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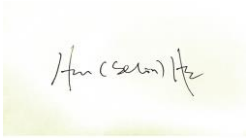

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The utility of multiple endoscopic techniques in the differential diagnosis of gallbladder adenomyomatosis from gallbladder malignancy with bile duct invasion: A case report and literature review

Abstract

BACKGROUND

Gallbladder adenomyomatosis (GAM) is a benign lesion, characterized by thickening of the gallbladder wall and a focal mass, which overlap with the features of gallbladder malignancy. Consequently, differential diagnosis of GAM from gallbladder cancer is difficult and approximately 20% of suspected malignant biliary strictures were postoperatively confirmed as benign lesions. Herein, we report a case in which preoperative diagnosis of GAM was made with a combination of endoscopic and imaging techniques.

CASE SUMMARY

A 40-year-old man was referred to our hospital chiefly for a fever and right upper abdominal pain with dark urine. Enhanced computed tomography (CT) showed thickening of the gallbladder wall and a mass in the gallbladder neck with involvement of the hepatic bile ducts, which was suspected to be malignant. Gallbladder malignancy with bile duct invasion was ruled out with

subsequent endoscopic examinations, including endoscopic retrograde cholangio-pancreatography (ERCP), intraductal ultrasound (IDUS), and SpyGlass. Endoscopic examinations showed a homogeneous hyperechoic lesion with smooth margins of benign bile duct stricture suggestive of inflammation stenosis of the bile duct. The patient underwent laparoscopic cholecystectomy (LC). GAM was postoperatively diagnosed and confirmed based on the histopathology results, which were consistent with the preoperative diagnosis. Notably, no malignant event occurred in the patient during a 12-month follow-up.

CONCLUSION

A combination of endoscopic techniques may help in the differential diagnosis of GAM from gallbladder cancer.

Keywords: Gallbladder adenomyomatosis; gallbladder cancer; differential diagnosis; endoscopic retrograde cholangio-pancreatography; intraductal ultrasound; SpyGlass; laparoscope ; case report

Core tips:

It remains a challenge to make an accurate pre-operative diagnosis of gallbladder adenomyomatosis (GAM) mainly due to the overlapping features between GAM and gallbladder cancer. In this case report, enhanced CT findings were initially indicative of malignant gallbladder lesions, which were subsequently diagnosed as GAM with a combination of endoscopic techniques. Our findings suggest that multiple endoscopies can improve the accuracy of GAM

diagnosis and help in differential diagnosis between GAM and gallbladder cancer.

Introduction

Gallbladder adenomyomatosis (GAM) is a benign tumor, and the imaging characteristics, such as thickening of the gallbladder wall and a focal mass, usually overlap with the findings in gallbladder malignancy. These similarities have posed considerable difficulties in making an accurate diagnosis of GAM, in particular, distinguishing GAM from gallbladder cancer. It has been reported that approximately 20% of suspected malignant biliary strictures were postoperatively confirmed as benign lesions[1]. Computed tomography (CT) is widely used in the preoperative assessment of gallbladder lesions[2]. However, CT imaging alone has been shown to reach an overall accuracy of only 70-80% for biliary stenosis[3]. Until now, there has been no definite consensus on the optimal clinical approaches for indeterminate biliary strictures. As such, it is necessary to improve the accuracy of GAM diagnosis and differential diagnosis between GAM and gallbladder cancer. In the present study, we illustrated a case which the preoperative diagnosis of GAM was made with a combination of endoscopic and imaging techniques.

Case presentation

Patient description

A 40-year-old male patient sought medical treatment mainly for a fever and pain in the upper

abdomen lasting for seven days as well as jaundice with dark urine for three days. The patient presented with right upper abdominal pain without abdominal distension or vomiting, as well as yellow sclera and film. The abdominal enhanced CT scan revealed a mass at the neck of the gallbladder involving the bile ducts (Fig. 1), for which he was referred to the Department of Hepatobiliary and Pancreatic Surgery for further diagnosis and treatment. He had no significant medical history.

Clinical examinations and diagnosis

Upon admission, physical examination was performed, revealing a body temperature of 37.5 °C, heart rate of 72 bpm, blood pressure of 116/68 mmHg, and respiratory rate of 15. Yellow sclera and film occurred without bleeding spots or petechiae. Diagnostic endoscopies, including endoscopic retrograde cholangio-pancreatography (ERCP) (Fig. 2), intraductal ultrasound (IDUS) (Fig. 3), and SpyGlass (Fig. 4) were undertaken, exhibiting a homogeneous hyperechoic lesion with smooth margins of benign bile duct stricture. The endoscopic findings were indicative of inflammation stenosis of the bile duct (Figs. 2 & 3). The laboratory test results were as follows: total bilirubin (TBIL) was 138.8 μmol/L, direct bilirubin (DBIL) was 117.3 μmol/L, carbohydrate 33 antigen 19-9 (CA19-9) was 161.3 U/mL, cancer antigen 12-5 (CA-125) was 15.76 U/mL, alpha-fetoprotein (AFP) was 1.77 ng/ml, carcinoembryonic antigen (CEA) was 1.29 ng/mL, C-reaction protein (CRP) was 81.3 mg/L, neutrophil granulocyte percentage (NE%) was 0.83, and

IgG4 was 0.2 g/L. GAM was postoperatively confirmed based on the histopathology results (Fig. 4).

Treatment, outcome, and follow-up

The patient underwent laparoscopic cholecystectomy (LC). Fortunately, neither recurrent GAM nor malignant tumors was observed in the patient during a 12-month follow-up.

Discussion

Gallbladder carcinoma is the most common malignant tumor in the biliary system[6]. Some benign gallbladder diseases are misdiagnosed as gallbladder carcinoma, resulting in unnecessary surgery. For instance, GAM is an excessively proliferative disease of the gallbladder epithelium with intramural diverticula (Rokitanskye Aschoff sinuses) extending into the thickened muscular layer[4] and its imaging features have some overlaps with those of gallbladder carcinoma when it presents as focal thickening at the body and fundus and a mass with irregularly soft tissue density in the gallbladder, which may simulate malignancy, resulting in a false-positive diagnosis of gallbladder carcinoma[5]. On the contrary, patients who suffer from gallbladder cancer may present with acute cholecystitis, misdiagnosed as a benign lesion. It has been reported that the hidden incidence of gallbladder cancer combined with cholecystitis ranges from 1-9%[6]. Gallbladder carcinoma originating from the neck can invade the cystic and extrahepatic bile duct,

making it difficult to distinguish from extrahepatic cholangiocarcinoma[7, 8]. When a stricture of the mid-portion of the extrahepatic bile duct is found in patients presenting with obstructive jaundice, careful evaluation of the cystic duct and gallbladder neck is necessary to rule out gallbladder cancer with metastasis.

With recently developed novel biomarkers and endoscopic techniques, unnecessary surgeries on benign strictures of bile duct have been greatly reduced. However, no single approach has been reliable in the differential diagnosis of benign and malignant lesions in the gallbladder mainly due to insufficient sensitivity, low specificity, and inaccuracy. From reviewing the published systematic reviews and meta-analysis, we identified the diagnostic indices for the evaluation of suspected malignant biliary strictures[1,9-13][1, 2]. We found that the clinical approach of various endoscopies in combination could significantly improve the diagnostic accuracy of indeterminate biliary stricture. In this case report and review of the literature, we propose a strategy for the evaluation and preoperative diagnosis of gallbladder-occupying lesions with bile duct invasion (Fig. 4), which may have great preoperative diagnostic utility. First, a detailed medical history should be obtained, with physical and laboratory examinations, along with an abdominal ultrasound to provide the initial evidence for a non-invasive imaging method such as CT or Magnetic Resonance Cholangiopancreatography (MRCP). These imaging modalities can reveal both the hilar bile duct and gall bladder, which can guide future treatment. Second, an invasive

method such as ERCP with IDUS/SpyGlass/Probe-based confocal laser endomicroscopy (pCLE)/Fluorescence in situ hybridization (FISH) or pathology can be used as the primary measure. If endoscopes and LC are positive, radical resection of hilar cholangiocarcinoma must be undertaken. If lymphatic metastasis or vascular invasion is found, ERCP stent implantation and radiofrequency ablation can be performed. Otherwise, 12 months of follow-up is usually necessary.

In summary, preoperative diagnosis of GAM is challenging, particularly when it presents imaging features similar to those of gallbladder carcinoma. The findings in this case study suggest that the use of multiple endoscopic techniques in combination may improve the accuracy of GAM diagnosis and benefit the differential diagnosis of GAM from gallbladder cancer.

Conflict of Interest

All authors declare no conflict of interest.

Figure legends

Figure 1 Enhanced CT imaging. (A) Thickening of the gallbladder wall, irregular density soft tissue invaded into the cavity and intrahepatic bile ducts extended from the neck with intrahepatic bile duct dilatation by approximately 2.5*1.3 cm; **(B)** The cystic duct lumen was narrowed and the

circular calcification-like high-density shadow was visualized at the end of the common bile duct at ~0.8 cm.

Figure 2 Endoscopic retrograde cholangio-pancreatography (ERCP). (A) Bile duct dilatation; **(B)** Gallstones at the end of the common bile duct**.**

Figure 3 Intraductal ultrasound (IDUS) imaging. Homogeneous hyperechoic lesions with smooth margins of benign bile duct stricture were visualized.

Figure 4 SpyGlass Direct Visualization System imaging. Inflammatory change in bile duct mucosa

Figure 5 Pathological examinations. Gallbladder adenomyomatosis with chronic cholecystitis and acute suppurative inflammation was present without signs of gallbladder carcinomas at the incisal margin of the liver and neck of the gallbladder.

Figure 6 Various endoscopic and radiological imaging modalities for evaluation and preoperative diagnosis of gallbladder occupying lesions with bile duct invasion.