The role of SpyGlass Direct Visualization System on Patient with Indeterminate biliary strictures: A case report

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ABSTRACT

Biliary strictures diagnosis has become a challenge where benign conditions could mimic a malignant process. Recently, SpyGlass DS overcame the limitations by allowing direct visualization of the biliary tree. A 65 years old Indian patient complaints of jaundice with total and direct bilirubin of 23.3 mg/dL and 16.2 mg/dL, respectively. Liver function test, gamma-glutamyltransferase and CA 19-9 were increased. Transabdominal ultrasound and abdominal CT supported dilatation of common bile duct (CBD) with abrupt narrowing showing periductal enhancement at supra pancreatic level and stricture. Endoscopic ultrasound showed intrahepatic CBD stricture with dilated proximal CBD and sludge ball. Endoscopic retrograde cholangiopancreatography showed mid CBD stricture. Although brush cytology results suggested low grade dysplasia and no definite evidence of malignancy, cholangioscopy using SpyGlass DS found nodularity with abnormal vascularity seen in mid of CBD suggesting malignancy, confirmed with histopathology as cholangiocarcinoma. We reported additional value of SpyGlass DS for detecting cholangiocarcinoma in an indeterminate biliary stricture patient.

Key words**:** *Biliary stricture, cancer, SpyGlass DS, cholangiocarcinoma.*

INTRODUCTION

Diagnosis of biliary strictures became a challenge due to the number of indeterminate biliary strictures after preoperative evaluation being up to 20%, thus definitive diagnosis demands further evaluation through surgical resection and pathologic examination.[1] Moreover, some benign conditions could mimic a malignant process, for example, post-inflammatory strictures and primary sclerosing cholangitis.[2] Iatrogenic injury, and post liver transplantation, post cholecystectomy are the most common cause of benign biliary strictures, whilst pancreatic cancer and cholangiocarcinoma are foremost sources of malignancy.[3] In general, around 13-24% of biliary strictures patients referred for surgery are ultimately found to be benign[4] and surgical resection proved that 20% of the suspected malignant strictures were actually benign conditions.[5] Excessive surgery for benign biliary disease should be avoided but delayed treatment of malignancy was also harmful for the patient. Therefore, preoperative evaluation plays an essential role to exclude malignancy.

Single ideal test regarding sensitivity, specificity and accuracy have not existed, despite

the variability of tests available recently. Several methods have been used as a diagnostic tool in the evaluation of biliary tree strictures, such as percutaneous trans-hepatic cholangiography or bile aspiration during endoscopic retrograde cholangiopancreatography (ERCP). Later, development of biliary tract brush cytology method has been commonly applied and became the method of choice. Brush cytology used air-dried cytologic material for Diff-Quick stain or fixed in ethanol for Papanicolaou staining. Recently, commercial SpyGlass direct visualization system from Boston Scientific Corporation (Marlborough, Massachusetts, United States) was available to overcome the limitations of previous methods. The system directly visualizes the biliary tree for diagnostic and therapeutic purposes by using a disposable digital scope with 120 degrees field of view. A tapered tip, a four-way tip deflection system, and a dedicated channel for water irrigation was featured on the scope, which enable unrestrained observation and biopsy procedures.[6] Direct visualization of the lesion with improved image quality and the ability to take targeted biopsies could be achieved by digital cholangioscopy. In malignancy, the findings obtained dilated of tumor vessels, tortuous vessels, infiltrative stricture, irregular margins with partial occlusion of the lumen, irregular surface, and easy oozing.[7] We reported a case in an Indian patient with indeterminate biliary strictures who underwent ERCP and SpyGlass DS examination.

CASE ILLUSTRATION

A 65 years old male, with Indian ethnicity was admitted to the hospital for jaundice 1 week ago. He also complaints of decreased appetite and generalized weakness. Past illness showed a history of chronic liver disease associated with chronic ethanol intake and cholecystectomy surgery. Physical examinations revealed a yellowish pigmentation of the sclera. The thorax was normal, abdominal was soft, non-tender with no ascites. The skin was turning yellow.

His routine blood investigations showed normal hemogram. Total, direct and indirect bilirubin were 23.3 mg/dL, 16.2 mg/dL and 7.1 mg/dL, respectively. The biochemical analysis revealed SGPT was 120 U/L, SGOT 127 U/L with increased alkaline phosphatase level (270 U/L). Total protein, albumin, globulin and renal function test were at normal limits. Hepatitis and acquired immunodeficiency syndrome (AIDS) viral markers were negative, alpha-fetoprotein of 4.5 ng/ml, gamma-glutamyltransferase of 986 U/L and CA 19-9 of 119.1 U/mL.

Transabdominal ultrasound showed post cholecystectomy state, increased and coarse echotexture of liver with minimal irregular contour suggested early change of hepatic parenchymal disease, common bile duct (CBD) and pancreatic duct were dilated (9.2 mm and 4 mm, respectively) with marginal splenomegaly. Triphasic abdominal CT showed atrophied left lobe with hypertrophy of caudate lobe and prominent fissures of liver with splenomegaly, suggesting chronic liver disease. Dilated CBD (1.54 cm) with abrupt narrowing showing periductal enhancement at supra pancreatic level and stricture.

Upper GI Endoscopy showed antral gastritis with superficial duodenal ulcers. Endoscopic ultrasound showed intrahepatic CBD stricture with dilated proximal CBD and sludge ball. ERCP showed mid CBD stricture, brush cytology was performed distal of CBD stricture with a CBD stent placed. Post procedure, patient was stable without any complications. He was treated with intravenous fluids, proton pump inhibitor and other supportive treatments. He was discharged in stable condition and advised to be in close follow up.

One week later, brush cytology result showed most of the cells are benign with round to oval nucleus and moderate amount of cytoplasm. Results suggest low grade dysplasia and no definite evidence of malignancy, suggesting repeat for definitive evaluation. ERCP was performed followed by cholangioscopy using SpyGlass DS (Figure 1). We found nodularity with abnormal vascularity seen in mid of CBD suggesting malignancy, and endobiliary biopsy was taken. CBD stent was placed.

Histopathology reported dysplastic cells with vesicular to hyperchromatic nucleus with inconspicuous nucleoli and moderate eosinophilic cytoplasm, and moderate nuclear

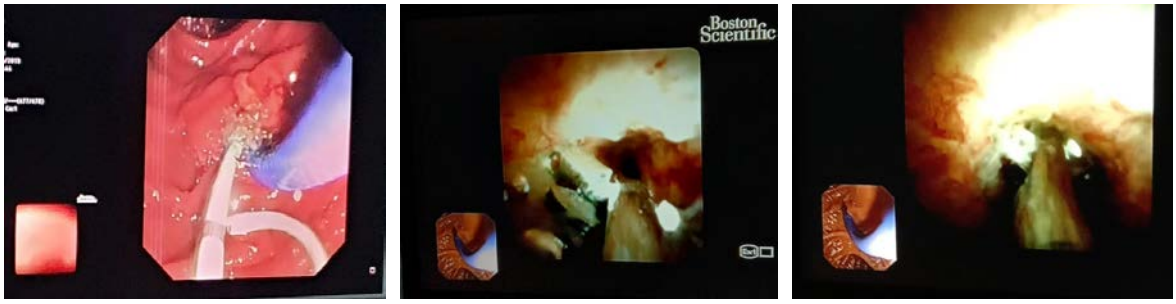

Figure 1. Cholangioscopy using SpyGlass DS showed nodularity with abnormal vascularity suggesting malignancy.

atypia suggesting positive for malignancy-cholangiocarcinoma. We plan further treatment for cholangiocarcinoma. Nature of underlying disease, long term prognosis and its complications has been explained in detail to patient and his attendants.

DISCUSSION

When the basic work-up (transabdominal imaging, endoscopic retrograde cholangiopancreatography and routine cytologic brushing) did not give diagnostic result, it is considered as an indeterminate biliary stricture.[8] We report an indeterminate biliary stricture patient and was diagnosed with cholangiocarcinoma using SpyGlass DS, previously detected as low-grade dysplasia by brush cytology. Although brush cytology of pancreatobiliary strictures has been the most common technique in the carcinoma diagnosis, the sensitivity was low from 48-68%.[9, 10] In contrast, a higher accuracy was observed in several studies used cholangioscopy. Using SpyGlass, a study in the United States reported sensitivity 97%, specificity 96%, positive predictive value 94%, and negative predictive value 98% for patients with indeterminate stricture.[11] The retrospective multicenter study also indicated a high sensitivity of 85% in 44 patients with indeterminate biliary strictures.[12] Asia-Pacific Expert Consensus suggested to use cholangioscopy in patients with indeterminate biliary strictures with Grade A recommendation.[13]

The presence of tumor vessels, indicative of malignancy are highly specific due to the different morphology with the normal vessels of the biliary mucosa that could be detected by experienced cholangioscopists.[14] Based on cholangioscopy findings, bile duct adenocarcinoma can be classified into nodular, papillary and infiltrative. A study reported that in 61% of patients with biliary malignancy, irregularly dilated and tortuous vessels was found but none were detected in benign biliary strictures cases.[15] Furthermore by using biopsy to confirm the malignancy, sensitivity was 80% and specificity was 100%. Thus, cholangioscopy finding is considered to be a general endoscopic marker for biliary malignancy. In contrast, a cholangioscopy biopsy as supplementary of tumor vessel observation might improve the ability to differentiate between benign and malignant biliary stricture. Although study found that tumor vessel ability to confirm malignancy only 61% for sensitivity and 100% for specificity, when tumor vessels and biopsy was combined, the sensitivity and specificity was improved to 96% and 100%, respectively.[15] Further, some studies suggested the on-site pathological evaluation for increasing the diagnostic yield of specimens.[12] Rapid on-site evaluation touch imprint cytology to cholangioscopy improve the sensitivity to 100%, specificity to 88.9%, with 86.7% of positive predictive value, 100% of negative predictive value, and 93.5% for the diagnostic accuracy.[16] Another issue is about biopsy size. The relatively low sensitivity of histology diagnosis was due to several limitations; inadequate number of obtained specimens, small size of the specimens as the result of SpyBite design and the absence of on-site cytology evaluation.[17]

Comprehensive evaluation on the patient's history is helpful to distinguish benign or malignant biliary strictures. A history of liver transplant, AIDS and cholecystectomy are the

frequent causes of benign biliary stricture. Careful observation on the clinical presentation is important because the patients may appear asymptomatic, but may also show abnormal liver test, pruritus, jaundice, right upper quadrant and fever (in several cases).[18] Weight loss and extensive fatigue symptoms require special attention because it may suggest a malignancy.

Transabdominal ultrasound examination provides low reliability of the distal part of the common bile duct due to the bowel gas interference. Meanwhile, abdominal CT may also useful but the sensitivity for early tumor was low. Magnetic resonance cholangiopancreatography ability to differentiate benign or malignant stricture was also problematic, even though it was relatively safe. Cholangiopancreatography procedure by magnetic resonance does not require injection of contrast, thus decreased the risk of cholangitis.[8] EUS-FNA was considered as a reliable option for vessels, perihilar lymph nodes, extrahepatic biliary tree and hilar masses, if the ERCP finding was inconclusive.[5] Serology diagnosis are also still controversial. Only 40% of the patients have elevated gamma glutamyltransferase and serum alkaline phosphatase and 40% of them are non-icteric.[19] As reported in a meta-analysis including 348 patients, another cancer marker CA 19-9 only yields has 69% sensitivity.[20] Importantly, increased serum CA 19-9 levels also occurred in benign cases including cirrhosis, cholestasis and cholangitis. Therefore, for cholangiocarcinoma diagnostic purpose, it is not recommended to use CA 19-9 as a single diagnostic tool but it could be combined with other tools to improve the reliability.[5] In general, ideal clinical, serological marker or radiological features was not available to distinguish benign and malignant biliary strictures accurately.

Several problems associated with cholangioscopy warrant precaution. Although it has detected similar complication rates of pancreatitis and perforation, cholangioscopy showed significantly higher cholangitis rate compared to ERCP (1% vs 0.2%).[21] The additional training required, cost and time consumed, limited area of working channel and inadequate image quality should also be noted.[3] The interobserver agreement was slight to poor,[22] suggesting validation and standardization of criteria for visual interpretation to improve the diagnosis of indeterminate biliary stricture.

CONCLUSION

We observed an additional value of SpyGlass DS for detecting cholangiocarcinoma in an indeterminate biliary stricture patient.

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