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Arrangements of Hepatobiliary Cystadenoma Complicated With Congenital Choledochal Cyst

A Case Report and Literature Review

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Abstract: Hepatobiliary cystadenoma complication with congenital choledochal cyst is extremely rare and has never been reported in literatures so far.

The aim of the study was to investigate the disease arrangements by analyzing the case and performing a systematic review of the literature.

This case report documents the details and clear patterns of the patient. A 65-year-old woman with fever (39.2°C), nausea, vomiting, and chronic hepatitis B imaging demonstrated a left hepatic multilocular cystic mass and cystic dilated common bile duct.

A regular left hemihepatectomy was performed with resection of the entire tumor and choledochal cyst.

The surgical margins were negative and a final diagnosis of hepatobiliary cystadenoma complicated with congenital choledochal cyst was established. The patient had an uneventful postoperative recovery and liver function returned to normal levels.

Main lessons learned from this case are: the awareness should be raised about the disease to avoid misdiagnosis; preoperative ultrasonography, computed tomography, magnetic resonance imaging, and magnetic resonance cholangiopancreatography play an important role in detecting the lesion; the scope and timing of the surgery should be determined, which provide the chance of cure to complete resection of the tumor.

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Abbreviations: AFP = α-fetoprotein, APBDU = anomalous pancreaticobiliary ductal union, CA = carbohydrate antigen, CEA = serum carcinoembryonic antigen, CT = computed tomography, IHBCAC = intrahepatic biliary cystadenocarcinoma, IHBCA = intrahepatic biliary cystadenoma, MRCP = magnetic resonance cholangiopancreatography, MRI = magnetic resonance imaging, US = ultrasound.

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The study was approved by the Second Affiliated Hospital of Nanchang University Ethics Committee and specimens were taken with the patient's full consent.
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INTRODUCTION

Hepatobiliary cystadenoma is an uncommon lesion, which is mainly seen in females.[1] The majority of the cases are localized in the right side of the hepatic parenchyma. Majority are intrahepatic, fewer are extrahepatic, and occasionally are seen to arise from the gall bladder.[2] Biliary cystadenomas are multiloculated cysts with an epithelial lining composed of biliary-type cuboidal or nonciliated columnar cells and are surrounded by a stroma that mimics ovarian stroma in 85% to 90% of patients.[1] Choledochal cysts are rare disease and of unknown etiology. These are typically a surgical problem of infants and children; the diagnosis is delayed in 20% of the patients until adulthood.[3] The surgical management of choledochal cysts is complicated by associated hepatobiliary pathology in adults.[4] To the best of our knowledge, such case of hepatobiliary cystadenoma complicated with congenital choledochal cyst has never been reported in the literature. This article reported the case to elucidate its clinical presentation, preoperative evaluation, and treatment.

Patient Information

A 65-year-old woman with fever (39.2°C), nausea, vomiting, and chronic hepatitis B was transferred to hospital on February 20, 2013 due to a 3-month history of right upper abdominal pain and mild jaundice. Initially she was admitted to a local hospital and had a history of 15-year hepatitis B. The local hospital diagnosed the illness as ''pancreatitis and cholangitis'' for the patient with paroxysmal recurrent right upper quadrant pain in 3 years, and misdiagnosed it as simple cyst; therefore, the patient was not treated with surgery. She had no history of intravenous drug use or tattoos or body piercing, excessive alcohol use or obesity, and working with toxic chemicals. There was no significant family history of biliary or liver diseases.

Clinical Findings

After admission, a detailed treatment plan was developed based on patient history. There was right upper quadrant tenderness by physical examination, but not touched the mass (Table 1).

Diagnostic Focus and Assessment

Laboratory results showed mild elevation of total bilirubin and liver enzymes, serum carcinoembryonic antigen (CEA), carbohydrate antigen (CA) 19–9, and normal α-fetoprotein (AFP) levels and positive serology for hepatitis B virus infection. Electronic duodenoscopy revealed increased duodenal papilla opening, a lot of jelly-like bile flowing, and no new neoplasms. Abdominal ultrasonography (US) revealed a left

TABLE 1. Timeline

Time	Treatment
February 20, 2013	Onset of intermittent abdominal pain, mild jaundice, fever, nausea
February 20, 2013	Physical examination, laboratory serology
February 21, 2013	Specialized imaging testing, US, CT, MRI (MRCP)
February 25, 2013	Multidisciplinary consultation, surgical planning
February 26, 2013	Surgery, intraoperative frozen sections of resection margin
March 15, 2013	Normal liver function
March 17, 2013	Postoperative recovery, leave hospital

US = ultrasound, CT = computed tomography, MRI = magnetic resonance imaging, MRCP = magnetic resonance cholangiopancreatography.

hepatic multiloculated cystic mass measuring $9.7 \times 8.1 \times 8.6$ cm with papillary lesion, and cystic dilatation of the left intrahepatic and common bile duct. An abdominal computed tomography (CT) imaging demonstrated a left hepatic multiloculated cystic mass measuring 9.5×8.6 cm; local cystic wall could show high-intensity shadows projecting into the intracavitary, less clear boundaries, and dilated left intrahepatic biliary tree (Figure 1). Followed by, the abdominal magnetic resonance imaging (MRI) showed high-intensity areas on T2-weighted images and a large cystic tumor measuring 9.7×8.4 cm, which originating from the left liver lobe and the visible papillary lesion of the local cystic wall protruding into the cavity. Magnetic resonance cholangiopancreatography (MRCP) demonstrated a multiloculated cystic lesion measuring 9.4 cm and cystic dilated common bile duct 8.6 cm in diameter, and the dilation of both right and left intrahepatic bile ducts lacked asymmetry (Figure 2). Based on these findings, the patient was diagnosed with hepatobiliary cystadenoma complication with congenital choledochal cyst (Type-IVA) per Todani classification.

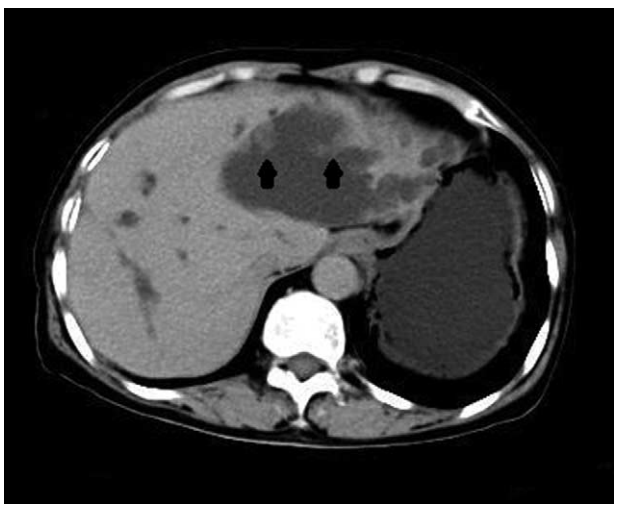

FIGURE 1. An abdominal computed tomography (CT) imaging demonstrated a left hepatic multiloculated cystic mass measuring 9.5×8.6 cm; local cystic wall could show high-intensity shadows projecting into the intracavitary, less clear boundaries, and dilated left intrahepatic biliary tree.

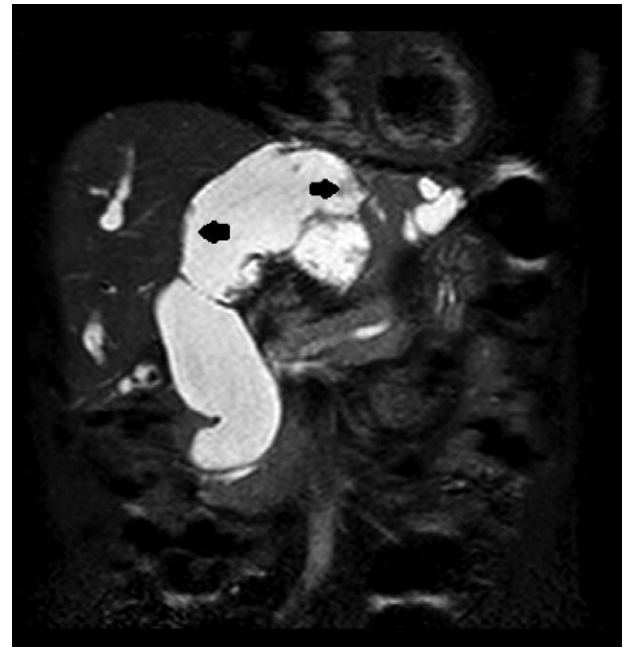

FIGURE 2. Magnetic resonance cholangiopancreatography (MRCP) demonstrated a multiloculated cystic lesion measuring 9.4 cm and cystic dilated common bile duct 8.6 cm in diameter, and the dilation of both right and left intrahepatic bile ducts lacked asymmetry.

Therapeutic Intervention

A large cystic dilated common bile duct, left intrahepatic biliary tree, and congestion and edema were observed after the patient treated with an exploratory laparotomy. Then a regular left hemihepatectomy was performed with resection of the entire tumor and choledochal cyst, meanwhile Roux-en-Y anastomosis was performed between right bile duct and jejunum.

Follow-up and Outcomes

On gross examination, the resected left liver specimen showed a multilocular cystic lesion measuring $11 \times 8 \times 3.5$ cm, covered with bullate nodules on the cutting surface (Figure 3). Cystic dilated common bile duct measuring 5×7.8 cm, multiple cystic dilations of the left hepatic duct, bile duct mucosal lesions, and many myxoma-like soft lesions which involved the entire hepatic and the upper common bile duct, and bile was jelly-like.

The cystic wall of dilated left intrahepatic biliary lesion was lined by a single layer of cuboidal and columnar epithelial cells, arrangement of papillary and adenoid, and some epithelial hyperplasia with severe atypia observed microscopically. A stroma with a dense layer of proliferating fibrous tissue was underlying the epithelium (Figure 4).

The patient had an uneventful postoperative recovery and liver function returned to normal levels.

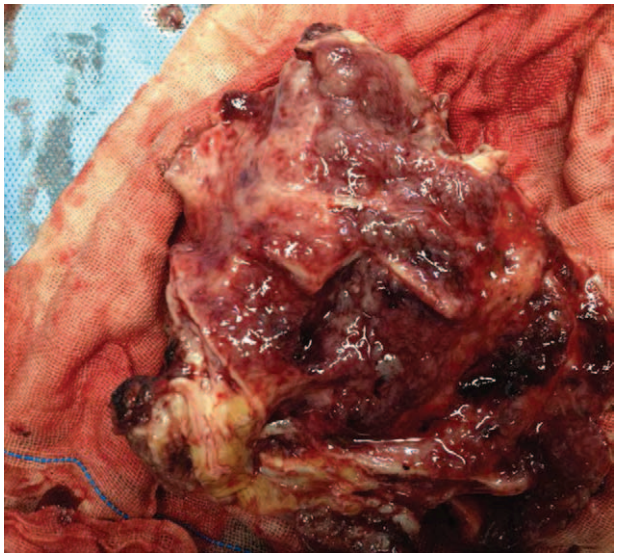

FIGURE 3. On gross examination, the resected left liver specimen showed a multilocular cystic lesion measuring $11 \times 8 \times 3.5$ cm, covered with bullate nodules on the cutting surface.

DISCUSSION

Hepatobiliary cystadenoma is a rare tumor of the biliary tract. It is mostly benign with potential for malignant transformation, less frequently in the extrahepatic biliary system, accounting for <5% of all cystic neoplasms found in the liver.[5] Although the etiology is unknown, many theories have been suggested that the tumors derived from ectopic remains of primitive foregut result from obstruction of congenital aberrant bile duct.[6] Choledochal cysts are believed to be congenital in origin; however, etiology still remains unclear. The most widely accepted theory is that cystic dilatation of bile ducts is related to an anomalous pancreaticobiliary ductal union (APBDU).[7] In this case, significant imaging findings could not prove the existence of APBDU due to the presence of abnormal function and spasm of the sphincter of Oddi associated with choledochal cysts, which may result in a functional obstruction to the common bile duct, thus predisposing to choledochal cysts. This study reported a patient who has mild dilation of the pancreatic duct with no mucinous filling defects and grape-like cystic space-occupying lesions. Confluence of pancreatic duct abnormalities or papillary sphincter dysfunction causes increased pressure within the pancreatic duct, which leads to dilation.[8] In addition, jelly-like bile originated from intrahepatic biliary cystadenoma causing obstruction, which leads to bile duct dilation, bile retention coupled with continued stimulation of pancreatic juice under reflux, bile duct inflammation and mucosal damage, bile duct epithelial cell hyperplasia, neoplasia, and dysplasia, which gradually forms hepatobiliary cyst adenoma. However, pathological specimens of pancreatic tissue are not identified; it cannot completely rule out the possibility of intraductal papillary mucinous neoplasm.

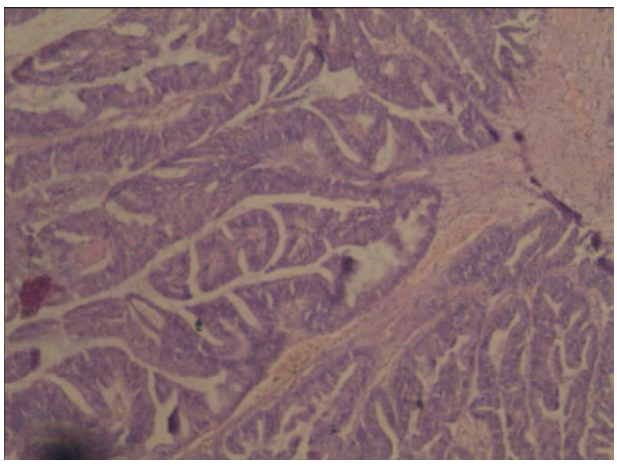

FIGURE 4. Intrahepatic biliary lesion was lined by a single layer of cuboidal and columnar epithelial cells, arrangement of papillary and adenoid, and some epithelial hyperplasia with severe atypia were observed microscopically.

Biliary cystadenomas are rare, multilocular cystic neoplasms of the liver that originate from the biliary epithelium.[9] On microscopic examination, the cysts that are lined with a single layer of cuboidal, columnar, nonciliated, and mucin-secreting epithelium resting on a basement membrane are found. The cysts often contain serous or mucinous fluid and may have a moderate-to-dense cellular stroma. A histological variant of biliary cystadenomas with mesenchymal stroma has been described. This variant is more common in females, which is characterized by the presence of spindle cells in the mesenchymal stroma.[10] These cells are capable of differentiating different types of cell with a high premalignant potential. The tumor may express receptors for progesterone, whereas histological characteristics include positivity for vimentin and cytokeratin.

Patients may present with abdominal pain and distention, dyspepsia, anorexia, nausea, and vomiting; however, patients may be asymptomatic at presentation.[11] Jaundice is either due to an extrinsic compression of the bile duct, biliary obstruction by an intraluminal tumoral mass, or accretion of mucus secretion from a communicating biliary cystadenoma.[12] Patient presented with fever and mild jaundice due to the improper discharge of jelly-like bile leading to the increased pressure of the bile duct and bacterial infections. On physical examination, an abdominal mass could be identified occasionally. Laboratory results are normal in most patients with hepatobiliary cystadenoma, but in this case, serum liver enzyme levels are mildly elevated; serum AFP, CA19-9, and CEA levels are within the normal range. Before surgery, CA19-9 and CEA levels may elevate in the cystic fluid and contribute to the diagnosis of hepatobiliary cystadenoma,[13] but definite diagnostic criteria established the need for statistically convincing data with comparisons of CA19-9 and CEA levels to simple cysts. It has been shown that serum CA19-9 level can be used as an indicator of tumor activity during regular follow-up after surgery.[14]

Because the clinical symptoms are not typical, nonspecific serology can easily lead to misdiagnosis, and delayed surgery. In this case, the patient was misdiagnosed as having a simple cyst, and not received timely surgery. Imaging studies by CT and MRI played an important role in detecting the lesion. Characteristic US, CT, and MRI findings including a multiloculated lesion with internal septa, a thickened and irregular wall, mural nodules, and papillary projections, calcifications, and wall enhancements have been well described.[15] US could reveal a thick-walled cystic mass, in which irregular septa can be demonstrated with perforator vessels by color Doppler flow imaging. Common features on CT scan include low-density, well-defined, lobulated, multilocular, thick-walled, cystic masses with internal septa, and occasionally mural nodules.[16]

Contrast CT demonstrates enhanced internal septations and mural nodules. MRI is a valuable tool for the diagnosis and differentiation of cystadenoma from other cystic liver lesions, whereas the combination of MRI with MRCP is even more useful. On T1-weighted images, the signal intensity may change from hypo to hyperintense as protein concentration increases. T2-weighted images demonstrate fluid collections within the tumor with homogeneous high signal intensity, whereas the wall of the mass shows a low-signal-intensity rim.[17] Demonstration of communication between the tumor and the biliary tract is of important diagnostic value in identifying the site of origin of the tumor and in differentiating biliary cystadenoma/cystadenocarcinoma from other hepatic cystic lesions.[18] However, CT and MRI have often failed to identify the narrow communication, which is easily detected during an intraoperative cholangiogram.[19] In fact, there are no dedicated imaging features to support the diagnosis of cystadenoma or cystadenocarcinoma. However, the presence of irregular wall thickening, mural solid nodules, thick calcification, and papillary projections is the indication of a cystadenocarcinoma.[20] In this case, enhanced mural nodules can be found on the cyst wall. However, the narrow communication cannot be found due to the lack of typical imaging features; hence, it is difficult to make a correct diagnosis. In addition, obviously dilated common bile duct and intrahepatic dilation in the left lobe of the liver were observed. Consistently, investigators have suggested that the incidence rate of patients with congenital choledochal cyst with co-existing intrahepatic dilation was 30.1% and consisted mainly of 2 types: one was cone-shaped dilation that tapered from the common bile duct to the beginning of the intrahepatic bile duct, and the other was cystic dilation. In this study, 53% of the patients were cystic dilation-type; among these, the dilation more frequently occurred in the left lobe of the liver.[21]

It is difficult to make an accurate diagnosis of biliary cystadenomas before surgery, and till date no publication has established presenting symptoms that differentiate biliary cystadenomas from other benign or malignant hepatic cystic diseases such as biliary cystadenocarcinoma, hepatic and hydatid cyst, Caroli disease, undifferentiated sarcoma, intraductal papillary mucinous tumor, and hepatocellular carcinoma.[11] In this case, the patient had been misdiagnosed as having a simple cyst and did not receive a timely surgery. The typical CT features of cystadenoma are usually a well-defined mass with low-density and internal septa. Its fibrous capsule and internal septations are often visible and help to distinguish the lesion from a simple cyst. The convex papillate can be seen on the septation, but it is more common in cystadenocarcinoma. There are no dedicated imaging features to support the diagnosis of cystadenoma or cystadenocarcinoma. However, there is a surgical indication for intrahepatic biliary cystadenoma (IHBCA), and definite preoperative diagnosis of IHBCA and intrahepatic biliary cystadenocarcinoma (IHBCAC) is not strictly required.[22] At present, imaging is the major diagnostic method for detecting hepatobiliary cystadenoma, but surgery is the only means of accurate diagnosis. Since it is believed to be premalignant, complete resection is the best treatment. The patient' condition was complicated with the principle treatment such as resection of the lesion, removing of the stricture, and unobstructed drainage. Then a regular left hemihepatectomy was performed with resection of the entire tumor and choledochal cyst, and Roux-en-Y anastomosis was performed between the right bile duct and jejunum. Complete resection of the tumor provided the chance of cure. It is also important for surgeons to determine the scope of the operation and for patients to receive a timely surgery.

In summary, hepatobiliary cystadenoma with congenital choledochal cyst is extremely rare complicated case. It typically causes nonspecific symptoms and is often incidentally detected. Cystadenoma can be mistaken for simple hepatic cysts on radiological imaging and can lead to inadequate treatment. Hepatobiliary cystadenoma combined with congenital choledochal cyst is easy to cause pancreatitis and cholangitis, and delay timing of surgery. Complete resection of the tumor provides the chance of cure. Preoperative US, CT, and MRI (MRCP) are suggested, and early referral for specialist hepatobiliary review is advised. Operative resection is also recommended and complete excision was achieved in these cases. Hence, the diagnosis and treatment awareness should be raised about the disease to avoid misdiagnosis in patients with biliary dilatation and jaundice; hence, best treatment plan should be developed in a timely manner for multidisciplinary consultation.

Patient Perspective

She was misdiagnosed as having simple cyst; therefore, she was not treated with surgery. However, complete resection of the tumor provides the chance of cure. Doctors should raise diagnosis and treatment awareness about the disease.

Informed Consent

A written informed consent was obtained from the patient for publication of this case report and accompanying images.

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