscopic cholecystectomy was performed. Pathologic evaluation of the gallbladder revealed a multiloculated mucinous cystic neoplasm.

**Discussion:** Mucinous cystadenoma of the gallbladder account for 0.02% of the total number of cases in the hepatobiliary system. They are more frequently seen in middle-age women with a mean age at presentation of 45 years. Symptoms vary depending on the location of the tumor, but it typically presents as acute or chronic right upper quadrant pain, epigastric pain, and nausea and vomiting. The multilocular form is more common than unilocular. The cystic lesions can be filled with serous, hemorrhagic, mucinous, or mixed fluids. Clinicians should be suspicious of mucinous cystadenoma of the gallbladder when common gallbladder disease is excluded because malignant features can be present in the lesion.

## INTRODUCTION

Mucinous cystic neoplasms (MCNs) of the gallbladder are extremely rare, benign, unilocular or multilocular cystic tumors that contain septations. The World Health Organization tumor classification defines MCNs as epithelial cystic neoplasms composed of cells that contain intracytoplasmic mucin.<sup>1</sup> The liver is the most common site of origin, followed by the extrahepatic biliary system. MCNs originating in the gallbladder account for only 0.02% of hepatobiliary cases.<sup>2</sup>

The aim of this report is to review the literature of previous cases to contrast with the present one. An online search of available databases, including MEDLINE/PubMed, was conducted. Terms used included *mucinous cystadenoma*, *mucinous cystic neoplasms*, *biliary cystic neoplasms*, *hepatobiliary cystadenoma*, and *mucinous cystadenocarcinoma*. Inclusion criteria comprised all cases identified in alive patients, and articles written in English.



Figure 1. Mucinous cystic neoplasm on ultrasound evaluation. Arrow indicates septae of the cystic lesion.

## CASE PRESENTATION

### Presenting Concerns

A 70-year-old African American woman with a history of chronic osteomyelitis of the lumbar spine was scheduled for an L4-L5 kyphoplasty. During hospitalization the day before her surgery, she reported severe, sharp, stabbing abdominal pain that radiated to her back and right shoulder. Vital signs were within normal limits. Physical examination was unremarkable except for severe right upper quadrant pain on palpation. Laboratory studies were remarkable for mildly elevated white blood cell count (11,800/mm<sup>3</sup>), anemia (hemoglobin, 9.3 g/dL), and mildly elevated amylase level (127 U/L). Liver enzymes and alkaline phosphatase were within normal limits. An ultrasonogram of the abdomen revealed a focal, predominantly hypoechoic mass in the gallbladder fundus measuring 2.7 cm × 1.8 cm × 2.7 cm (Figure 1) without central flow on Doppler analysis. Stellate hyperechoic septations were noted in the mass. The lesion demonstrated well-defined margins with no invasion. No gallstones, sludge, wall thickening, pericholecystic fluid, and ductal dilation were

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Figure 2. Gross specimen of the gallbladder. Yellow arrow indicates the cystic lesion.

present. The differential diagnosis included gallbladder polyp, septate gallbladder, adenomyomatosis, and cystadenocarcinoma of the gallbladder.

### Therapeutic Intervention and Treatment

The kyphoplasty was postponed, and a laparoscopic cholecystectomy was performed, during which the gallbladder was removed without any intraoperative complications. The patient's right upper quadrant pain improved greatly after the second postoperative day. The postsurgical course was uncomplicated, and the patient was taken back to the operating room for a kyphoplasty 5 days after the laparoscopic cholecystectomy.

### Follow-up and Outcomes

On pathologic examination, the gross specimen consisted of a partially opened gallbladder measuring 9 cm × 3 cm × 2 cm. The serosa was pinkish-gray with a cystic bulging mass in the fundus measuring 3 cm × 2 cm × 1 cm (Figure 2). The mass contained multiloculated cystic spaces with mucoid material (Figure 3), with sizes ranging from 0.2 cm to 1 cm. The epithelial lining was smooth, with spindle-shaped cells densely packed beneath an ovarian-like stroma (Figure 3). The gallbladder wall measured 0.2 cm in thickness. Final pathologic diagnosis was "multiloculated mucinous cystic neoplasm."

As of this writing, the patient has not shown any radiographic evidence of recurrence on computed tomography (CT) scans in 3 postoperative visits at 6 weeks, 3 months, and 6 months.

### DISCUSSION

MCNs are benign cystic proliferations of the hepatobiliary epithelium. Lesions originate in the liver in 85% of cases<sup>3</sup> and affect women more frequently, with a mean age at presentation of 45 years.<sup>4</sup> The first case of MCN of the gallbladder was reported by Bishop<sup>5</sup> in 1901, in which a 42-year-old woman presented with dull, sickly abdominal pain and intermittent biliary colic and jaundice. In addition, Devaney et al<sup>6</sup> reported 52 MCN cases, of which 50 were present in women (96%). They also found that when associated dysplasia was not present, 96% of cases occurred in females.<sup>6</sup>

Histologically, there are 3 main subtypes of MCNs described throughout the literature: Pyloric gland, intestinal, and biliary.<sup>7,8</sup> The pyloric gland type is most commonly found in the gallbladder, whereas the intestinal type is found in the extrahepatic bile ducts.<sup>8,9</sup> Some types of MCNs have ovarian-like stroma that contain estrogen and progesterone receptors, and these types affect women more often. The presence of ovarian-like stroma and spindle-shaped cells is important because it differentiates MCNs from intracystic papillary neoplasms of the gallbladder.<sup>10</sup> In contrast, other subtypes of MCNs lack ovarian-like mesenchymal stroma and affect men more often.<sup>7,8</sup>

Multilocular MCNs are more common than unilocular.<sup>8</sup> In our review, 12 cases were multilocular (13 including the current case), and 3 cases were not reported. Moreover, lesions can be filled with serous, hemorrhagic, mucinous (Figures 3 and 4), or mixed fluids. In our literature search, only 7 cases mentioned the content of the lesion: 4 mucinous, 1 serous, 1 described as "non-mucinous," and 1 described as "bile-stained hyalinized material."

The origin of MCNs remains unclear. Previous studies have hypothesized that MCNs originate from ectopic remnants of embryonal gallbladder tissue and aberrant hamartomatous bile ducts.<sup>9</sup> However, Devaney et al<sup>6</sup> did not support this hypothesis on the basis of the presence of simple columnar epithelium, which is characteristic of bile duct and/or gastric epithelium. Additionally,

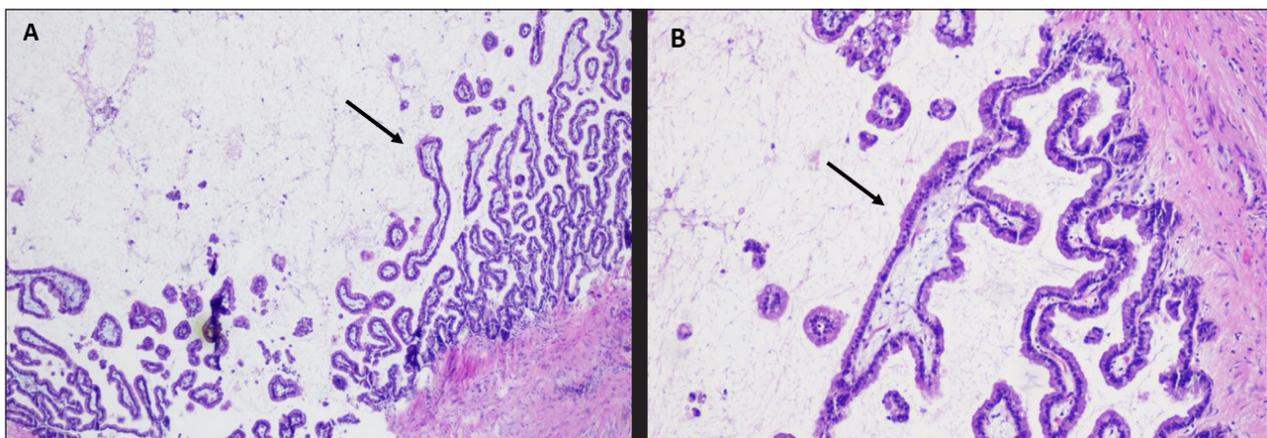


Figure 3. Hematoxylin/eosin stain showing adenomatous epithelial proliferation (arrows). (A) magnification 10x, (B) magnification 20x.

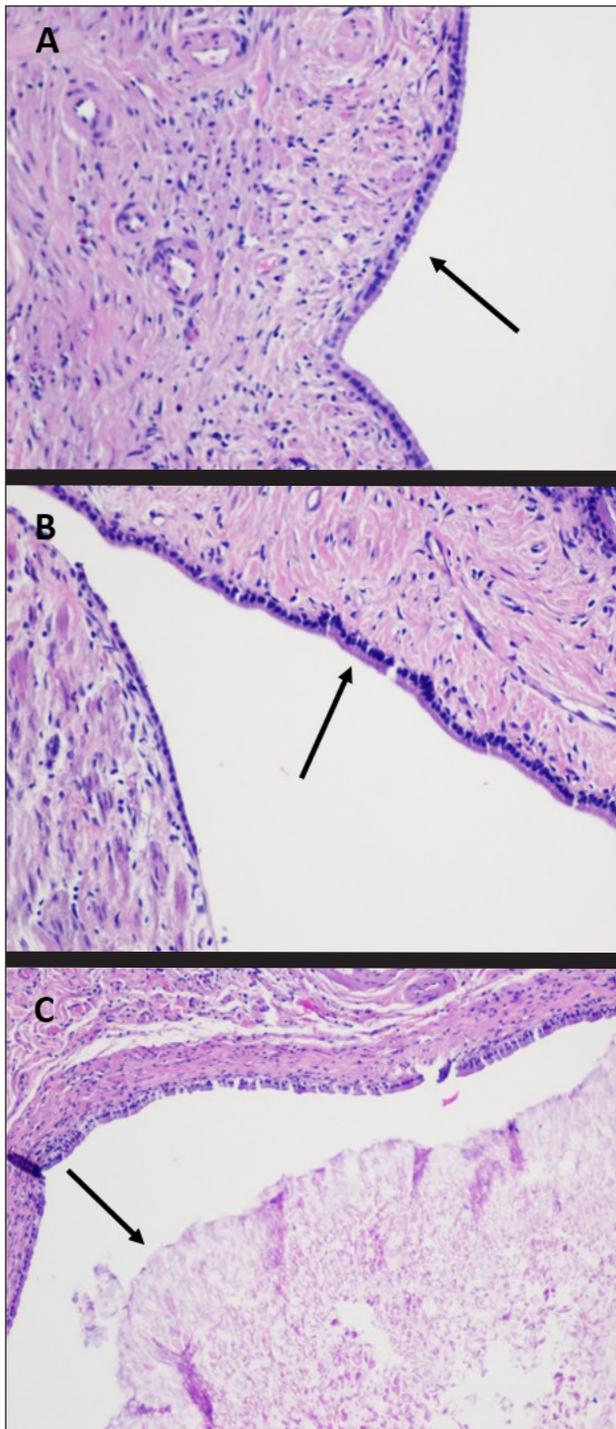


Figure 4. Hematoxylin/eosin stain showing cystic epithelium. Notice the basal location of the nuclei as well as the lack of nuclear dysmorphia and/or nuclear crowding, which is suggestive of benign proliferation (A, B); magnification 40x. Notice the arrow indicating intracystic mucin (C); magnification 25x.

MCNs have been considered acquired lesions because of their multilocularity and dense cellular walls accompanied by copious secretions.<sup>11</sup>

Discrepancies across the literature exist regarding the malignant potential. Some authors believe that approximately 13% of cystadenomas have dysplastic changes that can progress to a malignant form.<sup>12</sup> Transformation of Rokitansky-Aschoff sinuses has also been described.<sup>13</sup> However, in cases when dysplasias have been reported, lesions were noninvasive and contained only nests of malignant cells.<sup>7</sup> Albores-Saavedra et al<sup>14</sup> disagree with the malignant potential of MCNs. They suggest that carcinomas in the biliary tract arise from flat dysplasia and follow the dysplasia-to-carcinoma in situ sequence for invasion.

Most patients with MCNs are asymptomatic.<sup>14</sup> However, when symptoms develop, clinical presentation is widely variable and nonspecific (Table 1). In this literature review, right upper quadrant pain and previous chronic abdominal pain was present in 93% and 100% of patients, respectively. Jaundice was present in 6 (46%) of 13 reported cases, and bile duct obstruction was seen in 5 cases of 12 reported (41%). Findings of laboratory studies are also variable, with 6 cases having normal values, but it was noted that increased bilirubin levels were always present when other liver function tests were abnormal.

Across the literature,<sup>4-7,10,11,15-22</sup> case workup and diagnosis included right upper quadrant ultrasonogram and/or CT scan in most cases. Ultrasonography is considered to be more sensitive for internal features of the cysts (ie, septations and debris).<sup>15</sup> Typical ultrasonographic findings include anechoic cystic lesions with thickened irregular walls and internal septations.<sup>23</sup> The lack of central blood flow on Doppler ultrasonograms is suggestive of a benign cystic lesion.

CT scans are mainly used for definition of the anatomy, size, and extent of the lesions. In our case, repeated CT scans were performed to evaluate for possible recurrence or evidence of disease because of the lack of literature available regarding follow-up of MCNs. Endoscopic retrograde cholangiopancreatography (ERCP) is recommended when obstruction of the biliary tree is present or suspected, because it can be both diagnostic and therapeutic. However, despite its therapeutic potential, ERCP is not as effective as ultrasonography and CT for evaluation of the origin, infiltration, and extent of the tumor.<sup>15</sup> Because of the presence of mostly benign tissue with focal areas of malignancy, ERCP brushings, if performed, have a high likelihood of yielding false-negative results.<sup>24</sup> Importantly, ultrasound- or CT-guided fine-needle aspiration for biopsy is generally not recommended, because it increases the chances of seeding the tumor in the peritoneal cavity.<sup>25</sup>

Surgical management was the treatment modality in all cases in our literature review, with either open or laparoscopic cholecystectomy in most cases. The MCN in our present case was removed via laparoscopic cholecystectomy.

## CONCLUSION

MCNs of the gallbladder are rare, and no established guidelines for appropriate management have been developed. This case is an example of the lack of consistent presentation and

laboratory findings, which makes MCNs difficult to diagnose and to distinguish from other cystic lesions and gallbladder diseases. In addition, the lack of consistent evidence regarding the malignant potential of MCNs of the gallbladder makes this entity a diagnostic and therapeutic dilemma that requires good

clinical judgment for successful management of patients. The only consistent consensus across the literature is that all suspected MCNs originating in the gallbladder should be imaged, surgically removed, and evaluated under the microscope to determine the nature of the disease. ❖

**Table 1. Clinical characteristics of previously reported mucinous cystic neoplasms of the gallbladder**

Case no.	Author, y	Age, y/sex	Jaundice	Bile duct obstruction	Laboratory results	Size, cm	Management	Content	Loculation	Abdominal mass
1	Bishop, 1901 <sup>5</sup>	42/F	Yes	NR	NR	"Size of a child's head"	Partial removal of gallbladder mass	Mucin	Multilocular	NR
2	Kordenat, 1930 <sup>19</sup>	NR	NR	NR	NR	NR	NR	NR	NR	NR
3	Sambaugh, 1933 <sup>20</sup>	24/F	Yes	NR	NR	15	NR	Bile-stained hyalinized material	Multilocular	Yes
4	Ishak et al, 1977 <sup>10</sup>	52/F	No	No	NR	NR	Open cholecystectomy	NR	NR	No
5	Simmons, 1989 <sup>21</sup>	65/F	Yes	Yes	NR	NR	Open laparotomy	NR	Multilocular	NR
6	Devaney et al, 1994 <sup>6</sup>	NR	NR	NR	NR	NR	NR	NR	Multilocular	NR
7	Spector, 2003 <sup>22</sup>	47/F	Yes	Yes	Normal	4.6 × 4.2 × 4.4	Cholecystectomy, bile duct resection, and Roux-en-Y hepaticojejunostomy	Mucin	Multilocular	No
8	Terada et al, 2003 <sup>7</sup>	88/M	Yes	No	Elevated total bilirubin, alkaline phosphatase, liver enzymes; normal GGT	3.5 × 3 × 3	Cholecystectomy	Mucin	Multilocular	NR
9	Rooney, 2005 <sup>23</sup>	38/F	No	No	Normal	1.2 × 0.8 × 0.8	Laparoscopic cholecystectomy	NR	Multilocular	No
10	Waldmann et al, 2006 <sup>15</sup>	75/F	No	Yes	Elevated liver enzymes	17	En-bloc cholecystectomy, cystectomy, lymph node and liver wedge resection	Serous	Multilocular	Yes
11	McCague et al, 2008 <sup>11</sup>	32/F	No	Yes	Elevated alkaline phosphatase, direct bilirubin	12 (polyp)	Laparoscopic cholecystectomy	NR	Multilocular	No
12	Gokalp et al, 2010 <sup>2</sup>	33/F	No	No	Normal	0.67 × 0.28	Laparoscopic cholecystectomy	NR	Multilocular	No
13	Sistla, 2009 <sup>24</sup>	50/F	No	No	Normal	11 × 7.5 × 11.2	Cholecystectomy, partial liver resection	Nonmucinous	Multilocular	No
14	Zevallos Quiroz et al, 2014 <sup>4</sup>	75/F	Yes	Yes	NR	NR	Cholecystectomy and choledochoscopy	NR	Multilocular	No
15	Moussa, 2017 <sup>25</sup>	29/F	No	No	Normal	3	Open cholecystectomy	NR	NR	No
16	Rivero-Soto et al, 2018 <sup>a</sup>	70/F	No	No	Decreased Hb and Hct, mildly elevated amylase and WBC count	3 × 2 × 1	Laparoscopic cholecystectomy	Mucin	Multilocular	No

<sup>a</sup> Current study.

F = female; GGT = γ-glutamyl transpeptidase; Hb = hemoglobin; Hct= hematocrit; M = male; NR = not reported; WBC = white blood cell.

**Disclosure Statement**

The author(s) have no conflicts of interest to disclose.

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