

REVIEW

Diagnosis and management of chronic pancreatitis

V Gupta, P P Toskes

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Chronic pancreatitis represents a condition that is challenging for clinicians secondary to the difficulty in making an accurate diagnosis and the less than satisfactory means of managing chronic pain. This review emphasises the various manifestations that patients with chronic pancreatitis may have and describes recent advances in medical and surgical therapy. It is probable that many patients with chronic abdominal pain are suffering from chronic pancreatitis that is not appreciated. As the pathophysiology of this disorder is better understood it is probable that the treatment will be more successful.

virtually any diagnostic test will show large duct chronic pancreatitis. In the absence of radiological abnormalities or other imaging (ERCP, MRCP, CAT scan, ultrasound) abnormalities, it becomes imperative for physicians to recognise the presence of small duct pancreatitis. The typical tests used to diagnose large duct disease are often too insensitive to diagnose small duct disease. The disorder is poorly recognised by most clinicians for many reasons including a poor appreciation for the disorder and the unavailability of specialised testing at local centres.⁶ Given this, it is probable that the percentage of patients with chronic pancreatitis has been greatly underestimated and that a significant portion of patients with chronic abdominal pain may actually be suffering from small duct chronic pancreatitis.

Chronic pancreatitis is an inflammatory condition that results in permanent structural changes in the pancreas that ultimately leads to impairment of exocrine and endocrine function.¹ This is the fundamental basis why patients with this disorder commonly present with abdominal pain or maldigestion, or both. Although pain is the cardinal feature of chronic pancreatitis, its presentation varies significantly among patients. The “classic” pain is located in the epigastrium, radiates to the back, is associated with oral intake, nausea, vomiting, and is relieved by sitting forward. Many patients fail to exhibit this “classic” pattern, however, and this is why chronic pancreatitis must be included in the differential diagnosis of any unexplained chronic abdominal pain. Unfortunately, the treatment of pain in these patients is difficult as it is often complicated by alcohol misuse, narcotic dependence, and psychological factors.

PATHOPHYSIOLOGY

Chronic pancreatitis has numerous causes with chronic alcohol misuse responsible for most cases. While chronic alcohol misuse does represent about 70% of cases it is important for clinicians to recognise the other causes of chronic pancreatitis as well (table 1).

Although, these other causes are not as frequent as alcoholic and idiopathic chronic pancreatitis they warrant consideration. In particular the incidence of autoimmune pancreatitis has been found to be much greater than initially thought. The incidence seems to be increasing in some regions, particularly in Japan.⁷ However, it has been described in several countries in Europe as well as the USA and Korea suggesting that it is a worldwide entity.⁸

Chronic pancreatitis is a progressive disease process that causes irreversible pancreatic

About 20% of patients with chronic pancreatitis present with endocrine or exocrine dysfunction in the absence of abdominal pain.² Exocrine dysfunction leads to maldigestion causing patients to present with diarrhoea, steatorrhoea, and weight loss. Steatorrhoea typically occurs before protein deficiencies. Malabsorption of fat soluble vitamins and cobalamin (vitamin B12) may occur, although clinically significant vitamin deficiency is rare.³

The annual incidence of chronic pancreatitis has been estimated in several retrospective studies and ranges from 3 to 9 cases per 100 000 population.⁴ The only prospective study to date estimated the incidence to be 8.2 cases per year per 100 000 population.⁵ In most studies, alcohol misuse accounts for two thirds of all cases of chronic pancreatitis.

Large duct disease, most commonly associated with alcohol misuse, is well recognised by most physicians and diagnosed comparatively easily as

Table 1 Chronic pancreatitis causes

Type	% Of patients
Alcohol induced	70
Idiopathic	20
Other	10
Cystic fibrosis	
Hypertriglyceridaemia	
Tumour	
Pancreatic resection	
Familial	
Congenital anomalies	
Tropical	
Autoimmune	
Genetic defects	

Abbreviations: CCK, cholecystokinin; ERCP, endoscopic retrograde cholangiopancreatography; CT, computed tomography; EUS endoscope ultrasound,

See end of article for authors' affiliations

Correspondence to: Professor P P Toskes, University of Florida, Division of Gastroenterology, Hepatology and Nutrition, 1600 SW Archer Road, Room HD 602, PO Box 100214, Gainesville, FL 32610, USA; toskepp@medicine.ufl.edu

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damage and is pathologically characterised by chronic inflammation and irregularly distributed fibrosis. Conversely, acute pancreatitis typically involves reversible damage that affects a significant portion of the pancreas. The two disorders probably involve different pathophysiological processes with recurrent bouts of acute pancreatitis usually not leading to chronic pancreatitis, however this remains controversial.

Chronic pancreatitis is a multifactorial disorder that is probably started by two distinct events. The first event is attributable to functional or mechanical causes of decreased bicarbonate secretion. Functional impairment may be caused by genetic factors such as cystic fibrosis transmembrane conductance regulator and serine protease inhibitor *kazal* type 1 gene mutations and mechanical obstruction by tumour, strictures, and sphincter of Oddi dysfunction.⁹ The second event involves the premature activation of pancreatic exocrine enzymes within the pancreatic gland leading to interstitial fat necrosis and haemorrhage. This, in turn, starts a sequence of perilobular fibrosis, duct distortion, and changed pancreatic secretion.

Various genetic abnormalities have also been sought to further characterise the disorder. Chronic pancreatitis has been thought to be associated with over-expression of fibroblasts and growth factors, increased interleukin 8 expression, and disorders in cholecystikinin (CCK) homeostasis. These various factors, in conjunction, ultimately lead to irreversible damage to the organ.¹⁰⁻¹²

DIAGNOSIS

It is imperative in the diagnosis of chronic pancreatitis that patients be differentiated into having either large or small duct disease. This is important as there are significant differences in regards to the clinical course, treatment, and outcomes. In evaluating patients with chronic pancreatitis, testing is typically centred upon diagnosing abnormal structure and abnormal function. Table 2 summarises the findings seen on testing in large duct and small duct chronic pancreatitis. As stated previously, the diagnosis of large duct disease is comparatively easy, with a variety of diagnostic tests yielding positive results.

To fully assess the benefits of any diagnostic test there needs to be a gold standard or reference against which the sensitivity and specificity of testing is measured and this has typically been pathological specimens. In the case of chronic pancreatitis, the organ is comparatively inaccessible and biopsies carry a high risk. The only such series to examine this is a Japanese series of 108 patients who underwent a hormone stimulation test and pancreatic wedge biopsy as a reference standard. There was a significant correlation between histological examination and peak bicarbonate concentration. In addition, during subgroup analysis of 29

patients who had had endoscopic retrograde cholangiopancreatography (ERCP) performed, it was found that the sensitivity of the stimulation test was greater than that of ERCP.¹³

The secretin stimulation test is the most sensitive and specific testing available for the diagnosis of chronic pancreatitis.¹⁴ It has, unfortunately, been underused secondary to a poor understanding of its role as well as the fact that it is invasive and only performed in about 10 medical centres in the USA. Previously, the typical testing for chronic pancreatitis had focused on structural findings that, while sensitive at diagnosing large duct disease, proved to be comparatively insensitive at diagnosing small duct disease. It is important to note that about 30% of patients with small duct disease who have had a normal or near normal ERCP will be found to have an abnormal secretin stimulation test. These near normal pancreaticograms include subtle changes in the side branches that are seen at the time of ERCP and whose significance varies significantly between endoscopists. Furthermore, in elderly patients these changes can be seen and are thought to be related to aging.^{15 16} Our institutional experience is that secretin testing becomes positive when there is about 60% damage to the exocrine pancreas and ERCP findings suggestive of the disease occur with about 75% damage. Occasionally, the converse may be seen and patients may be found to have normal pancreatic stimulation testing and an abnormal pancreaticogram at the time of ERCP. This makes these tests not mutually exclusive, but, complementary in diagnosing chronic pancreatitis.

A discussion of the structural means of diagnosing chronic pancreatitis would be incomplete with discussing endoscopic ultrasound (EUS), which in recent years has emerged as a very sensitive test to aid in the diagnosis of chronic pancreatitis. The technology has a significant advantage over ERCP in that it is able to not only assess the intraductal system, but also the parenchyma. In addition it is safer, with the risk of post-ERCP pancreatitis being about 6.7% (range 1%–30%) as compared with the risk of serious complications related to diagnostic EUS, which is estimated at 0.5%.^{17 18} Table 3 summarises the EUS criteria for the diagnosis of chronic pancreatitis.

Various studies have examined the sensitivity and specificity of EUS in diagnosing chronic pancreatitis. When compared against ERCP there have been as high as 97% sensitivity, 60% specificity, and 75% negative predictive value.¹⁹ When compared against the traditional gold standard of histological examination, however, these percentages falter further and have been shown to have a 78% sensitivity, 73% specificity when using four or more features for the diagnosis.²⁰ In a preliminary study from our laboratory where EUS was compared with the secretin test EUS was shown to have a sensitivity of only 57% and a specificity of 64%.²¹

Table 2 Features of large duct and small duct chronic pancreatitis

Feature	Large duct	Small duct
Sex predominance	Male	Female
Diagnostic findings		
Secretin test	Abnormal	Abnormal
Serum trypsinogen	Often abnormal	Typically normal
Diffuse pancreatic calcifications on imaging	Frequent	Infrequent
ERCP	Often considerably abnormal	Minimally abnormal to normal
Natural history		
Progression to steatorrhoea	Frequent	Rare
Pain therapy		
Pancreatic enzymes	Poor to fair response	Good to excellent response
Surgical procedures	Sometimes helpful	Usually not indicated

Another preliminary study from the Mayo Clinic gave similar results.²² A second issue is the apparent overdiagnosing of chronic pancreatitis in patients who are shown to have normal pancreatic function testing and normal ERCP, but subtle changes on EUS. The actual accuracy of EUS to detect small duct chronic pancreatitis has yet to be fully defined.

Serum trypsinogen and fecal elastase are the tests of choice in patients with symptoms of malabsorption such as diarrhoea, steatorrhoea, and weight loss. If patients have enough damage to the exocrine pancreas to cause steatorrhoea and maldigestion, one of these tests will invariably be positive. It should be noted, however, that although both of these tests are excellent in detecting chronic pancreatitis with steatorrhoea, they do not consistently separate mild to moderate chronic pancreatitis from normals. In a study by Amann *et al*, all chronic pancreatitis patients with steatorrhoea had values of <100 µm/g of stool, but more than half of the mild to moderate chronic pancreatitis subjects had fecal pancreatic elastase 1 levels within the normal range.²³ Serum trypsinogen values of <20 ng/ml have an accuracy of 95% in detecting severe pancreatic insufficiency, but this test is not very sensitive.²⁴

In summary, to diagnose chronic pancreatitis with the wide variety of testing available the clinician must carefully select diagnostic testing that is relevant to the patients' symptoms. As stated earlier, in patients with symptoms of diarrhoea and steatorrhoea the initial testing should include a serum trypsinogen or fecal elastase as one of these tests will invariably be positive if severe exocrine dysfunction exists. In patients with chronic unexplained abdominal pain who are referred to institutions with secretin stimulation testing, typically basic radiological imaging (radiography or computed tomography) is performed first to rule out obvious large duct disease and after this, secretin testing. If the secretin stimulation test is positive then this obviates the need for diagnostic ERCP. This order of testing is safer, more sensitive, specific, and less expensive.

MANAGEMENT OF MALABSORPTION

Although complete correction of steatorrhoea is not commonly achieved, with appropriate treatment it can be controlled to restore a patient's fat absorption to an acceptable level, thereby allowing them to gain weight through a reduction in diarrhoea and steatorrhoea. Patients do not develop steatorrhoea until their lipase level decreases to less than 10% of normal. Given this, the cornerstone of treatment has evolved around the exogenous replacement of lipase through the use of pancreatic enzymes that have been primarily from porcine sources.

The site of pancreatic enzyme delivery (duodenum or jejunum) does not seem to be as important for the release of lipase as it does for protease. This is because fat absorption occurs throughout the small intestine. Given this, patients with steatorrhoea alone should be placed on two capsules of a potent high lipase enteric coated preparation before meals. If patients have an element of pain it will be necessary to treat

them with a non-enteric coated enzyme preparation but this will be discussed more extensively below.

MANAGEMENT OF PAIN

Although it has been suggested that the natural path of chronic pancreatitis is toward progressive glandular insufficiency and calcification with eventual pancreatic burnout and cessation of pain²⁵ this has not been found to be the case. In 1995, 318 patients were followed up over a median of nine years and after this time period 50% of alcoholic patients and 73% of non-alcoholic patients still reported pain.²⁶ Given this, it is unreasonable to passively monitor patients with pain from chronic pancreatitis in the hope of spontaneous pain resolution.

The treatment of chronic pain in patients with chronic pancreatitis can be frustrating for both clinicians and patients. The pathogenesis of the pain remains poorly understood, but has been thought to be associated with perineural inflammation, increased pressure in both large and small ducts, and in the pancreatic parenchyma, an abnormal feedback mechanism, or pancreatic carcinoma with duct obstruction. In addition, patients may develop the secondary complications of chronic pancreatitis such as a pseudocyst, duodenal obstruction, or duct obstruction that may exacerbate their pain. Lastly, these patients have a high incidence of dysmotility that may be worsening or causing their pain and that may be exacerbated by concurrent narcotic use.

Given the significant difficulty in treating patients with chronic pancreatitis, it becomes necessary to develop a systematic approach to the treatment of their pain. In patients with presumed pain from chronic pancreatitis it is important to first evaluate for the presence of large or small duct disease, as described above, as this will affect the treatment course. As well, secondary complications of chronic pancreatitis such as pseudocysts should be ruled out.

Although difficult, it is important for clinicians to avoid the use of narcotics analgesics in these patients. Unfortunately, narcotic dependence and addiction are common in these patients. Patients should be treated initially with a regimen of acetaminophen and non-steroidal anti-inflammatory drugs. After this, if necessary, this regimen may be supplemented with analgesics such as tramadol or propoxyphene. The use of narcotics typically only complicates the clinical picture in these patients and typically worsens or causes gastroparesis, which is common in these patients.²⁷⁻²⁸ It is our strong conviction that if the root cause of the pain is managed as described below, then narcotics may not be necessary.

PANCREATIC ENZYMES

Before discussing the use of pancreatic enzymes for the treatment of small duct chronic pancreatic pain it is important to understand the physiological mechanisms behind its use.

The exogenous replacement of pancreatic proteases is based upon the concept of feedback inhibition of pancreatic exocrine secretion through intraduodenal serine proteases.¹² In a subset of patients it seems that the pancreas is under constant stimulation by CCK.²⁹⁻³⁰ A CCK releasing peptide has been identified that resides in the proximal small intestine and is degraded by the serine proteases. As patients with chronic pancreatitis have decreased protease activity they may be unable to inactivate this releasing enzyme leading to perpetual pancreatic stimulation. These pathophysiological mechanisms illustrate the importance of exogenous protease to allow the pancreas to rest and afford pain relief.

To achieve feedback inhibition and thus have an impact on pain it is necessary to deliver exogenous protease to the

Table 3 Endoscopic ultrasonographic criteria for chronic pancreatitis

Ductal	Parenchymal
Stones	Echogenic strands
Echogenic ductal walls	Echogenic foci
Irregular ductal walls	Calcifications
Stricture	Lobular contour
Visible side branches	Cyst
Ductular dilatation	

proximal small intestine as the serine proteases and CCK peptide are found there. There have been six randomised trials with 193 patients examining the use of pancreatic enzyme preparations. The two trials using non-enteric coated preparations were shown to be effective³¹⁻³² while the four studies using enteric coated preparations were ineffective in reducing pain.³³⁻³⁶ This illustrates the importance of using non-enteric coated preparations for the treatment of chronic pancreatic pain. As these preparations are non-enteric coated, however, they are susceptible to degradation in the stomach by gastric acids and may be degraded before reaching the duodenum. For this reason, an acid suppressing agent such as an H₂ receptor antagonist or proton pump inhibitor should be added. A regimen of non-enteric coated enzymes taken orally with meals and at bedtime provides good clinical response in most patients.

The clinical course of patients with chronic pancreatitis receiving pancreatic enzyme replacement has yet to be fully delineated. Certainly the greatest success is seen in patients with small duct disease as this has been effective in decreasing abdominal pain in about 70% of these patients as compared with 25% of large duct disease. If a patient is found to have small duct disease they should be initially tried on a one month trial of pancreatic enzyme replacement. If they respond, they should continue to be given this medication, but if they do not, an EUS or ERCP should be performed to examine for an inflammatory stricture or other lesion that may be corrected endoscopically or surgically. Patients that respond to therapy should typically continue on enzyme therapy until a six month pain free interval has been achieved. This is necessary as after the withdrawal of medications, about 50% of patients continue to do well with no further relapses, however the remainder do relapse. These patients are continued with enzyme therapy with typically good results. Clear predictors for success off of medications has yet to be defined.

OCTREOTIDE

Octreotide was initially selected and examined for the treatment of chronic pancreatitis secondary to its therapeutic potential in improving small and large duct disease. As it is a somatostatin analogue, this drug inhibits pancreatic secretion and considerably lowers CCK levels. Initially, there were a number of small short term studies examining the use of this drug, but these resulted in variable findings.³⁷⁻⁴⁰ A multi-centre pilot study was performed in 1993 to examine various dosing regimens and showed that 200 µg of octreotide taken subcutaneously three times daily was superior to placebo.⁴¹ Octreotide significantly relieves pain in many patients with severe chronic pancreatitis that is refractory to other forms of therapy. Predictors of response remain unclear at this time, but it probably acts through reduction in CCK levels.

CHOLECYSTOKININ ANTAGONISTS

Cholecystokinin, originally thought to be confined only to the gastrointestinal tract, is now known to be found in both the gastrointestinal tract and central nervous system. McClean⁴² reported a novel treatment by treating patients with proglumide, a non-specific CCK receptor antagonist after noting that patients with abdominal pain from chronic pancreatitis had reduced analgesic response to morphine. He found that proglumide reversed tolerance to morphine analgesia, potentiated its effects, and even caused analgesia on its own. Based upon this, the author theorised that proglumide induced analgesia would be produced in chronic pancreatitis patients having raised CCK levels.

To evaluate the therapeutic efficacy of the CCK-A receptor antagonist, loxiglumide, a recent multicentre dose-response controlled trial was conducted in Japan.⁴³ In this study, 207

patients with abdominal pain induced by chronic pancreatitis were randomly assigned to oral treatment with loxiglumide at differing doses or placebo for four weeks. The overall clinical improvement rate was 46% in the 300 mg group, 58% in the 600 mg group, and 52% in the 1200 mg group.

These studies only further reaffirm the importance of CCK in feedback regulation and offer another prospective treatment for the control of chronic pancreatitis induced abdominal pain.

NERVE BLOCK

Unfortunately, we are unable to successfully medically manage all cases of chronic pancreatitis pain and secondary to this other forms of pain relief have been explored. Historically, through a blind translumbar approach a typical combination of long acting local anaesthetics and corticosteroids have been injected into the celiac plexus. With the advent of newer technologies, this has been largely replaced by computed tomography (CT) guided and now EUS guided approaches. In 1999, Gress *et al* performed a randomised prospective comparison of 22 patients treated with either EUS guided coeliac axis block compared with CT guided block using bupivacaine and triamcinolone. The study found that EUS guided block provided more initial (50% compared with 25%) and persistent (30% compared with 12%) pain relief than CT guided blocks.⁴⁴ In 2001, this same group prospectively examined 90 patients treated with coeliac axis block once again using bupivacaine and triamcinolone. They noted an initial response in overall pain scores in 55% of patients, but only 26% at 24 weeks, and 10% at 24 weeks.⁴⁵ As well it was noted that patients less than 45 years of age and those with prior pancreatic surgery were least likely to respond.

EUS guided coeliac axis block represents a comparatively safe and well tolerated option in the treatment of chronic pancreatitis pain. Given the fact that it is by nature invasive, with only short term benefits, and without long term follow up this procedure should be reserved for patients who have failed optimum medical management.

OXIDATIVE STRESSES

Stemming from the hypothesis that free radical formation may be contributing to pancreatic inflammation in chronic pancreatitis there have been two studies examining the use of antioxidants in this disorder. In the first, 20 patients with chronic pancreatitis were given antioxidant therapy (organic selenium, β carotene, vitamin C, and vitamin E, and methionine) daily in a double blind crossover trial for 30 weeks. They found that 0 of 20 patients receiving treatment developed pain during the study as compared with 6 of 20 in the placebo group.⁴⁶ This study was criticised for its methodology in the diagnosis of chronic pancreatitis in these patients however. In 2000, a small study of 10 patients treated for one year with daily antioxidants (L-methionine, β carotene, vitamin C, vitamin E, and organic selenium) showed a significant decrease in pain scores.⁴⁷ Unfortunately, these small studies while illustrating the possible benefits of antioxidant therapy fail to do so convincingly secondary to small sample sizes and questionable methodology. Given this, there is not significant current evidence to advocate or refute this treatment. Long term prospective randomised studies with significant power will be necessary to assess this further.

ENDOSCOPIC TREATMENT

Endoscopic pancreatic duct decompression via ERCP has been found to give pain relief in some patients.⁴⁸⁻⁵¹ The principle behind this approach is that by decreasing ductal pressure as seen in sphincter of Oddi dysfunction or pancreatic duct strictures, pain relief can be attained. The

largest body of evidence for this has been by Rosch *et al* in which 1018 patients were retrospectively identified and followed up for an average of five years after their therapeutic endoscopies.⁵⁰ In this study, obstruction of the pancreatic duct was found to be secondary to stricture in 47%, stones in 18%, and both in 32%. Endoscopic intervention consisted of pancreatic duct stricture dilatation, stone extraction, or pancreatic duct sphincterotomy. At the end of follow up, 60% had completed endoscopic therapy, 16% were still receiving therapy, and 24% had undergone therapy. Pain relief was 86% in the entire group, but only 65% in an intent to treat analysis.

The role of endoscopic pancreatic therapy is evolving. Certainly, in patients who have failed optimal medical management it should be pursued before considering surgical options as about two thirds of patients with pancreatic duct strictures will benefit from this form of treatment.

SURGERY

Refractory pain in patients who fail optimal medical and endoscopic therapies is an indication for surgical intervention. Thoroscopic bilateral splanchnicectomy entails transecting the nociceptive fibres originating in the pancreatic area at the thoracic level. There have been small reports of the use of this technique for the treatment of pain from adrenal cancer and pancreatic cancer. The only large series study with long term follow up to examine this has been in 44 patients with a median follow up of 36 months. In this series, pain scores significantly improved postoperatively, but at five years about 50% of patients had pain recurrence.⁵²

Surgical decompression is typically considered in refractory pain in the presence of pancreatic ductal dilatation >6 mm secondary to technical issues. Ductal decompression may be accomplished by the Puestow procedure (lateral pancreaticojejunostomy). There have been many variations of this procedure that preserve the duodenum and pylorus that have been used with varying results.⁵³⁻⁵⁶ Most studies initially report 80% pain relief, but long term pain relief occurs in only 30%–50%.

In recent years the operative morbidity and mortality for these procedures has improved. A study examining 231 pancreatic cancer resections that has been extrapolated to chronic pancreatitis has shown an operative mortality of 0.4%.⁵⁷ Another showed good quality of life and low morbidity after the procedure.⁵⁸ This makes these procedures viable options in the treatment of refractory pain.

PANCREATECTOMY AND AUTOLOGOUS ISLET CELL TRANSPLANTATION

The first autologous islet cell transplantation was performed in 1977 on a 39 year old patient with familial chronic pancreatitis.⁵⁹ Since that time, according to 2001 data from the International Islet Transplant Registry, only 140 islet cell autotransplants after pancreatectomy were performed between 1990 and 2001.⁶⁰ The current approach entails infusion of isolated islet cells after pancreatectomy into the portal vein with the goal of achieving decreased pain and decreased insulin requirements.

The first large series of patients was reported by the University of Minnesota, summarising the results in 48 patients undergoing the procedure between 1977 and 1995.⁵⁹ Of the 39 evaluable patients, 51% were insulin independent for at least one month, with the probability of sustained insulin independence decreasing to 34% after two years. However, of the 18 patients who received an autotransplant with islets prepared with the most recent techniques in islet cell isolation, the long term success rate was 55%. The most powerful predictor of insulin independence was the number

of islet cells infused, which in turn is inversely related to the degree of fibrosis of the pancreas.

More recently, Rilo *et al* reviewed 22 cases performed at the University of Cincinnati.⁶¹ In this small experience, at 19 months, 82% of patients were completely off narcotics (mean 78.4 (SD 105.9) morphine equivalents preoperatively compared with 9.5 (24) morphine equivalents postoperatively). In addition, 41% of patients were insulin free, 27% required fewer than 10 units/day, and the remaining 27% required 15 to 40 units/day postoperatively. Another study to examine this topic evaluated 40 patients with follow up ranging from six months to seven years.⁶² In this study, at two years after transplant, median HbA1c was 6.6% and median insulin requirement was 12 units/day as compared with six year data with median HbA1c of 8% and median insulin requirement was 43 units/day. In addition, most patients no longer required opioid analgesia and 68% were able to return to work.

In a follow up study, detailing their experience to date, the University of Minnesota reported data regarding 64 additional pancreatectomies and islet cell autotransplants performed since their initial study.⁶³ In this study, as was previously suggested, insulin independence was directly correlated with the number of islet equivalents/kg body weight infused. Complete insulin independence was achieved in 71% of patients without prior pancreatic surgery and in 100% of patients with a prior Whipple procedure. Furthermore, during subgroup analysis, patients with an islet yield of >2500 islet equivalents/kg body weight were found to have an 85% chance of complete insulin independence. Pain after pancreatectomy was found to be unchanged or worsened in 12%, improved in 32%, and resolved in 32%.

Pancreatectomy with autologous islet cell transplantation has been proposed as a therapy for pain associated with chronic pancreatitis. As can be seen from the few studies to date there is a wide variance in results regarding its efficacy in treating pain. It may be considered as a last option in patients with refractory pain who have failed conventional medical, endoscopic, and surgical options. Use in this subset of patients seems justified, however, this in itself is problematic as we now know that insulin independence is directly correlated to the amount of islet cells transplanted. Therefore the patients who have benefited most from this procedure to date have chronic pancreatitis without prior pancreatic surgery or evidence of islet cell insufficiency. The role of this procedure will still have to be further defined, but based upon current studies islet cell autotransplantation may be an option in lieu of ductal decompression surgery or partial pancreatic resection in patients with intractable painful small duct disease, particularly as the standard surgical procedures lead to decreased islet cell yield.

CONCLUSION

Chronic pancreatitis is an inflammatory condition with a poorly understood pathogenesis, multiple aetiologies, and varied presentations ranging from abdominal pain to steatorrhoea. These factors, have led to the ultimate under recognition of this disorder. Furthermore, for those who are recognised as having this disorder, the treatment has unfortunately been confusing and frustrating for clinicians and patients alike. Regrettably, the situation is often only exacerbated through alcohol and narcotics dependence as it is commonly seen in these patients.

Before beginning treatment regimens it is important to ascertain the aetiology of the disease and define it in regards to large duct compared with small duct disease as this will affect the treatment course. While large duct disease is easily recognised by a myriad of available testing, the diagnosis of small duct chronic pancreatitis requires the use of specialised

testing (direct hormone stimulation test) that may not be available in local communities.

A firm understanding of CCK homeostasis and its impact on pancreatic feedback inhibition is necessary to appreciate the role of pancreatic proteases, octreotide, and CCK antagonists in the treatment of painful chronic pancreatitis. With an understanding of the pathophysiology surrounding the disorder, comes a systematic approach to the diagnosis and treatment of these patients.

Authors' affiliations

V Gupta, P P Toskes, University of Florida, Division of Gastroenterology, Hepatology and Nutrition, Gainesville, Florida, USA

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Dermatology spot diagnosis

A 25 year old otherwise healthy man presented with painless lesions on the palmar side of both hands (fig 1A) and elbows (fig 1B). He was not taking any medication and his family history was negative. Laboratory studies disclosed the following values: total cholesterol 24.0 mmol/l (N: 3.8–5.2), triglycerides 17.4 mmol/l (N: 0.6–2.3), HDL-C 0.80 mmol/l (N \geq 0.90). Serum was lactescent at 4°C after a night in hospital. Serum aspartate aminotransferase, alanine aminotransferase, and thyroid stimulating hormone were normal. A lipoprotein electrophoresis showed the presence of a broad β band (cholesterol enriched chylomicron and VLDL remnants). The apo E genotype was confirmed to be E2/E2. Dysbetalipoproteinaemia (type III hyperlipoproteinaemia, broad-beta disease, or remnant removal disease) is a rare disorder affecting 1:5000 to 1:10 000 persons and is in part attributable to a mutation in the APOE gene resulting in reduced uptake of apo E-containing lipoproteins by the liver and impaired conversion of VLDL and IDL to LDL.^{1,2} The manifestations include tuberous xanthomas, deposits of cholesterol in the palmar creases (also called striae palmaris or xanthoma striata palmaris), and severe mixed hyperlipidaemia.³ Risk of atherosclerosis and its complications is increased, with onset in the fourth and fifth decade. Hypothyroidism and diabetes are known to be precipitating factors. Treatment of this condition is essentially lipid lowering diet complemented with lipid lowering drug treatment and avoidance of alcohol, oestrogens, and triglyceride raising agents.⁴ The patient was treated with a fibrate and a HMG CoA reductase inhibitor; his xanthomas have completely regressed.

P Maheux

Division of Endocrinology and Metabolism,
Université de Sherbrooke, 3001 12th Avenue
North, Sherbrooke, Québec, Canada
J1H 5N4;
Pierre.Maheux@USherbrooke.ca

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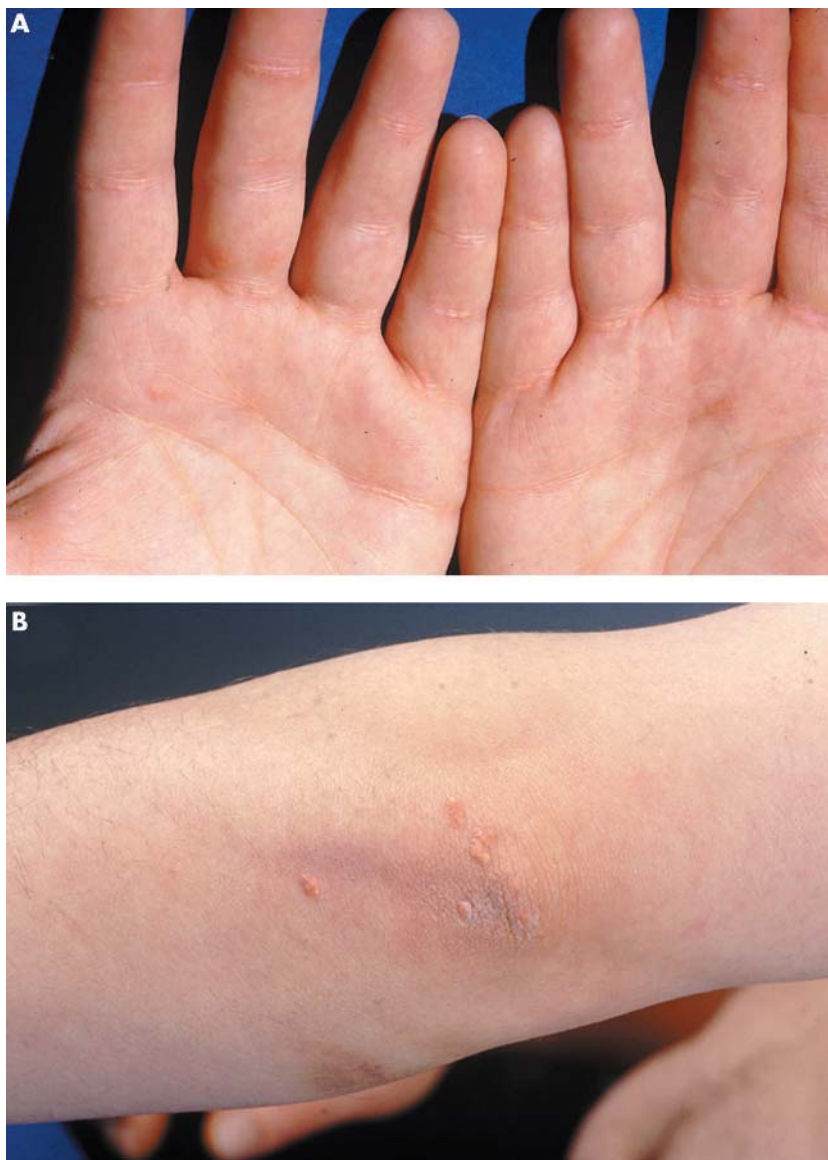


Figure 1 (A) Lesions on palmar face of both hands and (B) papules on extension side of left elbow (obtained with patient's permission).