Chronic Pancreatitis: Disease Forms and Clinical Picture

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The cardinal manifestations of chronic pancreatitis are recurrent or persistent abdominal pain that lasts for months to years, accompanied by diabetes, steatorrhea, and pancreatic calculi. Morphologically, the disease is characterized by destruction and loss of exocrine parenchyma that may be focal, segmental, or diffuse, as well as by fibrosis of the pancreas (Fig. 194-1). These changes may be associated with strictures and dilatation of segments of the pancreatic duct and with intraductal protein plugs or calculi.

The epidemiology of chronic pancreatitis parallels the prevalence of alcohol abuse in the community. In the United States, almost 75% of cases of chronic pancreatitis are associated with chronic alcoholism, which is thus the most important etiologic factor.

Although the pathogenesis of pancreatic injury is still speculative, current data indicate that acinar cells are injured first, with subsequent development of secretory changes and morphologic alterations such as fibrosis, ductular abnormalities, and stone formation.

Toxic metabolites, unopposed free-radical injury and genetic mutations that promote premature activation of trypsinogen to trypsin within the acinar cell are associated with the pathogenesis of chronic pancreatitis. Three genes are currently believed to play a major role: cationic trypsinogen gene (PRSS1, 7q35), CFTR, and SPINK1.

FORMS OF DISEASE
In chronic alcoholism, onset of chronic pancreatitis usually occurs after 15 or more years of 80 to 150 g of daily alcohol consumption. Individual susceptibility varies, and only about 10% of alcoholics who drink heavily develop chronic pancreatitis, but a larger number may have histologic changes in the pancreas. The susceptibility for pancreatic injury is increased with cigarette smoking and genetic abnormalities.

Tropical calculous pancreatitis (TCP) is a nonalcoholic form of chronic pancreatitis that occurs mostly in children and young adults of many developing nations. Cardi nal clinical manifestations of TCP are recurrent abdominal pain in childhood, followed by onset of diabetes mellitus a few years later. Diabetes, almost an inevitable consequence of TCP (in contrast to alcoholic pancreatitis, in which diabetes develops in 30%-60% of patients), is characteristically brittle. The etiologic factors for TCP are unknown, but genetic factors (mainly SPINK1 mutations) in association with other environmental factors are suspected.

Hereditary pancreatitis (HP) is one of the most common causes of recurrent pancreatitis in children, who may be as young as 7 years of age when HP is identified. Relatives of patients with HP may have painless disease, but more often they have pancreatic calculi, steatorrhea, or diabetes. A major milestone in the history of HP is the recent discovery of an abnormal gene and the feasibility of identifying the genetic abnormality. Mutations in the cationic trypsinogen gene (R1224, N291) cause the disease in 60% to 70% of kindreds. The most dreaded complication of HP is a 50- to 70-fold increased risk for pancreatic cancer.

Autoimmune pancreatitis (AIP) is a curable form of chronic pancreatitis that affects middle-aged men, in association with other autoimmune disorders (Sjögren syndrome, psoriasis, inflammatory bowel disease). AIP is characterized by elevated IgG1 levels in serum. Extrapancreatic involvement is common and includes sclerosing cholangitis and lymphoplasmacytic forms of kidney, salivary gland, and lung disease. Typical computed tomography findings are diffusely enlarged pancreatic gland with rim enhancement and irregularly attenuated main pancreatic duct. Response to steroid therapy is characteristic. (See Fig. 195-1.)

Idiopathic pancreatitis has two subsets. The juvenile form is characterized by male preponderance, age of onset before 25 years, and a long history of recurrent attacks of abdominal pain. Hallmarks of chronic pancreatitis, such as calculi formation, pancreatic insufficiency, and diabetes, develop 25 to 28 years after onset. The prognosis is poor because of the absence of a removable cause. Late-onset (usually after age 60) idiopathic chronic pancreatitis (senile pancreatitis) may be painless, diagnosed by incidental discovery of calculi during routine abdominal radiography or during workup of a patient with steatorrhea of uncertain etiology.

Other rare causes of chronic pancreatitis include obstruction, hyperlipidemia, pancreas divisum, hyperparathyroidism, gastrectomy, and celiac disease.

CLINICAL PICTURE
Recurrent Abdominal Pain
Postprandial pain is the dominant symptom in about 85% of patients with chronic pancreatitis and the most common reason they seek medical attention. Pain can be debilitating and intractable, often leading to functional incapacity, drug and alcohol addiction, poor quality of life, and even suicidal tendencies. Steady, boring, and agonizing pain in the epigastrium or sometimes in the left upper quadrant with radiation directly to the back, between the twelfth thoracic (T12) and second lumbar (L2) vertebrae, or to left shoulder is the typical presentation. Patients sit up and lean forward to the so-called pancreatic position or lie in the knee-chest position on the side. The severity and frequency of painful attacks vary. The duration of pain-free intervals is unpredictable, from weeks to many months. Pain may decrease or disappear, become stable, or worsen with advancing disease.

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Figure 194-1 Chronic Pancreatitis.
Pancreatic pain appears to be multifactorial in pathogenesis, accounting for the difficulty encountered in pain management. Intraductal or interstitial hypertension, neuronal hypertrophy, perineural inflammation, and ongoing pancreatic injury are proposed mechanisms. Treatable complications such as pseudocyst and common bile duct (CBD) obstruction may contribute to the pain.

**Malabsorption**

Steatorrhea does not occur until enzyme secretion is reduced to less than 10% of normal. Lipolytic activity decreases more quickly than does trypsic activity, and it explains why steatorrhea occurs sooner and is more severe than protein malabsorption. In addition to reduced secretion of pancreatic enzymes, patients with severe chronic pancreatitis have decreased bicarbonate secretion. The stools may be bulky and formed, in contrast to the frank, watery diarrhea seen in malabsorptive disorders secondary to small intestinal causes. Oil droplets in the stool are often reported in chronic pancreatitis. Fecal weight tends to be lower and fat content of the stool greater (>20 g/24 hr) in patients with pancreatic insufficiency than in patients with steatorrhea from other causes.

**DIABETES**

Diabetes develops in almost 30% of patients with alcoholic pancreatitis 10 years after onset of disease. Diabetes in chronic pancreatitis is an example of acquired beta- and alpha-cell insufficiency associated with insulin resistance. Ketosis is rare, but other complications (e.g., nephropathy, retinopathy) are as common as in type 2 diabetes, and neuropathy may be more common in view of the addictive effect of alcoholism.

**ADDITIONAL RESOURCES**