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Multimodal endoscopic evaluation of indeterminate biliary strictures

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Indeterminate biliary strictures, those whose etiology remains unclear after initial workup, require further endoscopic evaluation. The biliary endoscopist may utilize both endoscopic retrograde cholangiopancreatography (ERCP) and endoscopic ultrasound (EUS) in the evaluation of indeterminate strictures, maximizing the relative strengths of both procedures. Techniques to optimize ERCP yield, including brush cytology, forceps biopsies, needle aspiration and direct cholangioscopy, are described in this article. Ultrasound evaluation, intraductal as well as EUS with fine needle aspiration, may also be used in concert with ERCP and these techniques are also described. The goal of endoscopic evaluation is the identification of malignant lesions at a resectable stage.

Biliary strictures occur due to a myriad of reasons and the management of these strictures depends on their etiology. In some cases, it is not difficult to define the cause of a stricture. For example, patients with pancreatic adenocarcinoma in the head of the pancreas often have coexisting malignant distal common bile duct strictures. Similarly, a patient who has undergone a complicated cholecystectomy may present weeks later with a benign biliary stricture in the region of the cystic duct. Although it is critical to differentiate between malignant and benign biliary strictures, this differentiation may be occasionally challenging. If sampling of a stricture is confirmatory for malignancy, no further endoscopic evaluation is necessary. However, cytology or histology that does not initially demonstrate malignancy does not exclude malignancy. Sometimes, longer follow-up is required to ascertain whether a neoplastic process is present. A primary goal of endoscopic evaluation is to identify malignant lesions earlier in their presentation. The biliary endoscopist has a growing armamentarium of tools to evaluate indeterminate strictures.

Before embarking on an exhaustive endoscopic workup, it is helpful to consider the clinical scenario. Placement of the endoscopic findings in context with the medical history may alter clinical suspicion for malignancy. Specifically, it is helpful to inquire about a history of alcohol use (associated with chronic pancreatitis), recurrent pancreatitis history, symptoms of inflammatory bowel disease (associated with primary sclerosing cholangitis), systemic symptoms such as fever or weight loss (increasing suspicion for malignancy), or prior endoscopic interventions. Furthermore, in patients with jaundice, it may be helpful to obtain high-resolution cross-sectional imaging to guide therapy.

Both endoscopic retrograde cholangiopancreatography (ERCP) and endoscopic ultrasound (EUS) are helpful in the evaluation of indeterminate strictures. These modalities are considered complementary and can be performed during the same session to evaluate complex biliary strictures. Strictures that are associated with a mass on cross-sectional imaging are best evaluated with EUS-FNA. EUS-FNA has the highest yield in these patients and is not associated with the risks of ERCP. ERCP can then be subsequently performed for symptom palliation, if appropriate, after a diagnosis of malignancy has been confirmed. Strictures without an associated mass lesion, which are the primary focus of this review, are best evaluated by initial ERCP.

Initial ERCP evaluation of indeterminate strictures

ERCP is often the first endoscopic test performed in patients with jaundice and biliary dilation, particularly in

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the absence of a mass seen on cross-sectional imaging. ERCP allows both visualization and sampling of the stricture and it is important to optimize both components of the examination.

Cholangiography

Although the sampling of a stricture is critical, it is equally important to obtain excellent cholangiographic images. There are a few general principles to follow that will optimize cholangiography.[1] First, we favor taking frequent spot images early after contrast injection. If too much contrast is initially injected, there may be obscuration of the stricture, especially in lesions involving the bifurcation. For similar reasons, initial injection of contrast just below the stricture may be helpful. In cases involving the bifurcation it may be necessary to rotate the fluoroscopy machine or to rotate the patient, to obtain optimal imaging of the bifurcation and the left and right main hepatic ducts. For strictures involving the mid-common bile duct, placement of the endoscope in the "long" position, done by advancing the endoscope with leftward torque is often required to visualize the region of the common bile duct obscured by the endoscope. Once the stricture is clearly delineated, tissue sampling in an attempt to confirm or exclude a malignant diagnosis is appropriate.

Biliary brush cytology

The most commonly used cytologic sampling technique after identifying a biliary stricture is brush cytology. Although there are multiple brushes available, a difference in the yield of brush cytology is more likely to be obtained via optimizing technique rather than changing brushes. We prefer to use brushes that can be advanced over a guidewire to minimize the risk of complications and secure access to the biliary tree upstream of the stricture.

Technique

For brush cytology to be performed, a prior sphincterotomy is not necessarily required, but is often performed in anticipation of further interventions including forceps biopsy and stenting. Once the guidewire is positioned beyond the stricture, the brush catheter is advanced over the guidewire across the biliary stricture. The assistant then advances the brush out of the catheter, under fluoroscopic guidance. At this point, the bristles of the brush will be above the level of the stricture. We then slowly withdraw the brush catheter system so that the brush is within the stricture. The assistant then withdraws and advances the brush back and forth to collect cells. There is no consensus regarding the optimal number of passes. While some advocate a timed approach, we prefer to perform 10 to 15 controlled passes (Figure 1). It is important to not withdraw the brush into the catheter until all passes have been performed so that cytologic material is not lost and also to keep the floppy tip of the brush within the stricture tract as a guide for the brush. This requires fluoroscopic monitoring of this process. We do not routinely dilate strictures before brushing, as the data regarding increasing yield is conflicting. However, if it is felt that dilation will be required for management of the stricture, it is preferable to perform this before brush cytology given the possibility that dilation may increase cytology yield.

After the catheter and brush are withdrawn, it must be submitted for cytologic analysis. This is performed according to local institutional policies. Although a smear can be made onto a slide with the brush, most institutions have adopted a policy of simply cutting the brush off from the catheter and allowing it to fall into a fixative, allowing for the cells to be extracted by the cytology technician in the laboratory.

Although the yield of brush cytology is variable (30-88%),[2] it is relatively easy to perform, does not require a sphincterotomy, is wire-guided, and has high specificity. Therefore we perform this technique on all patients who present with an indeterminate biliary stricture.

Biliary forceps biopsy

Biliary forceps biopsies may be used in the evaluation of a biliary stricture. Although forceps designed for intraductal biopsies are more flexible than other traditional endoscopic sampling forceps, they remain more cumbersome to use as compared with brush cytology.

Technique

Free hand cannulation is required to pass the forceps into the biliary tree and typically requires a biliary sphincterotomy. The presence of a wire in the duct serves as a guide both for initial access into the biliary tree and subsequent advancement up the biliary tree. After successful cannulation is achieved with the closed forceps, the forceps are advanced to the stricture under fluoroscopic guidance. The forceps are opened immediately distal to the stricture and advanced into the stricture and closed under fluoroscopic guidance (Figure 2). One to two biopsies are taken at a time and up to three passes are often made. After this, the forceps are closed, withdrawn, and the samples submitted for pathology. Although forceps that open to the side exist (allowing biopsy of stricture when it is approached tangentially), there is no data demonstrating their superiority in clinical practice.

Complications

Complications from intraductal forceps biopsies, although rare, have been reported.[3] Cannulating the common bile duct with the forceps may be difficult and there is thus a theoretical risk of pancreatitis. However, this is less likely to occur if a sphincterotomy has been performed. Similarly, careful advancement of the forceps under fluoroscopic guidance through the bile duct lessens the chance of an iatrogenic injury. It may be helpful to "groom" the forceps, similar to a catheter, to aid in biliary cannulation. Sampling of a stricture can cause bleeding, which in rare cases may be severe. An endoscopically placed biliary stent can assist in