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Cholangioscopy in primary sclerosing cholangitis: a case series of dominant strictures and cholangiocarcinoma

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Background and Aims: Prompt and accurate differentiation of benign and malignant strictures in primary sclerosing cholangitis (PSC) is crucial. ERCP with brush cytology, the most common modality to achieve this, is hindered by a low diagnostic yield. Cholangioscopy can overcome this limitation by establishing a visual diagnosis based on the characteristic morphologic features of cholangiocarcinoma (CCA) and can aid in targeted biopsies of suspicious lesions. However, its role in PSC remains unclear. This case series demonstrates the performance of the latest generation of single-operator cholangioscope for this indication.

Methods: A single experienced endoscopist performed cholangioscopy for PSC cases referred for ERCP.

Results: Cholangioscopies of patients 1 to 3 demonstrate the features of extrahepatic duct dominant strictures (DS) and the cholangioscopic maneuvers undertaken in these cases, including advancement across the DS after balloon dilation, biopsy of the DS, and electrohydraulic lithotripsy of impacted stones. Cholangioscopies of patients 4 to 6 demonstrate the varied features of CCA ranging from focal stricture with tumor vessels, papillary frond-like projections, and features of an intraductal papillary biliary neoplasm. Also shown are the radiographic and histopathologic features of the disease.

Conclusions: Cholangioscopy allowed us to identify morphologic features of both malignancy and benign disease in PSC in the setting of extrahepatic duct strictures, and we were able to obtain adequate targeted tissue samples for histopathologic confirmation. (VideoGIE 2021;6:277-81.)

Primary sclerosing cholangitis (PSC) is a chronic inflammatory disease characterized by intra- and extrahepatic bile duct strictures. Strictures <1.5 mm in diameter in the extrahepatic duct or <1 mm in the intrahepatic duct are termed dominant strictures. Dominant stricture is the most common indication for ERCP in PSC,[1] not only to attempt balloon dilation to relieve the obstruction but also to rule out cholangiocarcinoma (CCA) because a high proportion of dominant strictures is thought to harbor CCA.[2] In fact, PSC is associated with a 400-fold higher risk of CCA compared with the general population.[2]

Prompt and accurate differentiation of benign and malignant strictures in PSC is crucial. ERCP with brush cytology remains the most common modality to achieve this, but it is hindered by low diagnostic yield.

Cholangioscopy can overcome this limitation by establishing a visual diagnosis based on the characteristic morphologic features of CCA and can aid in targeted biopsy of suspicious lesions.[3] However, its role in PSC remains unclear, based on studies of the previous generation of cholangioscopes with their inherent limitations of suboptimal image quality, restricted tip mobility, and smaller biopsy forceps. Current studies have extrapolated characteristic morphologic features of non-PSC CCA such as prominent or tortuous tumor vessels to establish a visual diagnosis of CCA in PSC.[4] Furthermore, cholangioscopy is deemed to be technically challenging in the setting of strictured ducts and hence is not routinely undertaken in PSC.[5]

In this case series, we present cholangioscopic features of dominant strictures and the varied and unique presentations of CCA in PSC.

DESCRIPTION OF TECHNIQUE

All procedures were performed using the duodenoscope (Olympus TJF-180, Olympus America, Inc, Center Valley, Pa, USA) and the third-generation single-operator cholangioscope (SpyScope DSII Access and Delivery Catheter, Boston Scientific Corp, Natick, Mass, USA). Intraductal biopsy specimens were obtained using the SpyBite forceps (Boston Scientific).

The technique of cholangioscopy in PSC is similar to non-PSC cases with the following exceptions. Advancement of the cholangioscope under direct visualization into the duct must be done with extra caution, especially if the stricture is in the distal common bile duct (CBD).

This helps avoid mucosal trauma, which can obscure the examination and thereby increase the need for irrigation, which can in turn lead to increased intraductal pressure and risk of cholangitis.[6] Whenever possible, free-hand cannulation and advancement without a guidewire is preferable to avoid guidewire-related mucosal trauma in an actively inflamed duct. In addition, the presence of the guidewire can limit the maneuverability of the cholangioscope; acute turns are often needed both in the extrahepatic duct and at the hilum because of the presence of fibrostenosis.

When the dominant stricture does not allow for safe advancement, balloon dilation followed by cholangioscope advancement can be successful. It is important to minimize irrigation to avoid displacing pigmented stones within the duct[7] and to anticipate the need for electrohydraulic lithotripsy of stones impacted proximal to the dominant strictures. To identify the morphologic features of CCA, it is best to examine the biliary tree before interventions such as guidewire advancement, stricture dilation, cytology brushings, and forceps biopsy. It is vital to examine as much of the hilar region as possible because CCA tends to predominantly affect this region.[8]

After examination of the extrahepatic bile duct, a cholangiogram of the intrahepatic biliary tree can be obtained via contrast injected through the accessory channel of the cholangioscope. This is best done with the cholangioscope positioned at the common hepatic duct or hilum. Contrast injection lower in the CBD is not optimal because contrast tends to flow out of the ampulla instead of opacifying the proximal ducts. This avoids the need for exchanging to a balloon catheter to obtain an occlusion cholangiogram. Selective guidewire cannulation of intrahepatic ducts is also possible through the cholangioscope if a particular intrahepatic biliary stricture is being evaluated. Finally, targeted biopsy specimens can be obtained using either the SpyBite or SpyBite Max forceps, depending on the luminal width.

All strictures were brushed for cytology and fluorescent in situ hybridization (FISH) analysis. This is a vital part of the procedure because cytology can uncover suspicious findings in cases in which histopathology results are nondiagnostic. All patients were given antibiotic prophylaxis during the procedure and for 3 to 5 days after the procedure to prevent cholangitis. Patients were also given rectal indomethacin 100 mg suppository to prevent post-ERCP pancreatitis.

VIDEO DESCRIPTION

Dominant strictures

The first case is a 71-year-old man with fatigue, new-onset cholestasis, and a normal CA 19-9 level. MRCP showed mild narrowing of the common hepatic duct with beading of the intrahepatic ducts. Digital cholangioscopy showed a high-grade stricture at the common hepatic duct (Fig. 1 and Video 1, available online at www.VideoGIE.org). The ductal mucosa distal to the stricture showed chronic inflammatory changes and luminal narrowing with a lack of vascular markings. After biopsy specimens were obtained, the stricture was dilated with a 6-mm balloon, allowing cholangioscope advancement past the stricture. Cytology showed atypical cells, but the patient has been doing well for 18 months with no evidence of malignancy on 3 subsequent ERCPs.

Figure 1. Common hepatic duct stricture and hilum in case 1.

The second case is a 53-year-old man with mild cholangitis, pruritus, fatigue, mildly abnormal liver function tests (LFTs), and normal CA 19-9 level. Magnetic resonance imaging (MRI) showed subtle irregularity of the left intrahepatic biliary ducts. Digital cholangioscopy showed a high-grade stricture in the common hepatic duct (Fig. 2 and Video 1, available online at www.VideoGIE.org). After biopsy specimens were obtained, the stricture was dilated with a 4-mm balloon. The stricture was then examined by cholangioscopy, which revealed mucosal trauma from the dilation but no features of malignancy (Fig. 3). Biopsy specimens of the stricture showed chronic inflammation with reactive changes but no dysplasia or malignancy. The patient is doing well at 7 months after ERCP.

The third case is a 71-year-old man with mild cholangitis, worsening LFTs, and normal CA 19-9 level. Ultrasound showed a CBD stricture. MRI and MRCP showed tapered loss of the proximal CBD with mild intrahepatic ductal dilation, particularly in the left lobe. A pinhole stricture was seen in the mid-CBD (Fig. 4 and Video 1, available online at www.VideoGIE.org), which was dilated with a 6-mm balloon, after which the cholangioscope could be advanced through the stricture. Biopsy specimens were obtained, and did not show malignancy. On carefully maneuvering

Figure 2. Common hepatic duct stricture in case 2.

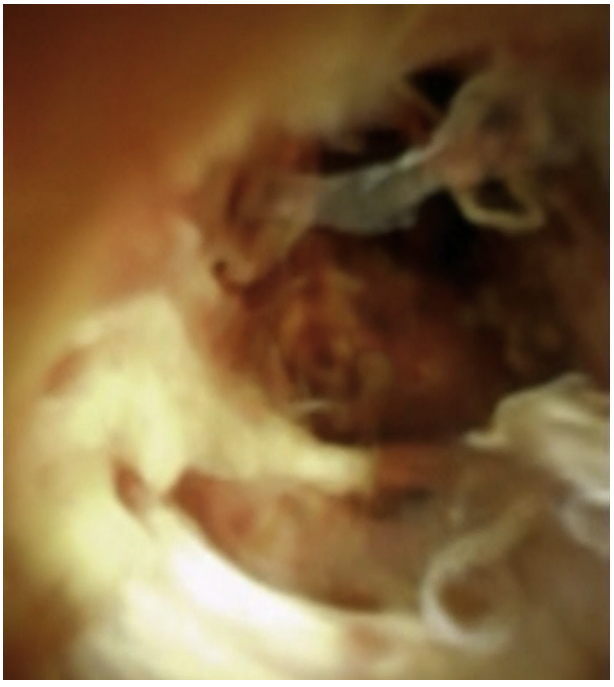

Figure 3. Postdilation appearance of common hepatic duct stricture in case 2.

through the stricture after dilation, an obstructing pigmented stone was encountered (Fig. 5), which was fragmented with electrohydraulic lithotripsy, followed by basket sweep extraction. No evidence of malignancy was noted on biopsy, cytology, or FISH analysis. On subsequent ERCPs, the patient was noted to have an additional dominant stricture involving the right hilum and common hepatic duct, without evidence of

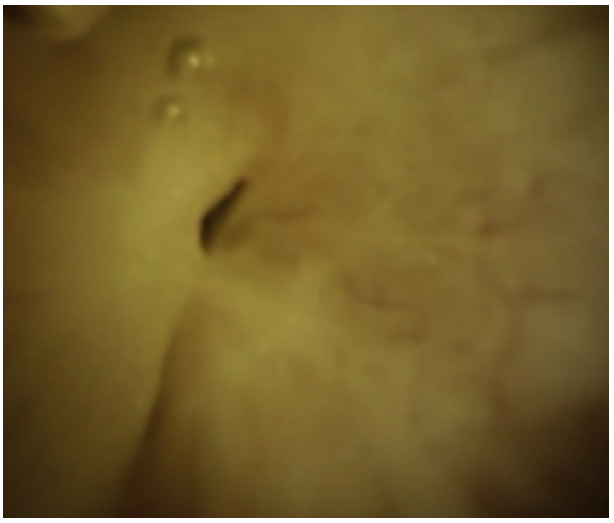

Figure 4. Common bile duct stricture in case 3.

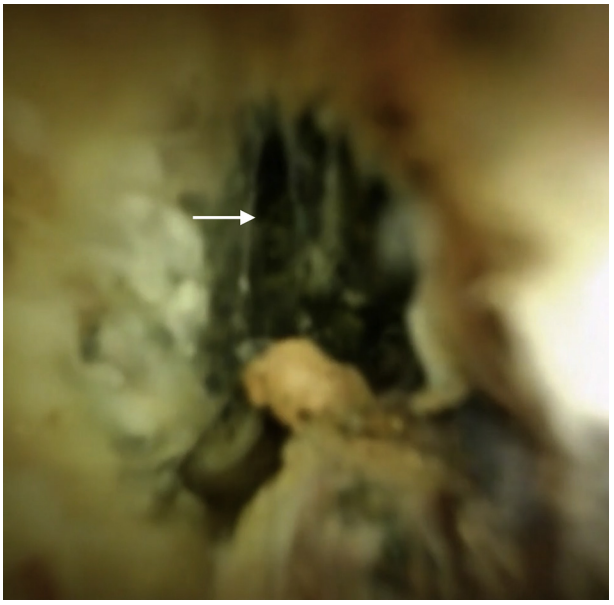

Figure 5. Postdilation finding of impacted pigmented stone (*white arrow*) proximal to the common bile duct stricture in case 3.

malignancy on biopsy or cytology, including FISH analysis. Owing to decompensated cirrhosis, he is awaiting living-donor liver transplantation.

Cholangiocarcinoma

The fourth case is a 63-year-old man with jaundice, pruritus, anorexia, and weight loss. His LFTs show predominant cholestasis with an elevated CA 19-9 level. MRI with MRCP shows diffuse ductal dilation and several bile lakes. Cholangioscopy showed a focal stricture at the common hepatic duct with increased vascularity and tortuous vessels (Fig. 6 and Video 1, available online at www.VideoGIE.org). Biopsy specimens were nondiagnostic, but cytology results from brushings were suspicious for

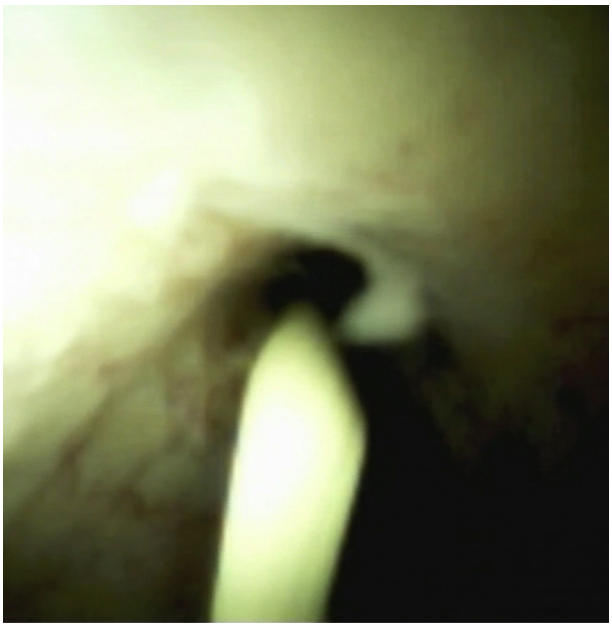

Figure 6. Common hepatic duct stricture with increased vascularity with guidewire coursing the duct in case 4.

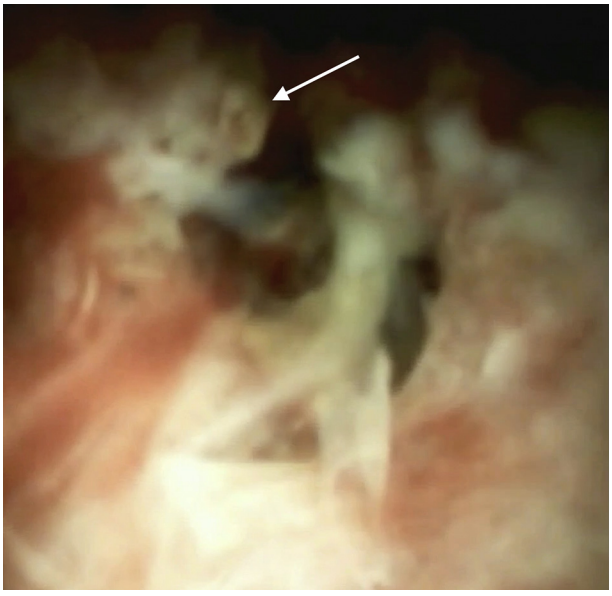

Figure 7. Frond-like papillary growths (*white arrow*) in the hilum in case 5.

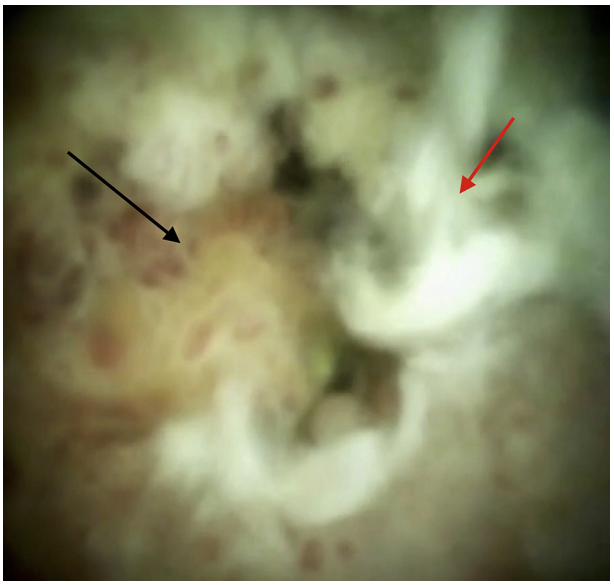

Figure 8. Papillary growths (*black arrow*) in the distal common bile duct with surrounding mucin (*red arrow*).

malignancy. Surgical specimen after hepaticojejunostomy confirmed invasive adenocarcinoma of the common hepatic duct.

The fifth case is a 62-year-old man with right upper quadrant pain, anorexia, and weight loss. MRI showed interval increase in intrahepatic dilation and relative atrophy of the left hepatic lobe with slight capsular retraction. Cholangioscopy was performed after balloon dilation of strictures in the extrahepatic bile duct and showed mucosal erythema. Frond-like papillary growths were seen at the hilum (Fig. 7 and Video 1, available online at www.VideoGIE.org). Biopsy examination showed granulation tissue. Cytology showed atypical cells suspicious for malignancy. He was diagnosed with cholangiocarcinoma on subsequent ERCP and underwent a liver transplant 2 years later.

The sixth case is a 48-year-old woman with right upper quadrant pain, anorexia, and weight loss. She had significant cholestasis and an elevated CA 19-9 level. MRI with MRCP showed a circumferential enhancing mass in the distal CBD with severe upstream dilation. On cholangioscopy, we saw features of an intraductal papillary neoplasm of the bile duct—papillary growths in the distal CBD (Fig. 8 and Video 1, available online at www.VideoGIE.org).[8] The uninvolved portions of the ducts showed mucosal scarring. Copious mucin was seen within a dilated duct. The disease was multifocal involving several areas of the extrahepatic duct and the left intrahepatic duct. Histopathology showed high-grade dysplasia with signet-ring changes. Cytology from brushing showed adenocarcinoma. Surgery was deferred in favor of chemoradiation because of her cirrhosis.

CONCLUSIONS

Cholangioscopy with biopsy is feasible and safe in PSC, despite the stricturing disease. Dominant strictures of the extrahepatic bile duct can be examined and traversed with the cholangioscope after balloon dilation. An adequate mucosal examination of the dominant strictures is possible to rule out features of malignancy, which can be confirmed on biopsy combined with brushings.

Cholangioscopy can also uncover findings that may not be seen on cross-sectional imaging, especially impacted pigmented stones that may need cholangioscopy-aided ductal clearance.

The morphologic features of CCA in PSC were different from conventional CCA and included a presentation identical to intraductal papillary neoplasm of the bile duct. Directed biopsy combined with brushings for cytology and FISH analysis can help with early diagnosis.

Accurate differentiation of PSC strictures with cholangioscopy can help customize endoscopic surveillance strategies, allowing for less-frequent endoscopic interventions for those with benign fibrostenotic disease, while monitoring those with suspicious findings more closely.

DISCLOSURE

All authors disclosed no financial relationships.

Abbreviations: CBD, common bile duct; CCA, cholangiocarcinoma; DS, dominant stricture; FISH, fluorescent in situ hybridization; LFTs, liver function tests; MRI, magnetic resonance imaging; PSC, primary sclerosing cholangitis.

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