Chronic pancreatitis

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Chronic pancreatitis causes destruction of the pancreatic gland which leads to diabetes and malabsorption. Its principal cause is alcohol abuse, and intractable pain is the main clinical feature. The incidence of pancreatic carcinoma is increased among patients with chronic pancreatitis.

Chronic pancreatitis (CP) is a condition where there is inflammation of the pancreas with fibrosis and formation of scar tissue which eventually replaces the whole gland, leading to exocrine and endocrine insufficiency. Thirty years ago it was considered a rare condition in the UK, but since then its incidence in Britain has increased fourfold with an incidence of 4 per 100 000 (Johnson and Hosking, 1991).

Alcohol abuse is considered to be the most important causative factor of CP and since pain is the main clinical feature narcotic abuse often aggravates it. A classification of alcoholic pancreatitis has been proposed, based on clinical symptoms and pancreatic function. This describes four stages of the disease:

Latent or subclinical
The period of alcoholism preceding the onset of symptoms.

Early
The stage of inflammatory complications following initial pain episodes (onset of CP in most cases).

Late
The stage of severe pancreatic insufficiency, pancreatic pain, pancreatic calculi and deterioration of pancreatic function.

Advanced
Painless pancreatitis after painful attacks disappear (Chari and Singer, 1994).

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AETIOLOGY

Alcoholism is the main cause of CP in the Western world, affecting nearly 75% of patients (MacLaren, 1990). Ethanol damages the pancreatic cells directly and also increases the concentration of proteins in the pancreatic juice which eventually leads to formation of protein plugs that can undergo calcification. One or more attacks of non-alcoholic pancreatitis can also lead to CP. Other causes that have been described are pancreas divisum and cystic fibrosis, and in 15–20% of cases the cause is unknown. Hereditary pancreatitis is an autosomal dominant disease. Acute attacks begin early in life and often progress to CP (Lowenfels et al, 1997).

CLINICAL FEATURES

Pain is the main feature in CP, together with progressive pancreatic exocrine and endocrine failure. By the time of surgical referral patients are often malnourished, diabetic and addicted to narcotic drugs and alcohol (Fleming and Williamson, 1995; Stapleton and Williamson, 1996).

The pain, which is normally epigastric and radiates to the back, is exacerbated by eating and partially relieved by sitting upright and leaning forward. The origin of the pain can be ductal and parenchymal hypertension, peripancreatic inflammation, nerve entrapment and pseudocysts (Williamson, 1991). There is generally a background pain which can be associated with sharp attacks of acute pain, generally during acute exacerbations, that normally present with an increased serum amylase level.

Complications
The main complications are jaundice, duodenitis with or without duodenal obstruction, pseudocyst, haemorrhage and cancer. Jaundice is the most common complication; it develops in about 20% of patients either as a result of

compression by a pseudocyst or narrowing of the duct. Pseudocysts happen in 30% of patients who require surgery for CP (Williamson, 1991). In contrast to the acute pseudocysts in acute pancreatitis they are usually contained within the capsule of the gland. Haemorrhage is a serious complication. It may result from concomitant disease such as peptic ulceration or oesophageal varices but sometimes arterial erosion in the vicinity of a pseudocyst can result in pseudoaneurysm formation, generally in the splenic or gastroduodenal artery, which can eventually bleed. The author's practice is to perform a preoperative angiogram in all patients who undergo surgery for pseudocyst.

Links between CP and pancreatic carcinoma

In prospective studies it has been found that pancreatic carcinoma develops in 0–5% of patients with CP (Hansen et al, 1995).

In CP there is chronic inflammation, which could play the same role as in Barrett's oesophagus or ulcerative colitis leading to cell replication. This may be one of the explanations for the excess risk of pancreatic carcinoma among the CP population (Ekbom et al, 1994).

There are three clinical scenarios where CP and pancreatic carcinoma can overlap. First, as a problem of differential diagnosis in a patient presenting with a mass in the head of pancreas and jaundice, showing an irregular stricture in the distal common bile duct and absence of calcifications, particularly when there is a short history with no obvious aetiology. In this situation biopsy will not be very helpful and therefore, when inflammation is found, one must be certain that distal reactive inflammation is not being sampled instead of the tumour. Resection of the pancreatic head is the only way to ensure that a tumour is not being left behind. Less often the diagnostic confusion occurs in a patient with a cystic mass in the pancreas and no previous history of pancreatitis. In this situation one has to rely on the computed tomography criteria, tumour markers and, ultimately, biopsy of the wall of the cyst before embarking upon derivative procedures (e.g. cystopancreatography or cystojejunostomy).

The second possibility is when cancer produces distal obstructive pancreatopathy. CP is often found upstream from the tumour, especially in slow-growing tumours, e.g. neuroendocrine tumours (Zografos et al, 1997).

Finally, when cancer arises in CP, is the latter an aetiological factor or it is just coincidental resulting from common aetiological factors?

Aetiological factor or coincidence?

There have been numerous studies that have tried to answer this question. In 1984 Amman carried out a longitudinal study on 245 patients with CP over 19 years. Seven patients (2.8%) developed pancreatic carcinoma. Six of these seven patients had calcific pancreatitis.

Lowenfels et al (1993) performed a multicentre historical cohort study where 2015 subjects who fulfilled criteria for CP were recruited from six countries. In order to avoid patients who already had pancreatic carcinoma at the time of the recruitment, 463 subjects with a follow-up of less than 2 years were excluded. Among the 1552, 29 pancreatic carcinomas were diagnosed instead of the 1.7 expected, giving a standardized incidence ratio (SIR) of 16.5. Even if only patients with a follow-up of longer than 5 years were considered, the number of pancreatic carcinomas found was larger than expected (18 *vs* 1.25; SIR=14.4).

Gold and Cameron (1993) commented on the difficulty of diagnosing CP back in 1946 when Lowenfels's study began. Aside from that, they pointed out that even assuming an SIR of 16, the attributable risk for the proportion of pancreatic cancer that is explained by CP may be only approximately 0.1% annually, compared to a risk of 30% for cigarette smoking.

In a population-based study of 7956 individuals, Ekbom et al (1994) found an SIR of 3.8 among patients with a diagnosis of CP and 4.8 among patients with more than one admission for acute pancreatitis.

Rather than investigate the incidence of pancreatic cancer among patients with CP, Bansal and Sonnenberg (1995) designed a case control study in order to compare the incidence of CP in 2639 patients with pancreatic cancer to a control group of 7774 patients, matched for age and sex. They found 93 and 99 patients with CP in the case and control subjects groups respectively (odds ratio 2.94), strongly suggesting that a history of pancreatitis represents a risk factor for development of pancreatic cancer. The author has had a similar experience with seven cases of pancreatic cancer among 300 cases of CP.

It seems from the literature and from the author's experience that the incidence of pancreatic carcinoma among patients with CP is higher than in the normal population. It is clear that hereditary pancreatitis is a premalignant condition (Lowenfels et al, 1997) and it is also clear that patients with alcohol-induced CP share a number of risk factors, not only for pancreatic carcinoma but also for other neoplasms. The

question to be answered is whether a screening programme should be implemented in patients with CP. This would involve performing a substantial number of pancreatoduodenectomies because of the unreliability of pancreatic biopsy in this population. It may be that with new genetic markers such as K-ras and p53 some subpopulations could be selected. However, because of the small number of cases of pancreatic carcinoma that are secondary to CP, this would not affect the overall survival figures for this neoplasm.

TREATMENT

Medical

Non-operative treatment is directed towards pain relief and replacement of pancreatic secretions. As mentioned previously, psychiatric support will be a crucial part of the treatment since 75% of patients are alcoholic.

Pain, which is the main clinical feature, has a role in maintaining the addiction in alcoholic patients, so control of the former will be important in treating the latter. Generally, ordinary analgesics are not very effective and it is important to control the pain before the patient becomes addicted to opiates. Other intermediate strength analgesics such as dihydrocodeine or buprenorphine are useful. Percutaneous coeliac plexus block consists of chemical neurolysis of the fibres which carry the pain from the pancreas to the splanchnic nerves. In expert hands this can be done with minimal complications but the results are variable and most of the time the pain relief is not permanent.

Other medical measures, such as carbohydrate restriction and oral hypoglycaemic agents, are directed towards control of the endocrine failure but unfortunately most patients will end up requiring insulin (Jalleh and Williamson, 1992).

The exocrine function should be assessed clinically (diarrhoea, steatorrhoea and need for enzyme replacement) or exocrine function tests (faecal fat, pancreatic stimulation, pancreolauryl test and faecal elastase). In general most patient are controlled by enteric enzymes (creon 10–15 tablets/day) (Williamson, 1991).

Surgical

Operative procedures can be classified as resective, derivative or denervations. The resective procedures can be partial (proximal or distal) or total pancreatectomy. Partial pancreatectomy is generally reserved for those patients with no dilatation of the duct or a localized mass.

In the author's experience, resection of the head of the pancreas was indicated mainly for pain (47 out of 52). Other indications were jaundice (19), suspicion of cancer (12) and duodenal stenosis (6). In 80% of patients, pain control was achieved (Stapleton and Williamson, 1996). Sometimes when the disease is more prominent in the tail, or for diagnostic purposes, the body tail is removed and this can be achieved in 40–45% of cases with preservation of the spleen (Aldridge and Williamson, 1991). The chance of insulin-requiring diabetes is unpredictable but increases if the line of transection goes to the right of the portal vein. In general distal resections impair the endocrine function more than the proximal ones (Jalleh and Williamson, 1992). Sometimes end-stage CP requires total pancreatectomy, performed in one or two stages. Again the main indication is pain and pain relief can be achieved after this procedure in 80% of cases, but there is a high rate of premature death, generally in alcoholics whose habit makes diabetic control erratic (Fleming and Williamson, 1995).

Drainage operations are ideal because they can alleviate the symptoms with no impairment of the pancreatic function. However, it is necessary to have either a pseudocyst or a dilated duct of at least 8 mm which can be opened from head to tail so that a Roux loop of jejunum can be anastomosed side to side. The same drainage can be appropriate for a pseudocyst with or without pancreatic ductal communication (Williamson, 1991).

Finally, splanchnicetomy should be mentioned among the denervation procedures. This was popular 50 years ago, but soon became unpopular because it required a painful thoracotomy scar. Now, however, video-assisted thoracoscopic surgery permits the section of splanchnic nerves

KEY POINTS

- The incidence of chronic pancreatitis has increased fourfold in the last 30 years.
- Alcohol abuse is its most important cause.
- Pain is the main clinical feature.
- Incidence of pancreatic carcinoma among patients with chronic pancreatitis is 5%.
- Addiction to opiates is often associated with chronic pancreatitis.
- The main complications are jaundice, duodenal obstruction, pseudocyst, haemorrhage and cancer.
- Sometimes resection of the pancreatic head is the only way to exclude a tumour.

through a minimally invasive and well-tolerated approach. Early experience of twenty four of these operations, with no mortality and minimal morbidity, was reported recently. However, the results were not very encouraging because only 25% of patients experienced an improvement in their pain (Usatoff et al, 1999). Nevertheless considering its minimally invasive character, it is worth trying splanchnicetomy before embarking upon major pancreatic surgery. **HM**

Conflict of interest: none.

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