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Symposium

Benign bile duct strictures

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Introduction

Bile duct stricture is an uncommon but challenging clinical condition that requires a multidisciplinary approach for management. The diagnosis of biliary stricture is often missed or delayed because of its indolent course, with up to 20% of patients presenting with subtle clinical manifestations 1 year after the initial injury. Up to 30% of patients with non-malignant strictures may have a protracted, complicated course necessitating intensive multidisciplinary management with its attendant significant health care costs.

Pathophysiology

Benign strictures develop due to damage to the bile ducts during surgery or trauma to the abdomen; a recurring condition, such as pancreatitis or bile duct stones; or a chronic disease, such as primary sclerosing cholangitis (PSC). After the injury, an inflammatory response ensues, which is followed by fibrosis and narrowing of the bile duct lumen. Atrophy of the hepatic segment or lobe drained by the involved bile ducts, associated with hypertrophy of the unaffected segments, can occur, especially with chronic strictures. These changes eventually progress to secondary biliary cirrhosis and portal hypertension.

Clinical presentation

Benign strictures of the biliary tract are associated with a broad spectrum of signs and symptoms, ranging from subclinical disease with mild elevation of liver enzymes to complete obstruction with jaundice, pruritus and cholangitis, and ultimately biliary cirrhosis.¹

Etiology

Postoperative injury after cholecystectomy

Approximately 80% of benign strictures occur following injury during a cholecystectomy. The incidence rate of major bile duct injury is 0.2–0.3% after open cholecystectomy and 0.4–0.6% after a laparoscopic cholecystectomy.^{2,3,4} Most of the benign biliary strictures following injury during cholecystectomy go unrecognized at the time of surgery (as many as 75% of cases). Presentation after more than 5 years may occur in 30% of cases. Most strictures after a laparoscopic procedure are short and occur more commonly in the common hepatic duct, distal to the confluence of the right and left hepatic ducts. After open cholecystectomy, strictures are more common in the CBD. The causes of benign bile duct strictures are usually surgical inexperience, failure to recognize abnormal biliary anatomy and congenital anomalies, acute inflammation, misplacement of clips, excessive use of cautery, and excessive dissection around the major bile ducts, resulting in ischemic injury.⁵

Pancreatitis

Jaundice due to obstruction of the intrapancreatic segment of the CBD occurs in patients with chronic pancreatitis and accounts for approximately 10% of the benign strictures.

PSC

PSC is a disease that causes strictures, beading, and irregularities of the intrahepatic and extrahepatic bile ducts. Approximately 70% of PSC cases are associated with inflammatory bowel disease.

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Orthotopic liver transplantation (OLT)

Bile duct strictures usually occur 2–6 months after OLT. Anastomotic strictures are more common, with choledochocolicostomy site strictures more common than choledochojejunostomy site strictures. Hepatic artery ischemia after OLT also can present as an anastomotic stricture, a hilar stricture, or diffuse stricturing of the biliary tree.⁶

Mirizzi syndrome

This condition is observed in 1% of patients. Extrinsic compression of the common hepatic duct due to a gallstone impacted in the Hartmann pouch or cystic duct results in jaundice and cholangitis. Repeated episodes of inflammation can lead to formation of a stricture (type I) or pressure necrosis leading to the formation of a cholecystocolic fistula (type II).

Radiation

Bile duct strictures can occur as a late complication of radiation therapy in the upper abdomen for cancer or lymphoma, sometimes presenting many years after treatment.

Blunt abdominal trauma

This can lead to bile duct strictures, which usually have a delayed presentation.

Portal biliopathy

Mechanical obstruction and ischemia of the biliary tract due to the large para- and epicholedochal venous plexus in cavernous transformation of portal vein. It is commonly seen in patients with extrahepatic portal vein obstruction.

Polyarteritis nodosa and systemic lupus erythematosus (SLE)

These are autoimmune diseases involving small- to medium-sized arteries. They can present rarely as extrahepatic biliary obstruction secondary to biliary strictures.

Tuberculosis and histoplasmosis

These conditions have rarely been reported to cause bile duct strictures in individuals who are immunocompetent.

Chemotherapeutic drugs

Hepatic artery infusion of 5-fluorodeoxyuridine (FdUrd, FUDR) or other chemotherapeutic drugs may cause bile duct strictures.

Sphincter of Oddi dysfunction or papillary stenosis

Patients usually present with biliary colic after cholecystectomy. The anomaly is in the smooth muscle surrounding the terminal portion of the CBD, with an abnormal basal sphincter pressure of greater than 40 mmHg.

Choledochal cysts

Choledochal cysts are uncommon anomalies of the biliary system manifested by cystic dilatation of the extrahepatic biliary tree, intrahepatic biliary tree, or both. This condition is found most frequently in Asian persons and in females. Associated hepatobiliary complications include recurrent cholangitis, bile duct stricture, cholelithiasis, choledocholithiasis, and recurrent acute pancreatitis.

Recurrent pyogenic cholangitis

This condition and hepatolithiasis are prevalent in Southeast Asia. It is characterized by recurrent attacks of suppurative cholangitis with strictures and dilatation of bile ducts and numerous pigment stones in the intrahepatic and extrahepatic bile ducts. It is thought to be precipitated by an infestation of liver flukes and round worms.

Inflammatory strictures

In addition to pancreatitis, choledocholithiasis can also cause chronic inflammation and fibrosis, leading to strictures of the CBD and sphincter of Oddi.

Endoscope-related strictures

Postendoscopic sphincterotomy stricture is possible.

HIV cholangiopathy

Sclerosing cholangitis with papillary stenosis is the most common (50%) finding. Patients present with right upper abdominal pain, fever, chills, marked elevation of alkaline phosphatase level, normal or moderate elevation of transaminases, and near-normal bilirubin value.

Idiopathic

A few cases of idiopathic benign bile duct strictures have been reported.

Miscellaneous

Strictures have been described in association with duodenal diverticulum, Crohn disease, hepatic artery aneurysm, cystic fibrosis with liver involvement, eosinophilic cholecystitis, and cholangitis.

Laboratory studies

The serum of patients with clinically apparent jaundice shows increase in total and conjugated bilirubin. Alkaline phosphatase levels are increased to more than 3 times normal. Elevated alkaline phosphatase levels are accompanied by increases in gamma-glutamyl transpeptidase and 5' nucleotidase, usually disproportionate to serum transaminase levels. Serum aminotransferase levels are usually less than 300 IU/mL. Patients with partial bile duct obstruction have

elevated serum alkaline phosphatase (ALP) and gamma-glutamyl transpeptidase (GGT). The prothrombin time (PT) and international normalized ratio (INR) may be prolonged and can usually be normalized with parenteral administration of vitamin K. Total cholesterol and lipoprotein levels may be elevated in patients with chronic cholestatic disorders.

Imaging studies

Ultrasonography

US is the imaging modality of choice for the initial screening of biliary disorders. It is more sensitive for detecting stones in the gallbladder. US can accurately detect dilatation of intrahepatic and extrahepatic bile ducts. However, US is less accurate for determining the etiology and level of obstruction. The sensitivity of US also depends on the degree of obstruction.⁷

CT scanning

Spiral CT (SCT) and multidetector CT (MDCT) scanning are highly sensitive for the diagnosis of biliary obstruction, particularly when these modalities are performed with oral and intravenous contrast agents.

The main value of CT scanning is its ability to detect the site of obstruction with greater accuracy than US and to help predict the cause of obstruction. CT scanning is rather insensitive for detecting stones in the CBD. CT scanning is superior to US in visualizing the distal CBD area, because intestinal gas may obscure this region when examined by US.

Magnetic resonance cholangiopancreatography (MRCP)

MRCP is a non-invasive technique of outlining the intra and extrahepatic biliary tree. The level of obstruction is correct in almost 87% cases.⁸ CBD strictures and stones can be differentiated as a cause of obstruction in most cases.⁹ Benign strictures due to sclerosing cholangitis are multifocal and alternate with slight dilatation or normal-caliber bile ducts, producing a beaded appearance. Side-branch ectasia is the most prominent and specific feature of chronic pancreatitis. MRCP does not currently allow any intervention to be performed, such as stone extraction, stent insertion, or biopsy.

Hepatic iminodiacetic acid scan

HIDA scanning is a non-invasive method of evaluating liver function and bile secretion and can help determine the clearance of bile across strictures and surgical anastomosis, thus providing a functional assessment of incomplete strictures and surgical anastomosis.¹⁰

ERCP

ERCP is a valuable technique in biliary disease because other diagnostic procedure (e.g., sphincter of Oddi manometry) and therapeutic interventions (e.g., stone extraction, biliary drainage, stent placement) can be carried out at the same time

as the primary diagnosis. The success rate of ERCP is often 90–95%, with a complication rate of approximately 3–5%. ERCP can help detect intrahepatic and extrahepatic biliary dilatation, stones, and the site of bile duct stricture with the highest sensitivity and specificity (both approximately 90–100%). ERCP findings are also valuable for helping differentiate malignant from benign biliary obstruction. Infectious causes of biliary obstruction can be diagnosed using collected bile samples or brushings.¹¹

Endoscopic ultrasonography (EUS)

EUS involves the use of echoendoscopes, which have a US transducer mounted at the end of a side-viewing or oblique-viewing endoscope. It also has color Doppler capability, enabling the endosonographer to be able to differentiate between vascular and fluid-filled structures. The pancreas, CBD, and the gallbladder are in close proximity to the distal stomach and the duodenum and can be viewed. EUS can help detect choledocholithiasis, especially small stones, with a sensitivity of more than 95%. The instrument also has a small biopsy channel for fine-needle aspiration (FNA) and fine-needle injection.

PTC

Indications for PTC in bile duct strictures are the presence of biliary-enteric anastomosis (e.g., Roux-en-Y anastomosis with hepaticojejunostomy, choledochojejunostomy, Billroth II gastrectomy), the presence of complex hilar strictures, or when ERCP is unsuccessful. The success rate of PTC approaches 100% when ducts are dilated. Therapeutic intervention, including biliary drainage, dilation of benign bile duct strictures, extraction of biliary tract stones, or placement of a stent across a malignant stricture also can be performed at the same time. PTC is contraindicated in patients with bleeding diatheses and significant ascites.

Fistulography

In postsurgery patients with an external biliary fistula or T tube, contrast medium can be injected into the biliary system through the tube or the fistula. This outlines the intrahepatic and extrahepatic bile ducts and delineates the site of stricture and the anatomy of the fistula. This study can precipitate cholangitis; therefore, patients should receive antibiotic prophylaxis.

Histologic findings

Surgically resected segments of the biliary tree will show the etiology of the bile duct stricture. In benign lesions the involved segment of the bile duct is surrounded by a collar of fibrosis causing a narrowing of the lumen. This is accompanied by a variable amount of inflammatory cellular infiltrate. The mucosa of the strictured segment usually is atrophic, with areas of squamous metaplasia. In autoimmune disease, the hallmark finding is dense lymphocytic infiltration.

Classification

Bismuth and Majno¹² proposed a classification for biliary stricture based on its location (Fig. 1). This classification helps the surgeon to choose the most appropriate surgical approach because it defines the level in which healthy biliary mucosa is available for repair and anastomosis. Type I biliary strictures, which occur more than 2 cm from the hepatic confluence, are the easiest to repair with a success rate of up to 100%.¹³

Type I strictures are located more than 2 cm distal to confluence of left and right hepatic ducts, whereas type II strictures are seen within 2 cm from hepatic confluence. Type III strictures affect confluence, which is patent; type IV strictures involve confluence and interrupt it; type V strictures involve the hepatic duct associated with stricture on aberrant right intrahepatic branch.

Medical care

Medical treatment consists of managing complications of bile duct strictures until definitive therapy can be instituted. Most patients who present with cholangitis have a response to antibiotics and supportive management. The common organisms that cause cholangitis are *Escherichia coli* and *Klebsiella*, *Enterococcus*, *Proteus*, *Bacteroides*, and *Clostridium* species. Empiric antibiotic therapy should be effective against these organisms. Traditionally, a combination of a penicillin, aminoglycoside (gentamicin), and metronidazole has been the preferred regimen. Newer penicillins, such as piperacillin/tazobactam or imipenem/cilastatin, also have excellent activity against anaerobes, enterococci, and gram-negative cocci.

Approximately 70–80% of patients respond to medical therapy and do not need urgent intervention. Patients not having a response to empiric antibiotic therapy within 24 h or those with hypotension requiring vasopressors, disseminated intravascular coagulation, or multiorgan system failure should be considered for immediate biliary decompression, which can be performed surgically, percutaneously, or endoscopically. Endoscopic or percutaneous decompression is often associated with lower morbidity and should be considered first.

Management

Patients with cholangitis whose conditions fail to improve with conservative treatment usually require urgent decompression of the obstructed biliary system. Treatment options for bile duct strictures include endoscopic or percutaneous balloon dilatation and insertion of an endoprosthesis or surgery.

Decompression of the biliary system is usually performed endoscopically, with placement of a nasobiliary tube or one or two 10F–12F stents after sphincterotomy. Thereafter, elective replacement of the stents seems desirable to prevent cholangitis by stent occlusion because polyethylene stents generally clog in 3–4 months. Alternatives to ERCP are percutaneous transhepatic biliary drainage and surgical decompression. Sphincterotomy and endoscopic balloon dilatation alone is not a reliable method of treating benign strictures. Percutaneous treatment by balloon dilatation followed by short- to intermediate-term stent placement appears to provide a more durable result.¹⁴ The role of metallic stents in this situation needs further evaluation.¹⁵

Operative treatment

Surgical management of benign bile duct strictures is necessary for patients in whom endoscopic therapy has failed. Surgical management consists of Roux-en-Y hepaticojejunostomy, choledochojejunostomy, or intrahepatic cholangiojejunostomy. Biliary-enteric anastomosis is a safe, effective, and lasting therapy for biliary strictures. However, before definitive operative therapy for bile duct strictures is performed, patients must be stabilized and, if possible, biliary drainage should be achieved either endoscopically or percutaneously. Patients with long-standing bile duct strictures due to pancreatitis may require pancreaticoduodenectomy. However, surgical drainage has been associated with considerable morbidity and mortality.

Endoscopic therapy shares an equal long-term success rate in comparison with primary surgery and hence is the preferred approach for the management of benign biliary stricture. Overall, an estimated 30% of patients require repeated hospitalization and invasive treatment of benign biliary strictures, and a small percentage of cases may progress to biliary cirrhosis requiring liver transplantation. Prompt

Fig. 1

diagnosis and management of these strictures are therefore recommended in spite of their “benign” nature.

Conflicts of interest

None identified.

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