JGH Open Open Access An open access journal of gastroenterology and hepatology

JGHF Journal of Gastroenterology and Hepatology Foundation

doi:10.1002/jgh3.12698

EDITORIAL

Progression from acute to chronic pancreatitis

Inflammation of the pancreas continues to be a significant health burden in most parts of the world. For example, in the United States, various surveys of gastrointestinal disorders have shown that acute pancreatitis is the most common reason for hospitalization.[1] Although there are well-recognized causes of infectious pancreatitis, almost all hospital admissions are caused by a non-infectious process that initially results in activation of harmful proteases within the pancreatic parenchyma. Categories of pancreatitis include acute pancreatitis, recurrent acute pancreatitis and chronic pancreatitis, although the reality is that these represent a continuum rather than discrete phases in a disease process.

In most surveys of acute pancreatitis in adults, biliary disease and alcohol abuse account for 60–70% of cases.[2] In the former, pancreatitis is usually attributed to obstruction of the pancreatic duct by bile duct stones, often during spontaneous passage into the duodenum. In the latter, the pathogenesis is less clear but a high intake of alcohol over several years results in toxic effects on pancreatic acinar and stellate cells, and biochemical changes in pancreatic secretions that facilitate the formation of pancreatic plugs. Acute pancreatitis unrelated to biliary disease or alcohol has been attributed to a variety of disorders including autoimmune pancreatitis, hereditary pancreatitis, drug-induced pancreatitis, pancreatic cancer, postoperative pancreatitis and pancreatitis induced by endoscopic retrograde cholangiopancreatography (ERCP). The remaining "idiopathic" group seems likely to include patients with small bile duct stones (microlithiasis), and patients with mutations in a variety of susceptibility genes such as the serine protease inhibitor Kazal type 1 gene (SPINK1). Whether the congenital anomaly, pancreas divisum, predisposes to acute pancreatitis is currently unclear.

Despite advances in intensive care, the overall mortality in hospitalized patients with acute pancreatitis is often approximately 10%, largely those with severe disease. In patients discharged from hospital, 20–30% have a further admission for pancreatitis, often within 1 month.[3] These patients are categorized as recurrent acute pancreatitis and are more likely to have alcohol abuse as the etiologic factor. However, a minority have an index episode categorized as biliary or idiopathic. Patients with recurrent acute pancreatitis are more likely to have had severe or complicated disease during the index episode with prolonged elevation of serum amylase or lipase. However, some of the idiopathic group have recurrent episodes of mild pancreatitis, usually with normal findings at ERCP. In this subgroup, endoscopic manometry has revealed changes in motility in the sphincter of Oddi: an association that has raised the possibility that pancreatitis can be caused by sphincter dysfunction with a degree of obstruction of the main pancreatic duct.

Chronic pancreatitis is the end result of continuing pancreatic inflammation and is characterized by extensive fibrosis that replaces exocrine cells and, to a lesser extent, endocrine cells in pancreatic islets.[4,5] Common clinical features are chronic pain, steatorrhea, nutritional deficiencies, analgesic addiction (particularly opiods) and diabetes. These features impact on quality of life and are associated with a reduction in life expectancy. The diagnosis of advanced chronic pancreatitis is usually straightforward in patients with steatorrhea and pancreatic calcification on a plain abdominal radiograph or computed tomography (CT) scan. However, in the absence of calcification, confirmation of the diagnosis may involve additional investigations including magnetic resonance imaging with magnetic resonance cholangiopancreatography (MRCP), with or without secretin stimulation, ERCP and endoscopic ultrasound (EUS). Fecal fat studies and various test of exocrine function are no longer in routine use.

The majority of patients with chronic pancreatitis have been previously diagnosed with acute and recurrent acute episodes. However, a substantial minority present with typical features of chronic pancreatitis without previous attacks, presumably because of long-standing subclinical acinar damage and inflammation. It has been estimated that approximately one-third of patients with recurrent acute pancreatitis will evolve into chronic disease over time. This time interval can be relatively short for alcoholic pancreatitis but is often prolonged to 10 years or more for idiopathic pancreatitis. The aetiology of chronic pancreatitis also varies widely in different populations. Alcohol abuse is the most common etiologic factor in most Western countries (40–70%), but idiopathic pancreatitis is the most common form in China (80%) and India (59%). Smoking has also emerged as a significant risk factor that is often associated with alcohol abuse in a synergistic manner. Yet another issue is genetic predisposition to chronic pancreatitis where studies from various countries have shown higher than expected frequencies of several gene variants linked to susceptibility to pancreatic inflammation.

In this issue of JGH Open, Drs Patra and Das from Kolkata, India, report longer-term outcomes in 122 patients who had previously been admitted to hospital with an index episode of acute pancreatitis.[6] After 5 years, outcomes were established in 100 patients. Four were known to have died (one from pancreatic cancer), 15 were categorized as recurrent acute pancreatitis and 13 had developed chronic pancreatitis. Seventeen patients had new-onset diabetes. Although idiopathic pancreatitis was the most common category for the index episode, recurrent acute pancreatitis and chronic pancreatitis were associated with alcohol abuse and with a more severe or complicated index episode. Although the study has limitations, a strength was the careful documentation of the severity of the index episode. Additional useful information may emerge with follow-up for 10 years or more.

An important issue for clinicians is the opportunity to intervene and alter the sequence of events as described above. One aspect is measures that decrease the severity and frequency of complications after acute pancreatitis. Although advances have occurred in our understanding of the pathogenesis of pancreatic inflammation, drugs such protease inhibitors, somatostatin and others have not shown clear benefit in randomized trials. An

exception is the reduced frequency of pancreatitis after ERCP in patients given non-steroidal, anti-inflammatory drugs or treated with pancreatic stents.[7] After acute alcoholic pancreatitis, cessation of alcohol and smoking reduce the risk of progression to recurrent acute and chronic disease.[8,9] In patients with mild biliary pancreatitis, same-admission cholecystectomy rather than later (interval) cholecystectomy (with or without ERCP) also reduces the risk of recurrence.[10] Longer-term treatment with corticosteroids may prevent progression to chronic pancreatitis in patients with autoimmune pancreatitis, although the natural history of this disorder is highly variable.[11] In idiopathic pancreatitis presumed to be caused by sphincter dysfunction, endoscopic or operative procedures to facilitate duct drainage continue to evoke debate and may not avoid progression to chronic pancreatitis.[12] Ongoing challenges include a better understanding of the pathogenesis of idiopathic pancreatitis, effective medication to avoid severe necrotizing pancreatitis and better ways to diagnose and treat the persistent inflammation that results in chronic disease.

Acknowledgments

I am grateful to Professor James Toouli for helpful suggestions for the manuscript.

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