



Case Report

Obstructive Jaundice Caused by Mucinous Cystic Tumor of Gallbladder: A Case Report and Literature Review

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Abstract

Mucinous cystic tumor of the gallbladder is an extremely rare benign tumor, with potential for malignant degeneration. Mucinous cystic tumors of the cystic duct are divided into mucinous cystadenoma and mucinous cystadenocarcinoma. Currently, cystadenoma is generally considered to be a precancerous lesion of cystadenocarcinoma. At present, there are few cases reported worldwide, and there are no relevant guidelines for diagnosis and treatment of this disease. This article presents the collected clinical data of a patient with mucinous cystic tumor of the gallbladder who was admitted to the First Affiliated Hospital of Hunan Normal University, with the characteristics of the disease summarized in combination with a focused literature review.

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Introduction

The cystic duct mucinous cystic tumor is a rare cystic duct tumor with latent malignant lesions, and represents a special pathological type in cholangiocarcinoma.^{1,2} Mucinous cystic tumors of the cystic duct are divided into mucinous cystadenoma and mucinous cystadenocarcinoma.³ Currently, cystadenoma is generally considered to be a precancerous lesion of cystadenocarcinoma, so patients in whom this disease is suspected should be decisively operated, with

their intraoperative fast frozen sections used to guide the operation.^{2,3} The etiology of mucinous cystic gland tumors of the bile ducts is currently unclear. Some believe that this is a congenital disease, caused by fluid retention as a result of inflammatory hyperplasia or obstruction of some abnormal ducts that occurs during embryonic growth; others believe that mucinous cystic tumors of the cystic duct are related to preembryonic intestinal residual or ectopic ovarian tissue.^{1–3}

The patient presented with painless jaundice that had lasted for a duration of 1 month. In this case, the large cystic duct tumor was found to have squeezed the common bile duct to cause obstructive jaundice and dilated intrahepatic and extrahepatic bile ducts.

Case report

The patient was a 57 year old female, with complaint nausea and vomiting for more than 1 month. She had been treated at a local community hospital 1 month prior to presentation at our hospital. However, after having received intravenous fluids and antibiotics, her symptoms did not alleviate. Laboratory examination upon presentation to our hospital showed the following: total bilirubin of 143.9 $\mu\text{mol/L}$; direct bilirubin of 109.6 $\mu\text{mol/L}$; alanine aminotransferase of 87.7 U/L; aspartate aminotransferase of 78.25 U/L; alkaline phosphatase of 201 U/L; gamma-glutamyltransferase of 682.0 U/L; carbohydrate antigen 19–9 of 252.02 U/mL; cancer antigen 72–4 of 7.76 U/mL; and, negativity for the panel of antinuclear antibodies. Findings for cancer antigen 125, blood routine, and serum C-reactive protein were basically normal. Abdominal computed tomography (Fig. 1A, B) showed obstruction of the lower part of the common bile duct, dilatation of the upper bile duct, and chronic cholecystitis. Magnetic resonance cholangiopancreatography (Fig. 1C) showed thickening of the lower part of the common hepatic duct with dilatation of the bile ducts inside and outside the liver. For preoperative jaundice reduction and cholangiography, percutaneous transhepatic cholangial drainage (referred to as PTCD) was performed. The PTCD angiography (Fig. 1D) showed filling defect in the common bile duct and bile duct dilation.

In order to clarify the nature of the space occupied by the bile duct and relieve the patient's biliary obstruction, abdominal cavity exploration, biliary exploration, preparation of biliary and enteral drainage were performed. A fro-

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Abbreviations: MCN, mucinous cystic neoplasm; PTCD, percutaneous transhepatic cholangial drainage.

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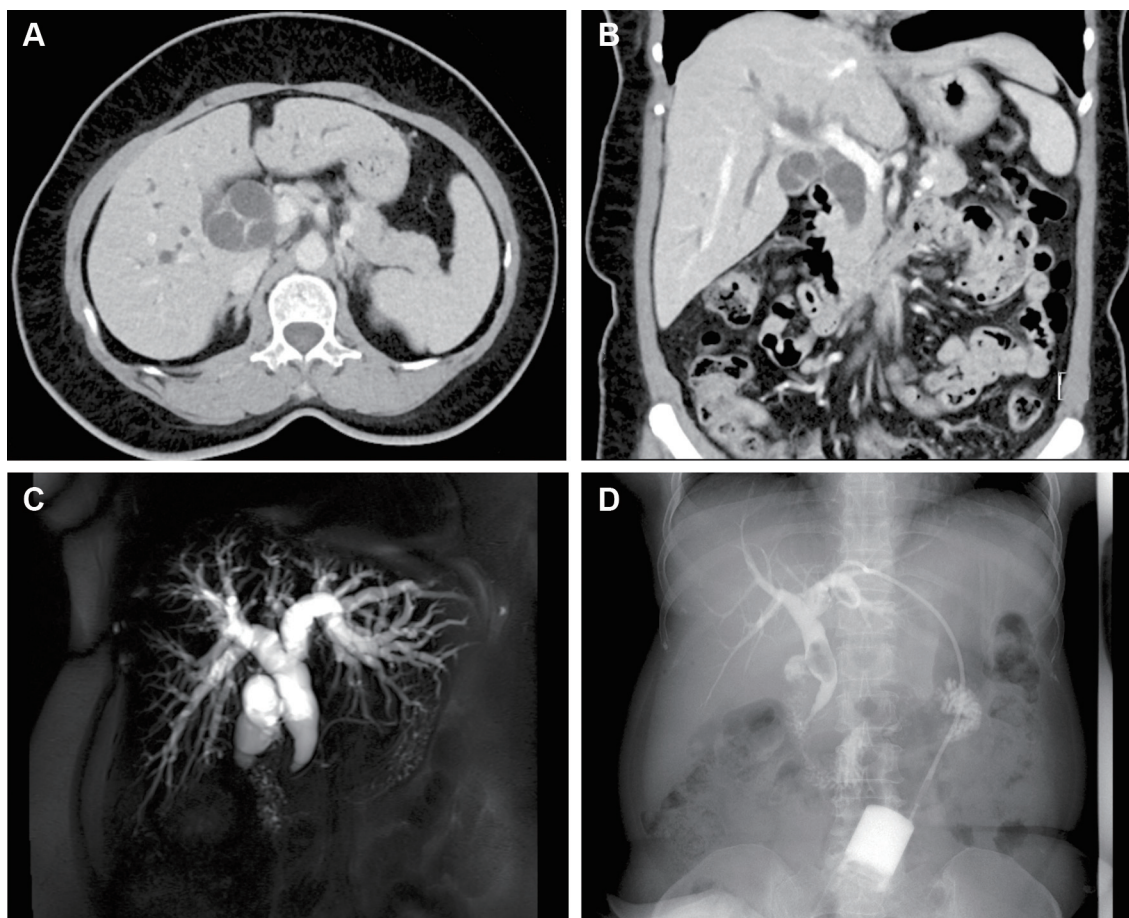


Fig. 1. Preoperative imaging revealed biliary obstruction. (A, B) Abdominal plain computed tomography scan plus enhanced (C) Magnetic resonance cholangio-pancreatography and (D) PTC angiography showed both intrahepatic bile duct dilation and common hepatic duct dilation, as well as a space-occupying lesion at the confluence of the cystic duct.

zen section was assessed intraoperatively, and the results were reported as: “*Consider gallbladder cyst adenoma*”. We then performed an open cholecystectomy, biliary exploration, and bile duct repair with shaping and T-tube drainage.

During the operation, a 4.0×2.0 cm mass of the cystic duct protruded into the bile duct lumen (Fig. 2A–D). The mass grew on the wall of the cystic duct with a pedicle, and a few stones were seen in the gallbladder.

The predischarge inspection showed that the total bilirubin was 25.8 μmol/L and the direct bilirubin was 18 μmol/L. Computed tomography of the abdomen showed that the dilatation of the bile ducts, inside and outside the liver, was significantly less than before. Postoperative pathology showed that there was a multicystic mass in the cystic duct, 4×2×2 cm in size, multicystic at the cut surface, and containing light-yellow, clear liquid in the cyst. The pathological diagnosis was mucinous cystic tumor with mild atypical hyperplasia with chronic cholecystitis immunohistochemistry of cytokeratin 7 (+), cytokeratin 19 (epithelial +), estrogen receptor (+), progesterone receptor (+), P53 (–), and Ki67 (scattered +) (Fig. 3).

Informed consent

Prior written informed consent was provided from the patient and this study was approved by the Ethics Review

Board of Hunan Provincial People’s Hospital/The First Affiliated Hospital of Hunan Normal University.

Discussion

Mucinous cystic neoplasms (MCNs) were first reported in pancreatic tissue and, subsequently, there has been much research devoted to investigating pancreatic MCNs. However, there are still many controversies about pancreatic MCN disease and even less is known about gallbladder MCN. According to the authors’ search of the PubMed database, the earliest case of gallbladder MCN was reported by Bishop in *The Lancet* in 1901,¹ and there have been 16 literature reports on gallbladder MCN (Table 1).

Similar to pancreatic MCN, gallbladder MCN can manifest unilocular or multilocular cystic changes, containing septa. In the World Health Organization Classification of Digestive System Tumors (2010 Edition), biliary MCN is listed separately, as a special tumor of the gallbladder, and is classified into “*mucocystic tumors with low-grade or medium-grade epithelium according to the status of intraepithelial neoplasia. Internal neoplasia (8470/0) (8470/2)*”, “*Invasive mucocystic carcinoma (8470/3)*”. The existing literature data divides MCN into at least two types.¹ One is non-invasive and has ovarian-like stroma under the epithelium, which is characterized by a high cell density. It appears as a dense

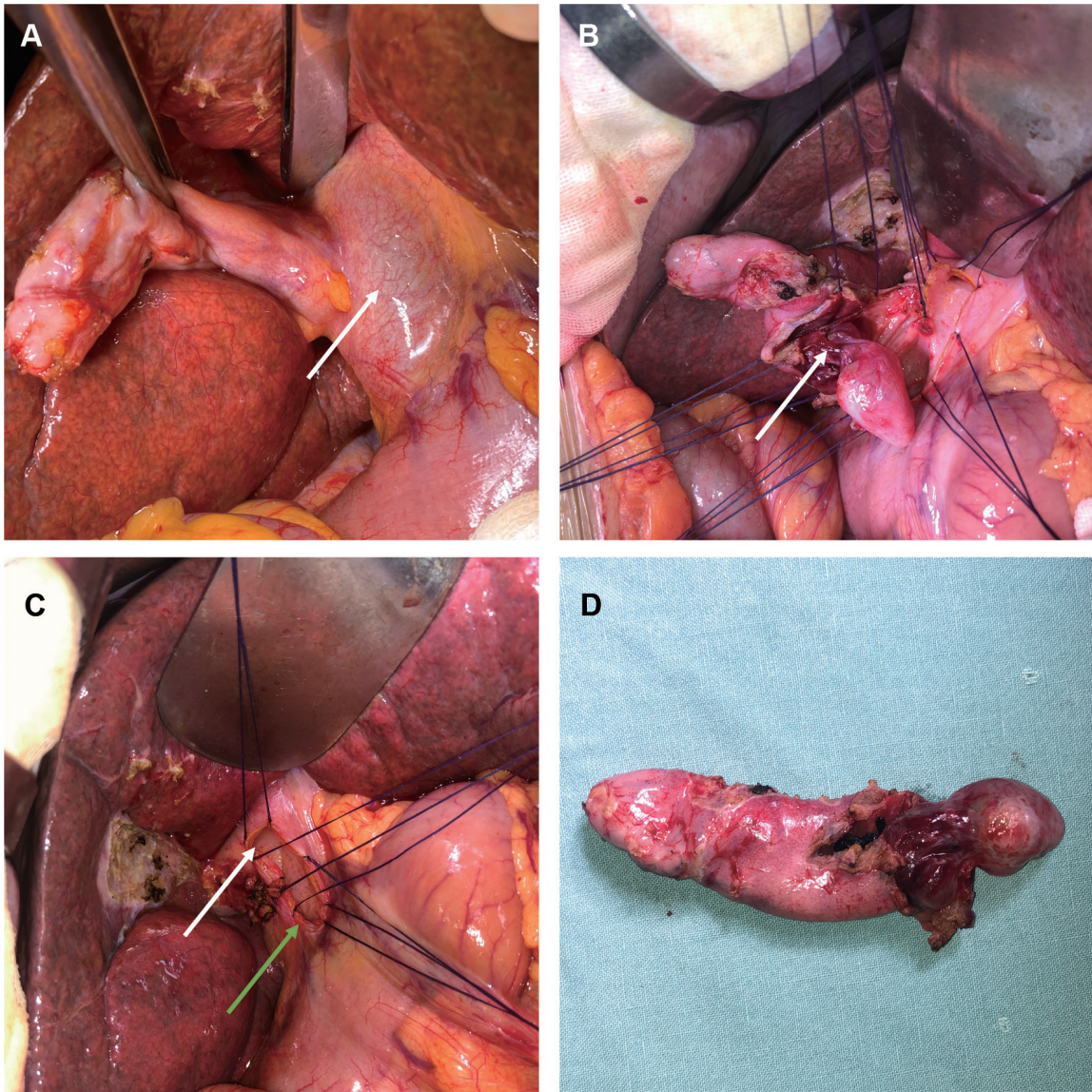


Fig. 2. A cystic duct-origin mass was found during the operation to block the common bile duct. (A) 4.0×2.0 cm mass of the cystic duct was seen protruding into the bile duct cavity (white arrow). (B) The mass was found on the wall of the cystic duct (white arrow). (C) The upper common hepatic duct (white arrow) and the lower common bile duct (green arrow) did not show stenosis nor any masses. (D) A cystic duct-origin mass was observed.

collection of spindle-shaped cells lacking cytoplasm and is immune to estrogen and progesterone receptors. This subtype affects middle-aged women. The other type is more aggressive, has no ovarian-like stroma, and affects men between 75 and 88 years-old. There are others who classify MCN using three subtypes, based on epithelial atypia and infiltration; the subtypes are mucinous cyst-adenoma, non-invasive mucinous cystadenocarcinoma, and invasive mucinous cystadenocarcinoma.²

Both gallbladder MCN and pancreatic MCN are common in women. The difference is that pancreatic MCN often occurs in the body and tail of the pancreas, which do not often cause obstructive jaundice.³ In the case of gallbladder MCN, as the tumor increases, some patients will show painful or painless jaundice.⁴ The overall prognosis of the disease is good, but there is a certain malignant potential. According to a Japanese study encompassing 156 cases of pancreatic MCN resection, the 10-year survival rate after resection was

95% for adenoma and 63% for cancer, among which micro-invasive carcinoma also reached more than 90%.⁴ Another study showed that the 5-year survival rate of untreated pancreatic MCN with invasive carcinoma was about 30% and the prognosis was poor.⁵ Such statistics are still lacking for gallbladder MCN. In pancreatic MCN, the maximum tumor diameter is an independent risk factor affecting malignant transformation, and the level of carbohydrate antigen 19-9 has greater diagnostic significance for male patients.³ In gallbladder MCN, as the tumor size increases, the likelihood of jaundice and malignancy increases together. In our case, the cystic duct tumor was large and it compressed the common bile duct, which then caused obstructive jaundice and intrahepatic bile duct dilation. Additionally, since gallstones were present, the case could have been misdiagnosed as common bile duct stones or Mirizzi syndrome.

Therefore, preoperative examination is particularly important. For this disease, ultrasound is more sensitive to the in-

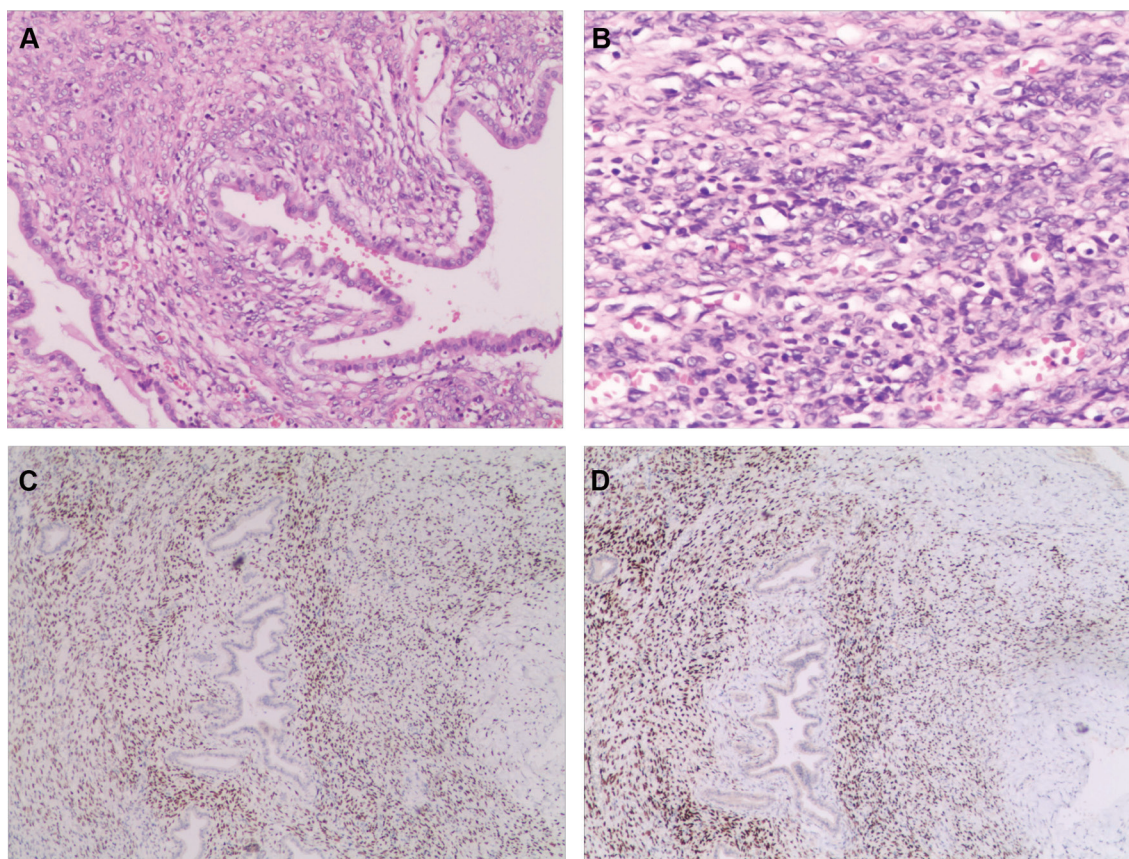


Fig. 3. Postoperative pathology showed that there was a multicystic mass in the cystic duct. (A) A 100× cyst, lined with a single layer of mucin-producing epithelial cells and showing low-grade dysplasia was observed. (B) Most segments of the 400× cyst wall contained ovarian-like stroma. (C, D) 40× ovarian-like stroma immunohistochemical analysis showed positivity for estrogen receptor (ER) and progesterone receptor (PR).

ternal features of the tumor (i.e. separation and fragments) and should be the first choice. Computed tomography can determine the location of the tumor and whether there is infiltration of surrounding tissues, which can help guide the scope of surgical resection. Magnetic resonance cholangiopancreatography can help determine the bile duct compression and involvement, determine the cause of jaundice in patients, and determine whether biliary reconstruction surgery is appropriate.⁶ Assessment of a quick-frozen section during the operation will help guard against the possibility of malignancy.

For asymptomatic patients, such as those who have tumors found on physical examination or imaging, one might use the pancreatic MCN endoscopic ultrasound-fine needle aspiration data on fluid collection to evaluate glucose (sensitivity of 92%, specificity of 87%, accuracy of 90%) and carcinoembryonic antigen (sensitivity of 58%, specificity of 96%, accuracy of 69%), for evaluation before an invasive operation, since there is always risk of tumor dissemination and surgical complications.³ It is important to comprehensively consider the patient's sex, age, family history, and surgical conditions. Interestingly, almost all gallbladder MCN patients are female^{1,7-21} (Table 1). In treatment, surgical resection is recommended for patients with clinical symptoms, such as abdominal pain, bloating, jaundice, or asymptomatic patients with gallbladder stones.²² It is important to send fast frozen sections during the operation to guide the operation method. After the surgical resection, it is recommended to check the confluence of the cystic duct, the wall of the gallbladder, and the common bile duct for other malignant tumors.

In summary, there is currently a lack of consistent evi-

dence for the malignant potential of gallbladder MCN, and there is also a lack of guidelines or consensus in diagnosis and treatment. However, the consensus reached after we compiled the literature is that due to the potential malignancy of gallbladder MCN, early diagnosis of such diseases should be paid attention to in clinical work, surgical treatment should be actively performed, and changes should be made according to the rapid intraoperative pathological examination results. Operating or expanding the scope of surgery will likely improve the prognosis and reduce recurrence and malignant transformation.

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Conflict of interest

The authors have no conflict of interests related to this publication.

Table 1. Gallbladder MCN reported cases

Case	Year	Age	Sex	Jaundice	Abdominal pain	Tumor size in cm	Carbohydrate antigen 19-9	Reference
1	1901	42	Female	Y	Null	Size of a child's head	Null	7
2	1930	Null	Null	Null	Null	Null	Null	8
3	1933	24	Female	Y	Null	15	Null	9
4	1977	52	Female	N	Null	Null	Null	10
5	1989	65	Female	Y	Y	14	Null	11
6	1994	Null	Null	Null	Null	Null	Null	12
7	2003	47	Female	Y	Y	4.6×4.2×4.4	Null	13
8	2003	88	Male	Y	Y	3.5×3×3	Normal	14
9	2005	38	Female	N	Y	1.2×0.8×0.8	Null	15
10	2006	75	Female	N	Y	17	High	16
11	2008	32	Female	N	Y	12	Null	17
12	2009	50	Female	N	Y	11×7.5×11.2	Null	18
13	2010	33	Female	N	Y	0.67 × 0.28	Null	19
14	2014	75	Female	Y	Y	Null	Null	1
15	2017	29	Female	N	Y	3	Null	20
16	2018	70	Female	N	N	6.7×6.8 ×7.2	High	2
17	2019	70	Female	N	Y	3×2×1	Null	21
18	2020	57	Female	Y	N	4.0 × 2.0	High	Current study

N, no; Null, not mentioned; Y, yes.

Author contributions

Patient management (CG), drafting of the manuscript (SL, ZZ, JK), statistical analysis (YS, SH), data collection (SL, ZZ, YS, ZY, CP, BJ), and revision of the manuscript for important intellectual content (YS,CP)

Data sharing statement

All data are available upon request.

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