Mechanisms of Acute Pancreatitis

Vascular Etiology

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Summary

Vascular mechanisms play an important but controversial role in the pathogenesis of acute pancreatitis. In experimental animals, injection of wax, powder, air, mercury, and microspheres into the pancreatic artery causes pancreatitis by end artery occlusion with resulting cellular infarction. Larger microspheres do not cause pancreatitis because collateral blood flow is preserved. Clinical evidence, such as microthrombi and atheromatous emboli in the pancreatic artery of patients with pancreatitis, supports pancreatic infarction as an etiologic agent. Experimental and clinical studies have suggested that pancreatic ischemia may also cause pancreatitis, but these studies have not been conclusive. We have compared five hours of total occlusion of the pancreaticoduodenal artery along with four hours of reperfusion to bile injection into the pancreatic duct as causes of pancreatitis. Bile injection caused a significant increase in serum amylase, activation of trypsin in pancreatic exudate, and histologic evidence of necrotizing pancreatitis. Pancreatic blood flow decreased as pancreatitis developed. Ischemia for five hours did not cause a significant increase in serum amylase or activation of trypsin in pancreatic exudate. Only edema was seen histologically, but there was no necrosis. Pancreatic blood flow increased with reperfusion. We believe ischemia aggravates, but does not initiate pancreatitis. Ischemia does not induce inflammation and necrosis in the pancreas, although infarction does.

Key Words: Pancreatitis etiology; pancreatic ischemia; pancreatic blood flow.

VASCULAR MECHANISMS OF ACUTE PANCREATITIS

Vascular mechanisms play an important but controversial role both locally and systemically in acute pancreatitis. The difficulty is whether these vascular factors initiate or promote pancreatitis, and whether they are a cause or an effect of pancreatitis. Acute pancreatitis is an inflammatory disease in which
digestive enzymes within the gland become activated and begin a process of autodigestion of the peripancreatic tissue and pancreatic parenchyma. Vascular mechanisms have been implicated in the etiology of acute pancreatitis since 1862, when Panum produced pancreatic hemorrhage by injecting small particles of wax into the pancreatic artery of experimental animals (1). Focal infarction of the pancreas with death from pancreatitis has been shown in experimental animals to follow pancreatic arterial injection of such diverse agents as lycopodium powder, air, oil, and mercury droplets (2).

Other studies, although confirming that pancreatic infarction could produce lethal pancreatitis, also pointed out the importance of collateral flow in preventing acute pancreatitis. Bunge in 1903 produced hemorrhagic infarcts by ligating the pancreaticoduodenal artery and then injecting air, petroleum, and oil through the ligated artery into the gland (3). However, animals with simple ligation of the pancreatic arteries remained well and did not die from pancreatitis. The animals with ligation and injection all died with infarcted pancreases. Pfeffer and coworkers (4) demonstrated in dogs that pancreatic arterial injection of sterile polyethylene microspheres caused pancreatitis. The degree of parenchymal damage was inversely proportional to the size of the microspheres injected. The most severe pancreatitis was produced with injection of microspheres that were 8–20 microns. Larger microspheres, i.e., 200–400 microns, produced little inflammatory change, suggesting that collateral flow could obviate the development of pancreatitis. Obstruction of the terminal arteriole bed by smaller microspheres led to parenchymal necrosis and subsequent pancreatitis. Redha and coworkers (5) have also shown that 20-micron polystyrene microspheres injected retrogradely into the splenic artery caused pancreatic infarction and death from pancreatitis in rats.

Clinical evidence lends support to pancreatic infarction as a cause of pancreatitis. Baer and Neu (6) described microthrombi in pancreatic blood vessels associated with pancreatitis in a patient who died during hyperparathyroid crisis. They suggested that high levels of serum-ionized calcium promoted thrombogenesis and subsequent pancreatic infarction. Probstein and coworkers (7) studied 12 patients with atheromatous emboli and found pancreatitis resulting from these emboli in all but two.

Certainly, pancreatic infarction can cause cellular disruption with release and activation of pancreatic enzymes. However, can ischemia do the same? Bunge's finding that pancreatic artery ligation alone does not cause pancreatitis was confirmed by Popper and coworkers (8). They occluded the pancreaticoduodenal artery in dogs for 45 min, but could not induce biochemical or histologic changes of pancreatitis. Likewise, Pfeffer and coworkers (4) found that permanent ligation of the pancreaticoduodenal artery alone rarely induced histologic changes of pancreatitis. Since occlusion of the main pancreatic artery itself did not induce pancreatitis, ischemia alone does not seem sufficient to cause pancreatitis. However, ischemia can serve as an important cofactor to potentiate and convert an initial insult to the pancreas into a frank pancreatitis. In the studies of Popper and coworkers (8), animals who