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Endoscopic Treatment of Biliary Acute Pancreatitis

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Pathogenesis of Acute Biliary Pancreatitis

Acute biliary pancreatitis (ABP) is caused by pancreatic duct obstruction mainly due to bile duct stones. Once a bile duct stone is impacted at the distal end of the bile duct or at the common channel, pancreatic duct outflow is obstructed directly or by the compression of the pancreatobiliary septum. Previous reports showed that bile duct stone impaction was found in 26–72% of patients who had ABP when surgery was performed soon after the attack [1]. Spontaneous passage of bile duct stones into the duodenum has been described in up to 50% of ABP cases [2,3]. Sphincter of Oddi spasm might be another cause of ABP. Therefore, the diagnosis of ABP is not always easy at the time of diagnosis of pancreatitis.

Biliary pancreatitis, as well as alcoholic pancreatitis, is a major etiology of acute pancreatitis. ABP accounts for 20–71.4% of cases of acute pancreatitis, but the rate varies depending on the country. Biliary pancreatitis is more common than alcoholic pancreatitis in Greece, Italy, the United Kingdom, Sweden, and the United States, whereas alcoholic pancreatitis is the most major cause in Hungary, France, Taiwan, Korea, and Japan [4–9].

Diagnosis

In addition to the increased levels of serum pancreatic enzymes, such as amylase and lipase, increased levels of hepatobiliary enzymes and bilirubin suggest the possibility of ABP. In such cases, imaging tests are strongly recommended for diagnosis. Although transabdominal ultrasound is the most convenient imaging modality, the extrahepatic bile duct is often difficult to visualize clearly due to the retention of gastrointestinal gas, especially in patients with acute pancreatitis. Abdominal computed tomography (CT) is also relatively convenient and has high sensitivity in detecting calcified stones (Fig. 33.1), but its sensitivity to detect small stones without calcification is limited. Endoscopic retrograde cholangiopancreatography (ERCP) may be indicated in highly suspected cases such as those with bile duct dilation and/or cholangitis. Magnetic resonance imaging (MRI) or endoscopic ultrasonography (EUS) can be performed before ERCP because they are safer and more convenient. In addition, magnetic resonance cholangiopancreatography (MRCP) can provide an image similar to ERCP. It has high sensitivity and specificity in detecting common bile duct stones (more than 90%) [10], but its sensitivity decreases in cases with dilated bile duct and small stones [11]. EUS is recognized as the most reliable imaging modality in detecting bile duct stones [12], has fewer complications, and shows higher sensitivity in detecting small bile duct stones than ERCP [13].

Indication of Endoscopic Treatment

Endoscopic treatments are indicated for patients in whom a bile duct stone was confirmed on imaging tests or highly suspected from clinical or laboratory findings. In addition, patients with persistent or repeated increasing levels of biliary and pancreatic enzymes are also indicated even if the presence of biliary stone was unclear. In such cases, a dysfunction in the sphincter of Oddi might be a cause of biliary pancreatitis.

The timing of endoscopic treatments is discussed later, but urgent ERCP should be considered when there is

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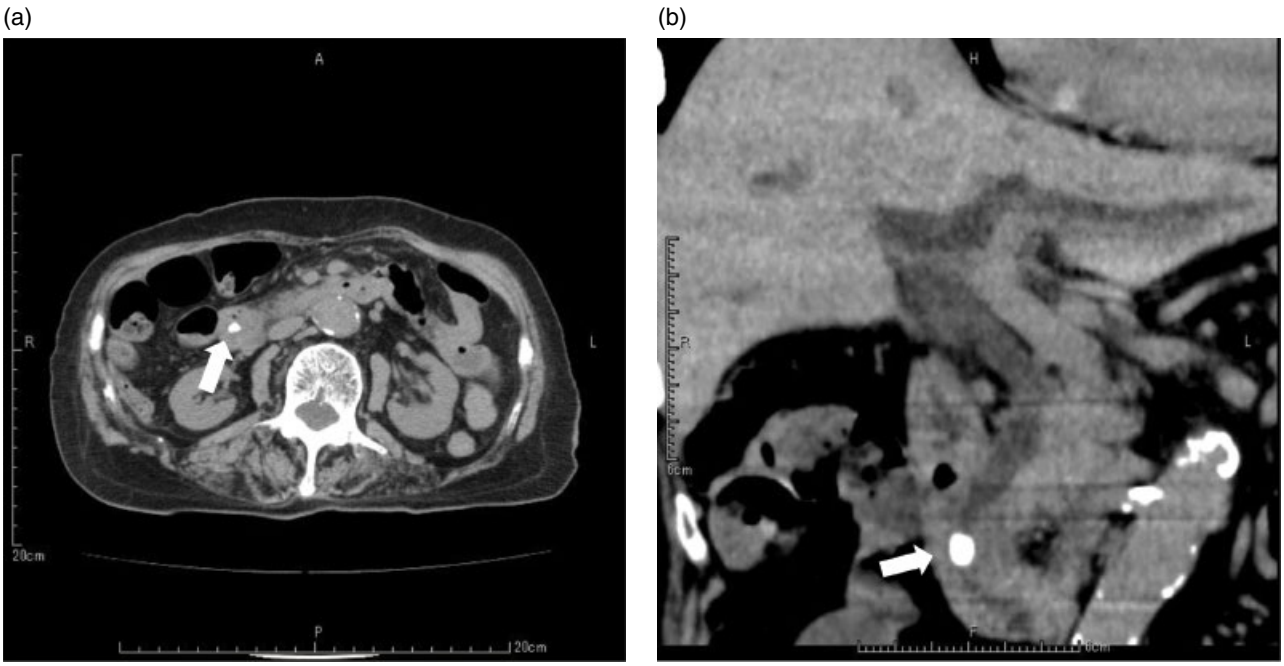

Figure 33.1 Computed tomography image of an impacted stone at the duodenal papilla. White arrow indicates an impacted stone. Axial image (a) and multiplaner reconstruction image (b).

evidence of severe cholangitis and/or ongoing biliary obstruction. However, conservative treatments such as fasting, rehydration, and administration of antibiotics may be attempted first in patients with mild clinical symptoms and with mild abnormal laboratory data.

Several previous studies suggested that EUS is helpful in narrowing down subjects. They showed that a preceding EUS avoided unnecessary ERCP in 71.2–75.4% of patients without increasing the risk of adverse events [13–16].

Techniques

The best way to treat biliary pancreatitis is the removal of the bile duct stone. Endoscopic sphincterotomy is generally performed for this. ERCP is initially attempted to confirm the stone in the bile duct, and endoscopic sphincterotomy is then performed using a sphincterotome if a stone is detected on cholangiogram. Subsequently, endoscopic stone extraction is performed using a retrieval basket or balloon. If the stone is impacted at the papilla, precut papillotomy using a needle knife would be preferred to conventional endoscopic sphincterotomy because cannulation into the bile duct is often difficult in such cases (Fig. 33.2).

Endoscopic sphincterotomy with subsequent stone extraction is currently a well-established technique with high success rate (approximately 90%) [17]. However, procedure-related adverse events, including pancreatitis, hemorrhage, perforation, and cholangitis, can occur in approximately 10% [18]. Aggravation of pancreatitis is a particularly big concern in patients with pancreatitis. Therefore, cannulation and contrast medium injection into the pancreatic duct should be avoided as much as possible; however, there is no evidence that accidental cannulation into the pancreatic duct harmfully affects the clinical course or outcome. Recently, the efficacy of pancreatic duct stenting was suggested in ABP following endoscopic sphincterotomy. In a nonrandomized study, complications were less frequent in the pancreatic duct stent group than in the control group without pancreatic duct stent (9.86% vs. 31.43%, $P < 0.002$) [19]. However, so far, there is no significant evidence to recommend pancreatic duct stenting after endoscopic treatment for ABP.

Outcomes and Timing of Endoscopic Interventions

Endoscopic treatments for ABP were initially described in 1981 [20,21]. Since then, a number of prospective randomized controlled trials (RCTs) have compared early endoscopic treatments with conservative therapy for ABP. However, the role and timing of endoscopic intervention in ABP remain controversial. A number of clinical trials and meta-analyses have provided conflicting evidence.

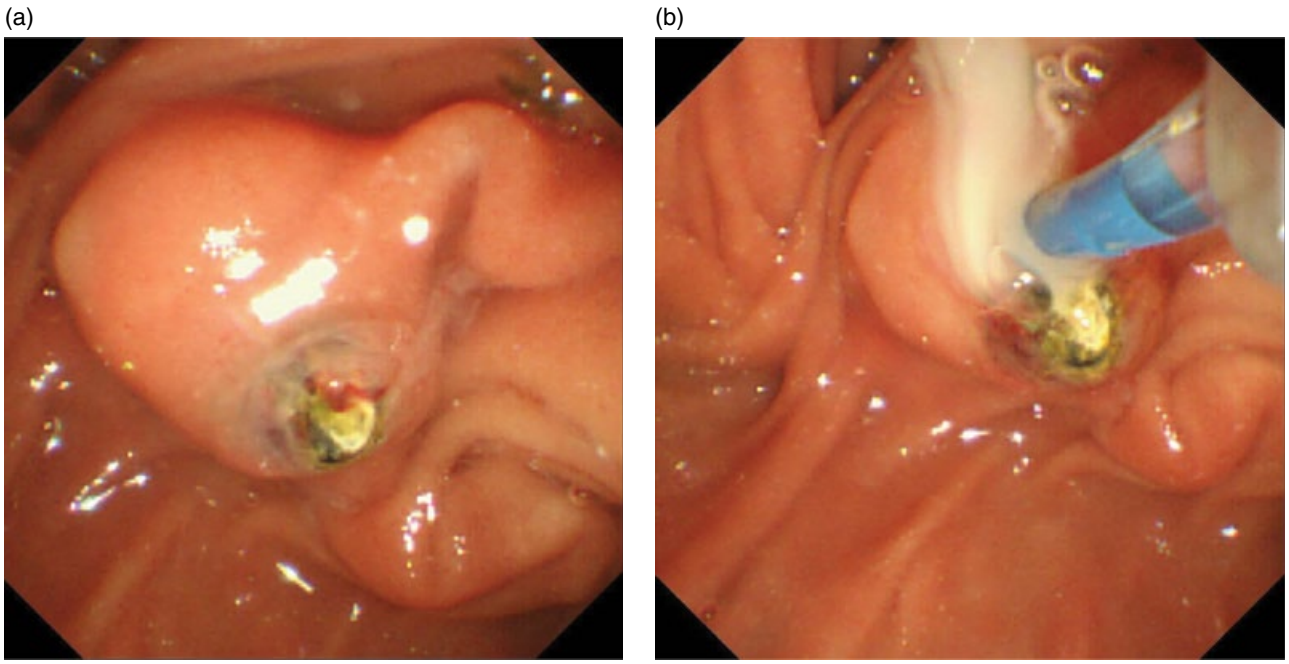

Figure 33.2 Endoscopic view of an impacted stone at the duodenal papilla. A stone is impacting at the biliary orifice (a). Needle knife papillotomy is preferably performed in such a case. Whitish pus is discharged after cutting up the papilla from the orifice using a needle knife (b).

Two early RCTs showed lower complication rate, shorter hospital stay, and lower mortality rate in the urgent ERCP group than in the conservative group [22,23]. However, another RCT showed that the overall rate of complications was similar in the two groups, and patients in the early ERCP group had more severe complications [24]. The first meta-analysis published in 1999 showed high success rate of ERCP (92%) and concluded that early ERCP significantly reduced morbidity (25.0% vs. 38.2%, $P < 0.001$) and mortality (5.2% vs. 9.1%, $P < 0.05$) in ABP [25]. However, later studies suggested that early endoscopic intervention was beneficial in further limited patients.

Several studies concluded that urgent endoscopic intervention should be considered only in patients with severe biliary pancreatitis [26–28]. In a meta-analysis by Ayub et al. [27], early endoscopic intervention was associated with significant reduction in complications only in predicted severe biliary pancreatitis (odds ratio [OR] 0.27, 95% confidence interval [CI] 0.14 to 0.53), whereas reduction of mortality was not significant in both predicted mild and severe biliary pancreatitis. Later, a meta-analysis by Moretti et al. [28] also reported that a significant difference in the pooled rate for complications was found only in predicted severe pancreatitis (38.5%, 95% CI −53% to −23.9%, $P < 0.0001$).

Meanwhile, several other studies suggested that the benefit of urgent endoscopic intervention was expected only in cases with cholangitis or cholestasis [29–34]. Petrov et al. [29] reviewed RCTs on early endoscopic intervention versus conservative management in patients with ABP without acute cholangitis. As a result, early endoscopic intervention in patients with predicted mild and predicted severe biliary pancreatitis did not lead to a significant reduction in the risk of overall complications and mortality. Later, van Santvoort et al. [35] conducted a prospective, observational multicenter study including patients with predicted severe ABP without cholangitis. They analyzed the outcomes in patients without and with cholestasis separately. As a result, endoscopic intervention was associated with fewer complications as compared with conservative treatment in patients with cholestasis (25% vs. 54%, $P = 0.020$), whereas it was not associated with reduced complications (45% vs. 41%, $P = 0.814$) in patients without cholestasis. A recent Cochrane review by Tse and Yuan [32] showed no evidence that early routine ERCP significantly affected mortality or local/systemic complications of pancreatitis, regardless of predicted severity. However, among trials that included patients with cholangitis, the early routine ERCP strategy significantly reduced mortality, local, and systemic complications. In addition, among trials that included patients with biliary obstruction, early routine ERCP strategy was associated with a significant reduction

in local and systemic complications. Finally, they concluded that early ERCP should be considered only in patients with coexisting cholangitis or biliary obstruction. From the latest systematic review [36] including 8 meta-analyses and 12 guidelines, there is consensus in guidelines and meta-analyses that early endoscopic intervention is indicated in ABP patients with coexisting cholangitis and/or persistent cholestasis. With the exception of the first meta-analysis [25], none of the included studies approved early ERCP in predicted mild ABP. Consensus is lacking on the role of routine early endoscopic intervention in patients with predicted severe ABP.

Cholecystectomy After Endoscopic Treatment

Recurrence rates of ABP of up to 61% have been reported when definitive treatment was not provided [37,38]. Therefore, subsequent cholecystectomy after endoscopic treatment of bile duct stones has been recommended to prevent recurrent attacks of ABP [39,40], although 25–50% of patients do not undergo cholecystectomy for various reasons [41–43]. In cases of severe ABP, the current consensus is to postpone cholecystectomy until after resolution of local or systemic complications [38–40,44].

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