14 Endoscopic Evaluation and Management of Primary Sclerosing Cholangitis

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Introduction

Primary sclerosing cholangitis (PSC) is a chronic inflammatory cholestatic liver disease that is characterized by fibrosis and progressive destruction of the intra- and extrahepatic bile ducts with an increased risk for cholangiocarcinoma (CCA) and eventual development of cirrhosis in the majority of patients [1]. In this chapter we review the central role of endoscopy in the initial diagnosis of PSC, endoscopic evaluation and endotherapy for dominant strictures, endoscopic evaluation for development of CCA, and endoscopic evaluation and management of recurrent PSC after liver transplantation.

Endoscopic Evaluation of PSC

PSC diagnosis is usually pursued after the incidental finding of persistent abnormal cholestatic liver function tests (most commonly, alkaline phosphatase) or presentation with suspicious symptoms (later in the course of the disease) such as abdominal pain, pruritus, fatigue, and weight loss [2].

Endoscopic retrograde cholangiography (ERC) was previously the de facto diagnostic tool in patients with suspected PSC; however, many studies have shown that magnetic resonance cholangiography (MRC) performs equally well with sensitivity and specificity of ≥80 % and ≥87 %, respectively, for the diagnosis of PSC. Given the noninvasive nature and lack of radiation exposure, MRC is currently considered the diagnostic modality of choice in patient with suspected PSC [3, 4].

Nonetheless, ERC may still have a role as a diagnostic tool in PSC, particularly in patients with early changes of PSC that could be missed by MRC, or when MRC visualization of the bile ducts is limited or equivocal [4] (Fig. 14.1).

The typical findings on cholangiography include multifocal, short, annular strictures alternating with normal or slightly dilated segments resulting in a "beaded" appearance (Fig. 14.2).

Confluent long strictures can also sometimes be seen and are worrisome for the development of CCA. Typically, both intra- and extrahepatic bile ducts are involved, although a subset of patients (<25 %) may have intrahepatic disease only. The gallbladder, cystic duct, and pancreatic duct may also be associated with PSC [5]. The classic cholangiographic findings mentioned above are not entirely specific and can sometimes be seen in secondary causes of sclerosing cholangitis such

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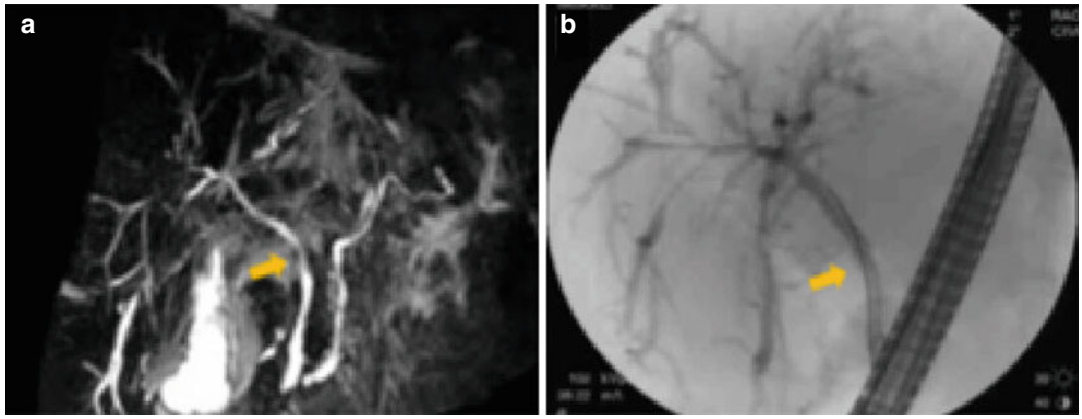

Fig. 14.1 (**a**) MRC images suspicious for a dominant stenosis in the mid bile duct (*arrow*). (**b**) Follow-up ERCP showed no evidence of stenosis in the bile duct (*arrow*)

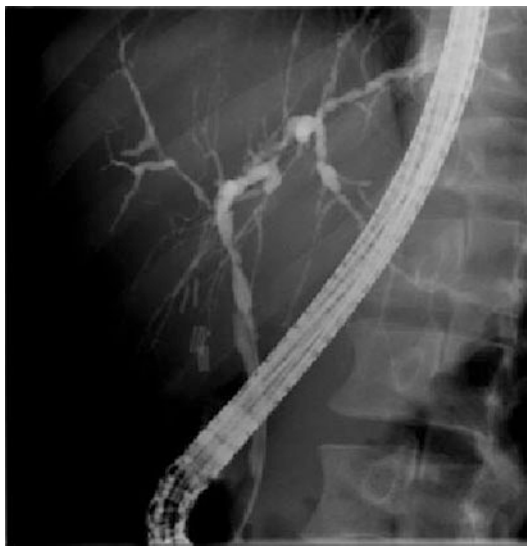

Fig. 14.2 Typical cholangiographic features of multifocal, short, annular strictures alternating with normal or slightly dilated segments resulting in a "beaded" appearance

as autoimmune pancreatitis, portal biliopathy, eosinophilic cholangitis, mast cell cholangitis, hepatic inflammatory pseudotumor, recurrent pyogenic cholangitis, primary immune deficiency, and AIDS-related cholangiopathy [6].

Endoscopic ultrasound (EUS) has also been studied as a minimally invasive tool for the diagnosis of extrahepatic PSC. Lutz et al. evaluated four sonographic parameters that are suspicious for PSC: wall thickening (≥1.5 mm), irregular wall structure (≥1 mm thickening in a duct length of maximum 5 mm), significant changes of the caliber of the common bile duct (≥2 mm change in a duct length of maximum 5 mm), and perihilar lymphadenopathy (≥10 mm). When two of these parameters were met, the sensitivity and specificity of predicting PSC were 76 % and 100 %, with positive and negative predictive values of 100 % and 79 %, respectively [7]. EUS-guided liver biopsy has been gaining more popularity as a safe and efficacious method to get adequate liver tissue samples and may be utilized more in the future when radiologic and endoscopic evaluation for PSC is inconclusive [8, 9].

Endoscopic Therapy for PSC

Endoscopic biliary therapy for PSC is primarily performed as a palliative measure and to exclude neoplasia. The presence of worsening symptoms (pruritus and RUQ abdominal pain), jaundice, cholangitis, rising cholestatic liver enzymes, or CA 19-9 in patients with PSC are typical indications for endoscopic retrograde cholangiopancreatography (ERCP) with the main goal of targeting a dominant biliary stricture for tissue sampling and endotherapy. If mass lesion or abscess is clinically suspected, abdominal ultrasound or MRI can be more helpful initial diagnostic tests.

A reasonable goal with endoscopic treatment is improving symptoms and excluding

malignancy. A surrogate marker for improved biliary drainage is serum alkaline phosphatase. Improvement of serum alkaline phosphatase to <1.5 upper limit of normal was found to predict a better outcome and reduce the risk of CCA in PSC [10, 11]. Predictors for successful clinical and laboratory improvement after therapeutic ERCP include a high bilirubin level and the presence of a dominant stricture, especially in the common bile duct location [12].

Although randomized, controlled data to evaluate the effectiveness of endoscopic therapy in PSC is not available, multiple uncontrolled case series have suggested favorable outcomes. Gotthardt et al. followed 171 PSC patients for up to 20 years. Patients with dominant stenoses underwent serial endoscopic dilations. The 5- and 10-year survival free of liver transplantation was 81 % and 52 %, respectively [13]. Another study that evaluated the impact of endoscopic therapy in PSC patients reported a significantly higher 5-year survival rate in patients undergoing endoscopic therapy than what was predicted by the Mayo risk score (83 % vs. 65 %). Multiple studies have supported this finding with 4- or 5-year survival rates that are 12–18 % higher than what was predicted by the Mayo risk score [14–16].

Endoscopic Sphincterotomy

Although the biliary sphincter could be involved by the inflammatory/fibrotic process in PSC and may contribute to biliary obstruction, sphincterotomy alone is seldom used as a sole treatment modality in PSC but rather to facilitate further interventions such as tissue sampling, stone extraction, balloon dilation, or stent placement [17].

Balloon Dilation vs. Stenting of Dominant Stenoses

Balloon dilation without stenting has been shown to be an effective modality to treat dominant strictures in PSC. In a prospective single-center study from Germany, 96 patients with dominant stenoses were treated with endoscopic balloon dilations, only five of which needed a short-term (1–2 week) stent due to complete biliary obstruction and cholangitis. Over the 20-year study duration, an average of 5.2 balloon dilations per patient were performed (range 1–17). Endoscopic balloon dilations allowed the preservation of a functioning common bile duct and of at least one hepatic duct up to 2 cm above the bifurcation in all patients. Progression of liver disease led to the need for liver transplantation in 23 % of patients [13].

Some experts, including our institution, advocate for endoscopic stenting to treat benign dominant stenoses in a similar fashion as benign postoperative biliary strictures [18] (Fig. 14.3).

One of the early reports of stent therapy in PSC revealed technical success in 21 out of 25 patients (84 %) with dominant stenosis. Stents were exchanged or removed either electively at 2–3 month intervals or because of symptoms attributed to clogging. Endoscopic stenting was followed by clinical and biochemical improvement in 16 of 21 patients (76 %) over a median follow-up of 29 months. However, it was noted that about half of the follow-up ERCPs were performed on a nonelective basis because of jaundice or cholangitis attributable to early clogging of stents [19]. As a result, most centers advocate earlier removal (e.g., 2–4 weeks) of indwelling biliary stents, though our practice has been to perform stent exchanges at 6–8-week intervals until the dominant stenosis has resolved. Etiology for stent failure in PSC may include the rapid occlusion of stents by inflammatory debris shed from the biliary tree. Moreover, in patients with dominant stenoses near the bifurcation, placement of one stent into a hepatic duct could potentially worsen the drainage of the unstented hepatic duct; thus, if a dominant stenosis extends into both the right and left hepatic ducts, we would advocate for bilateral stenting.

To compare balloon dilation and stenting, a retrospective single-center study of 71 patients found no significant difference in cholestatic parameters between patients who underwent endoscopic dilation alone versus those who received stenting in addition to dilation. However,

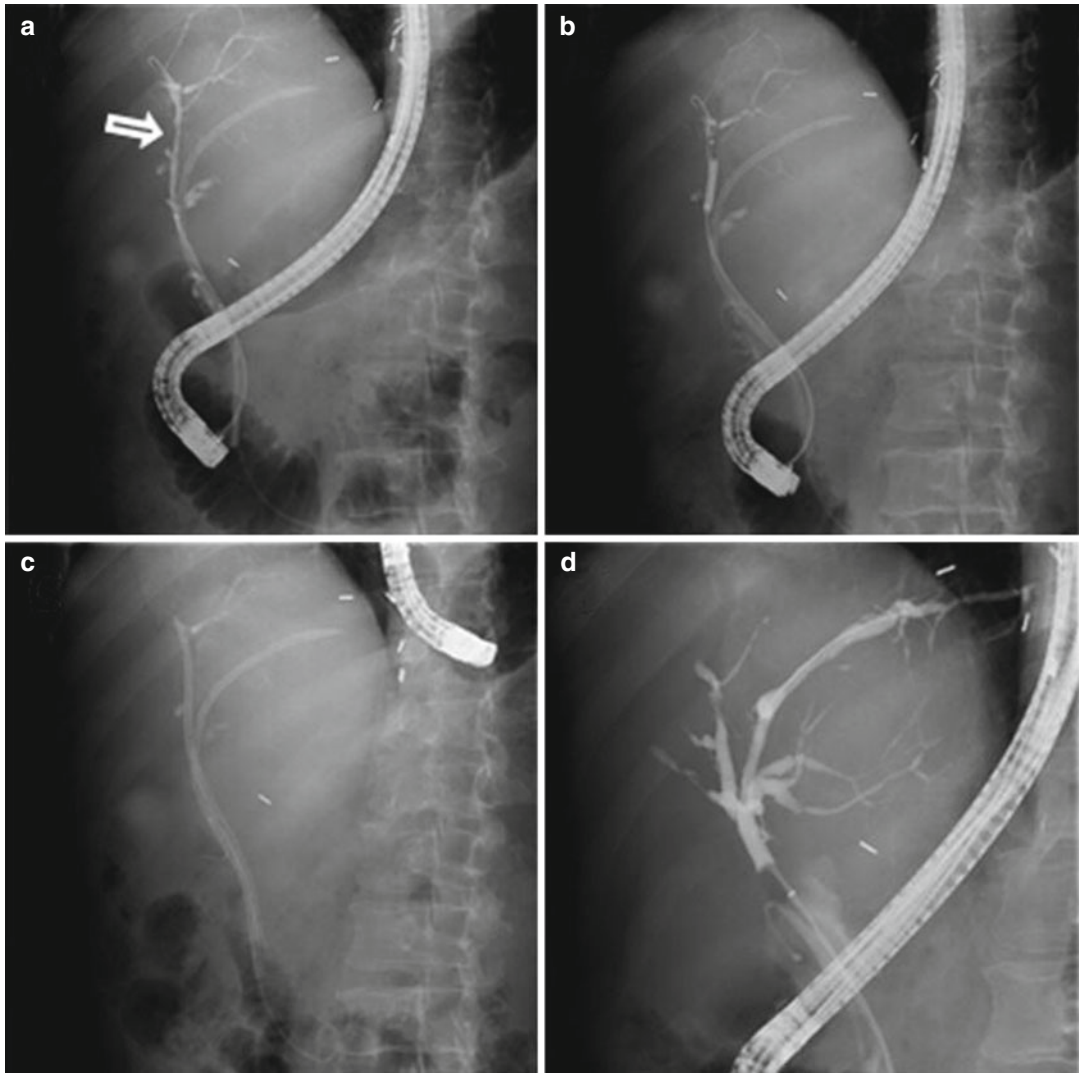

Fig. 14.3 Moderate localized biliary stricture in the right hepatic ducts (**a**) treated with balloon dilation (**b**) and stent placement (**c**) with resulting improvement of the stricture after 8 weeks (**d**)

a significantly higher rate of adverse events (AEs) such as cholangitis was noted in the stent group [20]. The authors concluded that there was no additional benefit from stenting after balloon dilation and that stenting was associated with more AEs. However, in this cohort of patients, stents were only placed in patients for whom biliary drainage was not adequate with endoscopic balloon dilation alone. Therefore, the patients in the stent group may have had more severe disease compared to the balloon-dilation-only group. It is also noteworthy that a subgroup analysis showed significantly higher AEs related to percutaneous biliary drains (such as cholangitis, bleeding, and bile duct perforation) compared to endoscopic stenting [20].

To overcome the problem of premature clogging of stents and resulting adverse events (AEs), some studies focused on reducing the duration of stent placement. In one study, sixteen patients with symptomatic PSC and dominant stenoses were treated with short-term stent placement (median duration, 9 days) and found that 81 % of patients remained asymptomatic

over a 19-month follow-up without recurrence of cholestasis [21]. In another study, 32 patients with dominant strictures were treated with short-term stenting (mean duration 11 days, range 1–23 days). Serum bilirubin normalized in 12 of 14 patients (86 %) who initially presented with jaundice, and 80 % of the patients remained intervention-free after 1 year [22].

Temporary plastic stents are the only type of stents used currently for the treatment of dominant strictures in PSC [23]. We would avoid the use of fully covered self expanding metal stent (SEMS) in this patient population due to often small diameter of ducts and risk of stent-associated changes that may be seen with indwelling fully covered SEMS.

Endoscopic Evaluation for Malignancy in PSC

The incidence of CCA in patients with PSC is higher than in the general population. Population-based studies show that the annual risk is about 2 % with cumulative 10-year and 30-year incidences of 6–11 % and 20 %, respectively [24–26].

CCA in PSC is usually detected at an advanced stage and has a very poor prognosis with a dismal overall median survival of just 5 months [27]. In appropriate candidates, if CCA is detected in an early stage, expedited consideration for curative liver transplantation may be pursued.

Patient- or disease-related risk factors that seem to increase the risk of CCA in PSC include older age at time of PSC diagnosis, longer duration of inflammatory bowel disease, history of colorectal cancer or dysplasia, history of variceal bleeding, tobacco smoking, and alcohol consumption [24, 26, 28–33].

If suspected, confirming (or excluding) CCA in PSC patients can be clinically challenging to the endoscopist. The presence of segmental fibrotic strictures throughout the biliary tree makes access to the areas of concern and adequate tissue sampling very challenging.

If CCA is suspected due to abnormal imaging studies, increasing LFTs or CA 19-9 the biliary tree should be evaluated for the presence of dominant strictures, as they appear to be a major risk factor for CCA [34]. A “dominant stricture” is defined as a stenosis with a diameter of 1.5 mm in the common bile duct or of 1 mm in the right or left main hepatic ducts (within 2 cm of the bifurcation) [35].

The prevalence of dominant bile duct strictures in PSC is 36–57 %, and up to one quarter of dominant strictures is malignant [35, 36]. Hence, these are the primary targets for tissue sampling at time of ERCP. One study that clearly showed the importance of dominant strictures in PSC followed 128 patients for a mean duration of 9.8 years. The survival was reduced in patients with dominant strictures (13 %) compared to those without (23 %). The difference in survival was mostly due to the development of CCA in patients with dominant strictures [36]. In the early stages of PSC, CCA may still develop without the presence of a dominant stricture. Further, according to population-based studies, around one-third of the hepatobiliary malignancies are diagnosed within the first year after the diagnosis of PSC [24, 26].

Diagnostic Workup

Non-endoscopic methods to diagnose CCA in PSC such as serum tumor markers and imaging studies lack both sensitivity and specificity for the detection of CCA.

The most commonly used tumor marker in clinical practice is CA 19-9. In a prospective observational study from Germany that included a cohort of 106 patients who were followed for a median of 5 years, CA 19-9 was elevated (>100 ng/ml) in 24 % of patients; however, CCA developed in only 3 %. It is also not uncommon to see a drop in CA 19-9 level after treatment of biliary obstruction and caution should be exercised in its interpretation in the setting of acutely worsening cholestasis (e.g., cholangitis or jaundice) as it may inappropriately alarm both patient and provider [37]. Moreover, it is noteworthy that CA 19-9 testing will have no value in patients with negative Lewis antigen (7 % of the general population) as they cannot express CA 19-9 [38].

Imaging studies seem to perform poorly as well. A study that followed 230 patients over 6 years reported sensitivity to ultrasound, computed tomography, and magnetic resonance imaging for CCA of 57 %, 75 %, and 63 %, respectively [39].

Endoscopic Evaluation of Dominant Biliary Strictures in PSC

Brush Cytology

This includes the use of conventional cytology brush during ERCP to obtain cells from a concerning stricture for cytology analysis (Fig. 14.4).

This method is considered relatively easy and has a very high specificity (95–100 %), but unfortunately has a disappointing low sensitivity that ranges from 29 to 73 % [40, 41].

These findings were confirmed by a meta-analysis of 54 studies that revealed a pooled specificity of 97 % but a pooled sensitivity of only 43 % [42]. It is likely that the low sensitivity is due to severe periductular fibrosis and stricturing in PSC limiting access and adequate sampling of concerning areas.

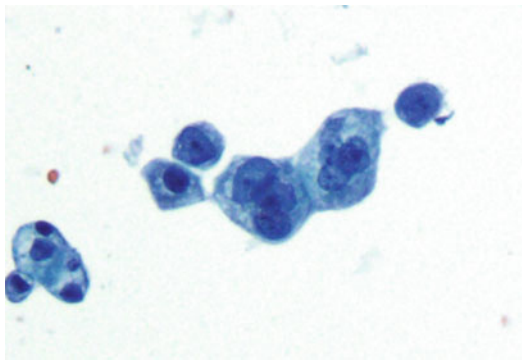

Fig. 14.4 Cluster of malignant cells from a common bile duct brushing (*arrow*) in PSC. In comparison to the adjacent benign cells (*arrow head*), the malignant cells are larger, with dark nuclei and high nucleus to cytoplasmic ratios than the benign cells. Papanicolaou stain, 200× (Image courtesy of Paul Dimaggio, MD, University of Colorado Department of Pathology)

Endoscopic Ultrasound

EUS-guided fine needle aspiration (EUS-FNA) can be a valuable diagnostic tool for suspected malignant biliary stricture when brush cytology and biopsy are inconclusive with a sensitivity and specificity up to 89 % and 100 %, respectively [43, 44]. EUS-FNA can also be utilized for evaluation and sampling of suspicious lymph nodes. Given the rare possibility of tumor seeding with FNA [45], most institutions feel that EUS-FNA of suspicious biliary strictures is a contraindication to liver transplantation.

Fluorescence In Situ Hybridization (FISH)

In this technique, fluorescently labeled DNA probes are used to assess cells obtained using biliary brushings for chromosomal abnormalities. At our center, we provide two brushing specimens of the stricture and submit to cytology who will then divide the specimens for routine cytology and FISH evaluation. The probe set used assesses the pericentromeric regions on chromosomes 3, 7, and 17, and a locus-specific probe on chromosome 9p21 [46, 47]. The results of FISH testing can be classified as normal, polysomy (if five or more cells show gains of two or more of the four probes), tetrasomy (if 10 or more cells showed four copies of all probes), and trisomy (if 10 or more cells showed three copies of chromosome 7 or 3 and two or fewer copies of the other three probes) [46] (Fig. 14.5).

FISH polysomy is highly associated with CCA; however, trisomy and tetrasomy are not considered independent predictors for CCA, and patients with these changes seem to have a similar outcome to patients with normal FISH testing [46–49].

In a Mayo clinic study of 235 PSC patients, FISH polysomy had a sensitivity of 46 % and specificity of 88 % for the diagnosis of CCA [46]. These findings were confirmed by a meta-analysis of eight studies involving 828 patients [50]. An interesting subsequent study from the same center showed that in patients with an index

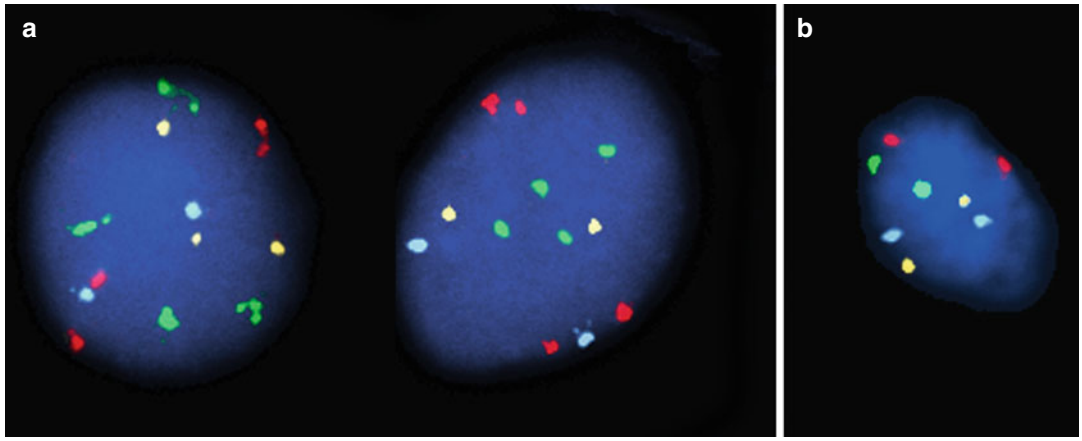

Fig. 14.5 A chromosome enumeration assay for interphase cells was performed using a mixture of DNA sequence probes specific for the centromeres of chromosome 3 (*red*), 7 (*green*), and 17 (*aqua*) and for the 9p21 (p16) locus on chromosome 9 (*gold*) along with a DAPI counterstain on ThinPrep slides of bile duct brushings. (Panel **a**) Two polyploid interphase cells from the same patient demonstrating four copies of chromosome 3, four copies 7 centromere, and two copies of 9p16 and 17 centromere sequences. (Panel **b**) A normal interphase cell with two copies of each signal for 3, 7, and 17 centromere and 9p21 (p16) sequences (Image courtesy of Billie Carstens, Colorado Genetics Laboratory)

polysomy FISH study who had subsequent non-polysomy results, only 18 % ended up developing CCA. For those patients with subsequent positive polysomy FISH (so-called serial polysomy), 69 % subsequently developed CCA [47]. This study emphasizes the limitation of a single polysomy FISH result and the importance of repeating the FISH testing for risk stratification. Further, in liver transplant centers that propose treating PSC patients with suspected CCA utilizing the Mayo protocol, the proposal is based on suspicious cholangiographic appearance of a stricture, elevated CA 19-9 (greater than 100), and/or FISH polysomy to support the upgraded listing [51].

Another study that attempted to improve the utility of FISH testing in PSC showed that finding of positive FISH testing in multiple areas of the biliary tree, so-called multifocal polysomy (MFP), was the strongest predictor of CCA (when compared to unifocal polysomy and suspicious cytology). The 1- and 3-year cumulative incidence rates of CCA among MFP patients were 65 % and 83 %, respectively. This study suggested that brushing multiple areas of the biliary tree (even without the presence of dominant stricture) and placing the specimens in separate jars help risk stratify these patients and may improve the ability to detect CCA. Interestingly, this study did not find an elevated CA 19-9 (>129 U/ml) to be an independent predictor of CCA [48].

Intraductal Endoscopy

Cholangioscopy provides direct visualization into the biliary tree. However, it has a limited role in PSC due to narrowed ducts and inability to traverse strictures without pre-inspection dilation, which could alter mucosal characteristics [52]. Further, inflammatory changes in the setting of PSC or stent changes could make it difficult to distinguish from malignant changes and nodular mass-like villiform changes are not uncommon in benign PSC [52, 53]. However, select studies have suggested that cholangioscopy might increase the ability to differentiate between malignant and benign strictures in PSC [54]. In a prospective observational study from Germany that included 53 PSC patients, cholangioscopy (2D-Microendoscope ERCP, Almikro Ltd., Bad Krozingen, Germany) had a higher sensitivity (92 % vs. 66 %; $P = 0.25$) and specificity (93 % vs. 51 %; $P < 0.001$) for detecting CCA, when

compared to endoscopic brush cytology alone [55]. However this degree of neoplasia detection utilizing cholangioscopy has not yet been duplicated. Liu et al. reported a sensitivity of 75 % and specificity of 55 % for cholangioscopy (SpyGlass system, Boston Scientific, Natick, MA, USA) in 18 PSC patients with suspected CCA [54]. Another recent small report described the use of video cholangioscopy and NBI (Olympus Tokyo, Inc) during cholangioscopy. Despite a 48 % increase in the rate of detecting suspicious lesions that led to more biopsy specimens being obtained, NBI-directed biopsies did not improve the dysplasia detection rate compared with white-light imaging and overall did not confirm a true value for the use of cholangioscopy in this patient population [56]. Further, we reported our data on the use of cholangioscopy in 41 patients with PSC. Cholangioscopy identified one extrahepatic CCA but missed two intrahepatic CCAs. In this report, cholangioscopy was very helpful to detect biliary stones in 56 % of patients (30 % of which were missed on cholangiography) which could contribute to recurrent cholangitis [52].

Transpapillary intraductal ultrasound was used to analyze dominant strictures in 40 PSC patients and showed a sensitivity of 87.5 % and specificity of 90.6 % for detection of CCA. Larger studies are needed to confirm the utilization of this technique in PSC patients and fragility of the probes have limited its use [57].

Probe-Based Confocal Laser Endomicroscopy (pCLE)

Due to the limitations of conventional tissue sampling and direct visual inspection of mucosal changes by cholangioscopy, investigation in the subepithelial changes that may help exclude malignancy has been sought. The technique of pCLE provides a real-time in vivo microscopic images of the bile duct epithelium using a small (2.8 F) diameter probe but requires direct contact to the mucosa and a minimally tangential approach for optimal imaging. Due to the probe size, pre-inspection dilation is generally not required. The probe can be placed either through a cholangioscope or through the lumen of a standard cannula that permits tip deflection (Swing Tip, Olympus America, Inc). The Miami classification was developed for indeterminate non-PSC biliary stricture. It includes five malignant imaging characteristics: thick white bands (>20 μms), thick dark bands (>40 μms), epithelial structures, dark clumps, and fluorescein leakage [58, 59] (Fig. 14.6).

Our group evaluated a total of 20 strictures specifically in patients with PSC. The use of pCLE was feasible in 95 % of examinations. The sensitivity was 100 %; however, specificity was only 61.1 %. This was likely due to inflammatory ductal changes in the setting of PSC. Interestingly, in two patients with positive pCLE but only

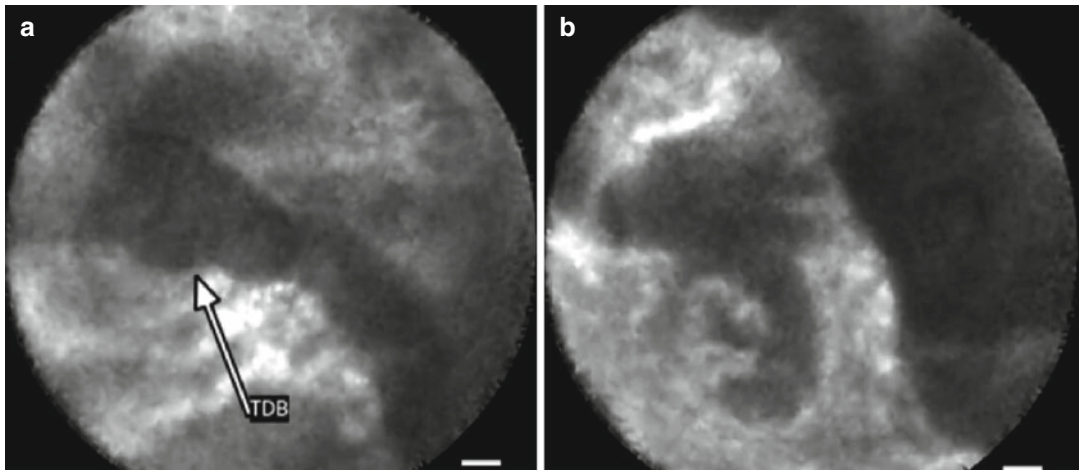

Fig. 14.6 pCLE images in malignant dominant stricture. (**a**) Showing thick dark band and (**b**) showing dark clumps

"atypical" cytopathology who underwent liver transplantation, dysplasia was noted in the segment of the explanted duct that corresponded to the location of abnormality during pCLE examination [60]. A multicenter study of 102 of indeterminate pancreaticobiliary strictures (PSC patients were excluded) showed that combining two or more of the Miami criteria significantly increased the sensitivity and predictive values. The sensitivity, specificity, positive predictive value, and negative predictive value were found to be 97 %, 33 %, 80 %, and 80 %, respectively. So, if a dominant stenosis shows benign pCLE features, then it is more reassuring to reduce the frequency of surveillance sampling required [59]. Another study supporting the above findings included 10 pCLE experts who reviewed pCLE findings from 46 patients with PSC strictures. Combining pCLE and tissue sampling yielded sensitivity and negative predictive value of 100 % [61].

A multicenter registry study utilizing pCLE specifically in PSC patients with dominant stenoses is ongoing.

The Paris classification attempts to take into account inflammatory or reactive changes that may be seen in biliary strictures. It included criteria for benign inflammatory conditions (vascular congestion, dark granular patterns with scales, increased inter-glandular space, and thickened reticular structure) that may help improve the specificity of pCLE findings and may be more relevant in patients with PSC [62].

Antibiotic Prophylaxis

Given the often diffuse, segmental intrahepatic structuring associated with PSC, injecting contrast during ERCP into obstructed ducts may increase the risk for post-ERCP cholangitis. Cholangitis in PSC can be life-threatening and lead to liver decompensation due to an inability to decompress intrahepatic segmental biliary obstruction [63]. Thus, pre-procedure IV antibiotics or oral antibiotics started 48 h prior to ERCP followed by a 3- to 5-day course post-ERCP are considered the standard of care and despite randomized, controlled data [64, 65]. At our institution, we routinely administer an IV dose of a quinolone or ampicillin/sulbactam prior to ERCP and give a 5- to 7-day course of quinolone or amoxicillin-clavulanate after the procedure. Further, in patients who have had post-ERCP cholangitis, we will provide oral antibiotics for 48 h prior to a repeat ERCP and anecdotally have found it to help reduce the risk of cholangitis in these more susceptible individuals.

Adverse Events of ERCP in PSC

The largest reported series of PSC patients with long-term follow-up reported an AE rate of 7.3 % among 317 ERCPs performed on 117 PSC patients over a mean duration of 8 years. The most common AEs were post-ERCP pancreatitis, cholangitis, sepsis, biliary tract perforation, post-sphincterotomy bleeding, and liver abscess. The complications were mild without a need for surgical intervention. There were no procedure-related deaths [15].

Role of Endoscopy in Recurrent PSC After Liver Transplantation

A German study that followed 335 PSC patients for 98.8 months after liver transplantation showed that recurrent PSC was diagnosed in 20.3 % of the patients after 4.6 years. Risk factors for recurrent PSC were older donor age, IBD, and INR at time of transplantation [66]. Diagnosis of recurrent PSC can be challenging, particularly in differentiating it from many other conditions that could cause biliary strictures (ischemia, hepatic artery thrombosis, chronic ductopenic rejection, ABO incompatibility, bacterial/fungal cholangitis, etc.). Biliary strictures after liver transplant can be classified into anastomotic and non-anastomotic strictures. Non-anastomotic biliary strictures occur more often after liver transplantation for PSC than for other indications [67]. Given involvement of extrahepatic bile ducts in PSC, Roux-en-Y choledocho- or hepaticojejunostomy (as opposed to duct-to-duct anastomosis) or more recently choledochoduodenostomy

is considered the method of choice for biliary reconstruction [68]. The Roux-en-Y anatomy makes endoscopic access for diagnostic and therapeutic purposes challenging; however, the recent advances in biliary endoscopy using balloon-assisted deep enteroscopy (single and double balloon) after Roux-en-Y reconstruction was shown to be feasible and highly efficacious [69]. These techniques are not widely available and are mostly performed in specialized tertiary centers. Given the aforementioned factors, MRC is considered the first choice for evaluation of biliary strictures after liver transplantation. Anastomotic strictures can be treated successfully with balloon dilation and stenting [70]. Non-anastomotic strictures can also be treated with balloon dilation and stenting but appear to be more difficult to treat [71]. Most of the published data, however, are for complications involving liver transplantation with duct-to-duct anastomosis. Percutaneous transhepatic biliary drainage (PTBD) can also be used for the management of biliary strictures after liver transplantation, particularly if endoscopic approach is not successful [72]. Preliminary data from our institution (DDW 2016, Poster Tu1572) showed that at a median 2-year follow-up, deep enteroscopy ERC compared to percutaneous transhepatic biliary drain is associated with fewer procedures, fewer post-procedure hospitalization days, and a shorter time to resolve anastomotic strictures in patients with long limb surgical biliary bypass including Roux-en-Y reconstruction after liver transplantation.

There are no published data to show the overall efficacy of endoscopic treatment on the progression of recurrent PSC aside from symptomatic management of biliary strictures and their complications. Retransplantation for progressive, recurrent disease is often an unfortunate consequence.

Conclusions and Future Directions

The best approach to treat dominant strictures in PSC is still unknown. Endoscopic balloon dilation (along with short-term stenting for severe strictures and patients presenting with cholangitis) seems to be the best approach. We perform serial upsizing of stents to treat dominant stenoses until their resolution. Studies are underway to clearly define and compare the role of each modality in treatment of PSC (Short-term Stenting Versus Balloon Dilatation for Dominant Strictures in Primary Sclerosing Cholangitis, NCT01398917).

Despite the availability of multiple diagnostic tests for CCA, confirming or excluding CCA in PSC is still a major challenge to clinicians. There have been some exciting developments in finding biomarkers for CCA that could play a role in the future. Among those are promising early studies for markers that can be studied in the bile aspirated at the time of ERCP such as oxidized phospholipids, volatile organic compounds, and DNA methylation [73–75]. For now, we advocate the use of brush cytology, biopsy/histology, and FISH analyses and consider pCLE for all dominant stenoses [76].

Recurrent PSC following liver transplantation is problematic, but advances in deep enteroscopy techniques provide minimally invasive options for symptomatic patients.

Conflict of Interest Dr. Shah is on the medical advisory board and has received unrestricted educational grants from Boston Scientific, unrestricted educational grants and prototype endoscope loans from Olympus, Inc. and unrestricted educational grants and honoraria from Mauna Kea Technologies, Inc.

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