

Leading article

Pancreatic inflammatory disease

'When I use a word, it means precisely what I want it to mean, neither more nor less.'

Words used to describe diseases or their complications mean different things to different people. Definitions are crucial, especially in case reporting and comparative studies. In pancreatology, for example, studies on patients with chronic pancreatitis may lack strict criteria and the groups studied are rarely homogenous.

Attempts to define and classify pancreatic inflammatory disease have continued for years. The impact of histology, followed by ultrasound, endoscopic retrograde cholangiopancreatography, and eventually computed tomography have each refined thinking and thus diagnosis and treatment.

An ideal definition should be exclusive and universally agreed and the perfect classification system simple, easy to use, unequivocal, and include information implying treatment and prognosis.

The initial effort at definition and classification some 30 years ago,¹ predated modern imaging and is morphologically based. It made the crucial distinction between the reversibility of the lesions of acute pancreatitis and the irreversible and possibly progressive nature of chronic disease. It relied on function tests or histological examination, which was not very precise. With the advent of modern imaging attempts were made to provide something more user friendly: the Cambridge² definitions were entirely clinical; in Marseilles³ histopathology was included but in clinical practice it is rarely available. A recent classification of pancreatitis was based on molecular pathology.⁴ The latest effort was undertaken in 1992 and focused on acute pancreatitis.⁵ The reason for this upsurge in interest was the notion that an infected pancreatic necrosis carried a high mortality and if diagnosed, could be treated surgically with benefit. If the production of precise diagnostic criteria could lead to useful treatment (or, better, an avoidance of unnecessary medical interference), then this would be helpful. The terminology had become confused and complicated and it was felt that the classifications currently available had to be more user friendly.⁶

What is acute pancreatitis?

An acute inflammatory process of the pancreas, which may subsequently involve other regional tissues or remote organ systems; the process can be mild or severe, mild being associated with minimal organ disruption, an uneventful recovery without the features of severe disease (see later). Three of four cases of acute pancreatitis fall into this 'mild' category.

Severe acute pancreatitis is associated with multiple organ abnormality or a local complication, such as necrosis, abscess or pseudocyst, or both.

The pathological basis for this is that mild acute pancreatitis shows microscopic interstitial oedema and fat

necrosis (the so called 'oedematous' pancreatitis), whereas severe acute pancreatitis is associated with macroscopic areas of pancreatic and peripancreatic necrosis and haemorrhage.

Is it pancreatitis at all?

The diagnosis of pancreatitis is accepted if the serum concentration of pancreatic amylase is three to four times the upper limit of normal, the differential diagnosis (perforation or infarction of the bowel, ruptured ectopic pregnancy or dissecting aneurysm), usually becomes rapidly apparent. If there is diagnostic doubt then a plasma lipase test is helpful. Once the diagnosis has been considered and an increased amylase concentration found, problems relate not to diagnosis but to severity.

What is the prognosis?

Patients with severe acute pancreatitis exceed three Ransom criteria at 48 hours,⁷ or five Apache II criteria at any time during the disease⁸; severity is directly related to the intensity and extent of the inflammatory process. The two crucial issues are whether and when the patient requires intensive care treatment, and whether or when surgical intervention is appropriate. Experience suggests that an infected necrosis (diagnosed by fine needle aspiration, microbiology, and culture⁹), is best treated surgically and improved survival has been reported,¹⁰ although surgical techniques are not standardised.

Definition of complications

Complications are usually diagnosed by computed tomography. Not every hospital has a scanner but, as complications usually occur a few days after the onset of the disease, those patients requiring scanning can be selected by the application of the simple criteria of Ransom or Apache II and then referred appropriately.

Pancreatic necrosis

This is an area of non-viable pancreatic parenchyma, often associated with peripancreatic fat necrosis. The gold standard for making this diagnosis is dynamic contrast enhanced computed tomography. This will show well defined areas of non-enhanced parenchyma >3 cm in size or >one third the area of the gland. Contrast density is <50 Hounsfield units in areas of necrosis after administration of intravenous contrast (normal enhancement should be between 50–150 Hounsfield units).¹¹ The overall extent of pancreatic fat necrosis cannot be reliably determined by computed tomography but is not usually overestimated.

It is crucial to distinguish between sterile and infected pancreatic necrosis because infection in necrotic tissues trebles mortality.¹² Infected pancreatic necrosis carries a bad prognosis without surgical drainage.

Acute fluid collection

Acute fluid collection occurs early in the disease in about one third to one half of patients and represents the early development of acute pseudocysts or abscess but lacks a defining wall of granulomatous or fibrous tissue. More than one half of the fluid collections regress spontaneously.

Pseudocyst formation

A pseudocyst is a collection of pancreatic juice enclosed by a defined wall of granulation or fibrous tissue usually more than four weeks from the onset of the episode. They are further subdivided into acute (occurring in a patient who has had an episode of acute pancreatitis), or chronic (occurring where there is no antecedent episode and invariably in the context of chronic pancreatitis). Bacteria may be present in a pseudocyst but may be of no clinical significance.

Pancreatic abscess

A pancreatic abscess is a circumscribed intra-abdominal collection of pus usually near the pancreas, containing little or no pancreatic necrosis, which arises as a consequence of acute pancreatitis or pancreatic trauma. The distinction between an abscess and infected necrosis is important because the death risk for an infected necrosis is greater than that of an abscess. Necrosis usually requires surgery but an abscess may be treated by percutaneous drainage.

The terms phlegmon, infected pseudocyst, haemorrhagic pancreatitis, and persistent acute pancreatitis find no place in the Atlanta terminology. Thus a simple classification with implications for treatment and prognosis is suggested.

Chronic pancreatitis

The continuing inflammation in the gland with loss of exocrine parenchyma, fibrosis, and destruction of endocrine tissue may be complicated by acute episodes, but, after some time, signs of endocrine and exocrine insufficiency appear and the acute episodes relent. A common mechanism for aetiology of all types might be the precipitation of protein within the duct which, in contact with the ductal epithelium, may cause duct cell atrophy and subsequent periductal fibrosis with stricture and thus upstream loss of exocrine tissue. A transudate of protein and calcium rich interstitial fluid occurs, which permits increasing calcium deposition, hence chronic calcified pancreatitis. If this precipitation of protein is the basic lesion than chronic pancreatitis might be defined as an irreversible destruction of exocrine and endocrine tissue resulting from ductal obstruction consequent on protein precipitation, this process having various causes.

Chronic calcifying pancreatitis

The commonest form seen in Europe, the United States, and Japan. It is usually caused by alcohol, possibly a result of a combination of the stimulatory effects of alcohol producing a viscid juice and the production of protein plugs in such profusion as to obstruct the flow of juice and cause the typical patchy histological effect. As only a proportion of alcoholic subjects have pancreatitis, it may be that there is a genetic susceptibility, perhaps mediated

through the lack of production of a stabilising protein that can prevent calcium precipitation.

Tropical pancreatitis

The diagnosis rests on the geographical location of the patient, who is usually young, of either sex, and comes from a region where there is protein and fat malnutrition. This problem affects both children and adults, particularly mothers so these neonatal malnutrition may be an important factor.

Hereditary pancreatitis

This rare condition may result from a lack of protein stabiliser, which permits the formation of calcifying plugs. The condition may be familial and is seen in children of either sex.

Obstructive pancreatitis

In these conditions an obstruction of the main pancreatic duct occurs gradually and exists before the development of the disease. The obstruction may be caused by a small lesion such as a scar, stricture or tumour and the lesions are uniformly distributed with a paucity of intraductal plugs without calculi. Chronic main pancreatic duct hypertension is the underlying problem and may be reversible.

A successful and useful system of definition and classification must provide signposts for treatment. It remains uncertain which patients with chronic pancreatitis will become pain free if treated conservatively, indeed the relations between pain, function, and histopathology remain far from clear. The dynamics of chronic pancreatitis require study and agreed criteria for mild, moderate, and severe disease are necessary, as are new techniques to provide insight into function, given the limited sensitivity of existing tests.

What is certain is that if the doctors can talk the same language we should have a better chance of offering effective help to patients with inflammation of the pancreas.

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