

ENDOTHERAPY OF CHRONIC PANCREATITIS

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Abstract : Chronic pancreatic, characterized by chronic inflammation and fibrosis, is a progressive disease. It is most commonly caused by alcohol, other causes being metabolic, autoimmune, hereditary and idiopathic. The diagnosis can be made on CT scan, MRI with MRCP and ERCP. Though, exocrine and endocrine insufficiency is common in later stages, it is the persistent severe pain which needs the maximum efforts. Medical therapy consists of cessation of alcohol, dietary modifications and NSAIDs and narcotic analgesic. In non responsive and complicated cases, endotherapy plays an important role. Endotherapy combined with ESWL provides pain relief in over 3/4th cases. Also, pancreatic pseudocysts, ascites and biliary obstruction can be managed endoscopically.

INTRODUCTION

Chronic pancreatitis is an inflammatory process characterized by destruction of pancreatic parenchyma and ductal structures, leading to fibrosis. It is most commonly *caused by* chronic and heavy alcohol intake in the West (accounting for 70% of cases)¹. In most cases, patients have had a history of consuming more than 150 g/day of alcohol for more than 5 years. Only 10 to 20% of the chronic alcoholics develop chronic pancreatitis. Other known causes of chronic pancreatitis include tropical pancreatitis, hereditary, autoimmune, hyperlipidemia, hypercalcemia and pancreas divisum. Ten to 30% of patients with chronic pancreatitis have no obvious cause. This group is considered as idiopathic. The most common *presenting symptom* of chronic pancreatitis is pain, occurring in two third to 80% of patients. Other presentations which occur late in the disease include steatorrhea due to pancreatic enzymes deficiency and diabetes mellitus. Patients may also present due to associated complications. The *management* of patients involves determining the etiology, confirming the presence and assessing severity of chronic pancreatitis and presence of complications so as to guide the treatment. Besides detailed clinical and routine examination, these patients require morphologic and functional evaluation. Plain x- ray of abdomen may reveal pancreatic calcification while CT examination is more sensitive at picking even smaller acinar calcification, ductal stones and dilatation, and presence of pseudocyst, biliary and duodenal obstruction. MRI with MRCP has the advantage over ERCP of not only providing good quality delineation of MPD, side branches, presence of strictures and stones but also parenchymal changes. Results can further be improved by giving secretin injection². ERCP is considered as the gold standard for diagnosis of chronic pancreatitis. It involves injection of contrast, visualization of the entire MPD and side branches. The ERCP findings are used for grading the severity of chronic pancreatitis, the Cambridge Criteria (table)³.

The endoscopic ultrasound (EUS) is less invasive and safer than ERCP for diagnosis of chronic pancreatitis. It evaluates the ductal system and the parenchymal changes⁴. It can also pick mass lesions less than 2cm in size and also do FNA from suspicious mass lesions.

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Cambridge criteria for grading severity of chronic pancreatitis				
Grade	terminology	MPD	abnormal MPD	additional features
0	Normal normal	normal	none	
I	equivocal	normal	<3	none
II	mild	normal	3 or more	none
III	moderate	abnormal	>3	none
IV	severe	abnormal	>3	one or more: large cavity, obstruction, filling defects, severe dilatation or irregularity

MPD: main pancreatic duct, MPDB: main pancreatic duct branches.*

If pathologic changes are limited to one third or less of gland, they are classified as local and designated as being in head, body or tail; if more than one third of gland is involved, changes are classified as diffuse.

Management of chronic pancreatitis is mainly directed at *pain relief*. The origin of this pain is multifactorial, important factors being increased pressure in the ductal system and interstitium besides neural entrapment in fibrotic process. Medical measures include cessation of alcohol intake, dietary modifications, pancreatic enzyme replacement therapy and analgesic (non narcotics and narcotic opioids).

In those patients where medical therapy fails, **endoscopic and surgical options** can be given. Endoscopic management is preferred as it provides good short and long term pain relief, has lower morbidity and minimal mortality. Surgery, though has better short results, is better reserved for failed endotherapy, associated mass lesion and disease mainly in tail or distal body region. It is associated with significant morbidity and mortality. (Fig.1&2)



Fig.1: ERCP—Large calculi in the MPD and side branches



Fig.2: Post pancreatico jejunostomy

ENDOSCOPIC MANAGEMENT

Though in a given patient, multiple pathologies might be contributing to symptoms, for the purpose of discussion, following pathologies will be dealt individually

Pancreatic duct strictures, pancreatic duct stones, leaks (pseudocysts, ascites, pleural effusions, internal and external fistulae), biliary obstructions and celiac plexus blockade.

Pancreatic Duct strictures

Benign pancreatic duct strictures are common in chronic pancreatitis. At times they need to be differentiated from malignant disease. Presence of dilatation of MPD and side branches both proximal and distal to stricture, multiple strictures and stones indicates benign stricture. If in doubt, brush cytology and serum CA 19-9 can be done.

Asymptomatic strictures do not require any treatment. Patients with pancreatic duct strictures associated with recurrent pain, pancreatitis attacks or upstream leaks need intervention. Strictures predominantly in the head and body region of pancreas should be considered for endotherapy. Symptomatic strictures can be treated by dilation and/ or pancreatic duct stenting following pancreatic sphincterotomy. The pancreatic sphincterotomy can be done either by needle knife or pull type sphincterotome. Stricture dilation can be done either using wire guided balloons (size varying from 4 to 8mm) or graduated catheter dilators. The size of the dilator used depends on the tightness of the stricture and diameter of the distal pancreatic duct. Majority of the patients with stricture also require stenting after dilation (Fig.3).



Fig.3: MPD stricture with dilatation managed with pancreatic duct stenting

The stents are placed over the guidewire across the stricture. The diameter of the stent used should not exceed the diameter of the duct downstream. The pancreatic stents used are available in 7, 8.5, 10 and 11.5F sizes and variable lengths. They have flaps on either end to prevent migration.

Results

Reported initial outcomes of endoscopic therapy in main pancreatic duct strictures has been encouraging with successful stenting being reported in 72 to 100% of cases and pain relief in 75 to 95% of stented cases⁵. Weber et al⁶ reported successful outcome in 17 out of 19 patients, while Binmoeller et al⁷ reported 2/3rd patients free of pain at 5 years. Costamagna and colleagues treated⁸ 19 patients with severe chronic pancreatitis aggressively. Strictures could be successfully treated in 95% of patients. During a mean follow up of 38 months after stent removal, 84% of patients

were asymptomatic and 10.5% had symptomatic stricture recurrence. The optimum duration of stent placement, stent number and diameter, and degree of balloon dilatation are not established. In a randomized trial comparing the endoscopic treatment with surgical pancreaticojejunostomy, pain relief was achieved in 32% in the endoscopic group and 75% in surgical group⁹.

Complications are common after pancreatic endotherapy and include bleeding (after sphincterotomy), pain, pancreatitis, stent block, stent migration, infection and stent induced stricture and stone formation¹⁰.

Pancreatic Duct Stones

Pancreatic stones are seen in over half the patients with chronic pancreatitis. They form primarily in the main ductal system. They obstruct the flow of pancreatic juice and contribute to the pain and repeated episodes of pancreatitis in patients with chronic pancreatitis. The therapeutic options for the treatment of pancreatic stones include *endoscopic removal*, *extra shock wave lithotripsy (ESWL)*, and *surgery* either alone or in combination. The treatment choice depends on the information obtained from imaging results. Factors affecting the treatment include – stone size and number, location, degree of impaction, presence of strictures and ductal tortuosity and dilatation.

Patients who have stones less than 1cm in size and less than 3 in number, are not impacted and there are no downstream strictures can be managed directly with endotherapy. Patients with larger and more than 3 stones, impacted stones, especially located in body and tail and with strictures should initially be managed with ESWL. Endotherapy involves pancreatic duct sphincterotomy followed by stone removal either using balloons or soft baskets. In some cases mechanical lithotripsy and stricture dilation may be needed. In patients with failed initial endotherapy, ESWL can be done followed by repeat endoscopic removal. Stone clearance has been reported in 70 to 80% of cases. In successful cases, pain relief occurs in 80 to 100%. At 5 years, pain relief continues in 55 to 85% of cases^{11, 12}. Complications are seen in 5 to 15% of cases and include bleeding, infection, pancreatitis and rarely perforation. ESWL involves delivery of shockwaves produced by electromagnetic or electrohydraulic generators, to the stones leading to their fragmentation. This is safe procedure done under conscious sedation on outpatient basis. This is followed by ERCP and removal of stone fragments. Most patients require 1 to 3 sessions. A recent review of the ESWL role in pancreatic ductal stone management concluded that the ESWL can result in complete stone clearance in up to 50% of cases. Combined ESWL and endotherapy results in complete ductal clearance in 50 to 75% of cases and partial in an additional 5 to 30%.clinical improvement is seen in 62 to 86% of cases^{13, 14}. One large series of 1000 patients with chronic pancreatitis with long term follow up found that 65% of patients with strictures or stones, or stones with strictures had improvement in pain after endotherapy. Twenty four percent of patients ultimately required surgery to treat their chronic pancreatitis¹⁵.

Pancreatic duct leaks

Pancreatic duct leaks occur as result of chronic pancreatitis with

blowout proximal to a strictures or stones. They can result in pancreatic pseudocysts, ascites, pleural effusions and fistula formation.

PANCREATIC PSEUDOCYSTS

Pancreatic pseudocysts occur in 20 to 25% of patients with chronic pancreatitis¹⁶. They can be asymptomatic or can produce symptoms due to compression or complications. Pseudocysts which are enlarging, producing pain or causing biliary or gastric outlet obstruction, or are complicated (infection or hemorrhage) need intervention. Treatment can be endoscopic, radiologic or surgical. The *endoscopic technique* is preferred as it has high success rate and is minimally invasive. The pseudocysts can be drained transmurally either into the stomach or duodenum depending upon its location. The pseudocyst wall should be well formed and the distance between the pseudocyst and stomach or duodenal wall at puncture site should be less than 1cm. Endoscopic ultrasound may be helpful in selecting the site of puncture and avoiding any blood vessel. Using duodenoscope, the site for cystogastrostomy is selected. Then a puncture is made into the pseudocyst either using a needle papillotome or polypectomy snare or sclerotherapy needle, followed by balloon dilation of the tract and then placement of 1 or 2 10F double pigtail stents into the pseudocyst cavity. The technical success rate of transmural drainage ranges from 90 to 100%, with pseudocyst resolution occurring in 80 to 100% of cases. Pseudocyst recurrence is seen in 10 to 15% of patients^{17, 18, 19, 20}. Complications of transmural drainage include bleeding, infection and perforation. Stents are usually removed after 8 to 12 weeks. Transpapillary approach is done in cases where transmural approach is not possible either due to small size or anatomic location. The pseudocyst must be communicating with the main pancreatic duct. It involves ERCP, cannulation of main pancreatic duct, demonstration of leak followed by placement of stent or nasopancreatic drain either across the leak or into the pseudocyst cavity. This technique carries low risk of bleeding but high risk of infection. It has carries a technical success rate of 94% and a complication rate of 12%^{18, 19}.

Percutaneous drainage is done in cases of infected pseudocysts or failed endotherapy. It should be avoided in patients with strictures. Surgery is reserved for failed endotherapy cases or not amenable for endoscopic drainage.

Pancreatic ascites and pleural effusions

Pancreatic ascites usually results either from disruption of pancreatic duct or leaking pancreatic pseudocyst. The ascitic fluid is rich in proteins and amylase levels are very high. Treatment consists initially of TPN, nil orally and octreotide. In unresponsive cases, endotherapy in the form of pancreatic stenting can be done with success rate of about 60%^{21, 22}. In cases of pleural effusion, besides pancreatic stenting patients also require intercostal drainage. In failed cases, surgery can be done.

Biliary obstruction

Symptomatic distal bile duct obstruction occurs in 10% of patients, though 35% of patients may have biochemical or radiological evidence of obstruction. Untreated, this can result in jaundice, cholangitis and secondary biliary cirrhosis. Endotherapy

in the form of placing multiple stents in the bile duct has shown good short term results but surgery appears more definitive and effective treatment in these cases^{23, 24, 25}.

Celiac plexus blockade

In many patients with chronic pancreatitis and debilitating pain unresponsive to medical and endoscopic therapy, celiac nerve plexus blockade can be tried. This can be done under endoscopic ultrasound or CT guidance, involves injection of local anaesthetic agent (bupivacaine) and steroid (triamcinolone) into the celiac plexus. Because only 50% of patients can be expected to respond to any form of celiac plexus blockade, many patients will still require analgesic medication^{26, 27}.

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