Recent Trends in the Management of Acute Pancreatitis

Essay

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Master Degree in General Surgery

By

Ayman Abd EL Monem Ameen
M.B, B.Ch

Under Supervision Of

Prof. Dr. Ashraf El Zoghby
Professor of General Surgery
Faculty of Medicine – Ain Shams University

Prof. Dr. Amr Ahmed Abd El Aal
Professor of General Surgery
Faculty of Medicine – Ain Shams University

Dr. Hany Said Abd El Baset
Lecturer of General Surgery
Faculty of Medicine – Ain Shams University

Faculty of Medicine
Ain Shams University
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Introduction

Acute pancreatitis (AP) is a non bacterial inflammation of the pancreas caused by the activation, liberation and the digestion of the gland by its own enzymes ***(Reber, 1999)***.

In about 80% of cases, AP is a mild self –limiting disease characterized by minimal local and systemic effects and an uneventful recovery. In 15% to 20% of cases, sever AP develops that is accompanied by an exaggerated systemic response characterized by release of inflammatory cytokines and other mediators, also known as the Systemic Inflammatory Response Syndrome(SIRS) ***(Bhatia et al., 2005).***

The two major causes of AP are biliary calculi, which occur in 50%-70% of patients, and alcohol abuse which account for 25% .The remaining cases may be due to rare causes as (idiopathic, drug induced, hyperparathyroidism, autoimmune, post-ERCP) ***(Chang et al., 2003)***.

The diagnosis of acute pancreatitis depends on a combination of clinical assessment and laboratory testing. Serum amylase has relatively low sensitivity. Serum lipase is more sensitive ***(Yousaf et al., 2003).***

In patients with clinically severe disease, imaging provides a significant contribution to the diagnosis and identification of local complications and serves as a guide for therapeutic interventions. Conversely, imaging plays only a limited role in patients with mild disease ***(Mofidi et al., 2006)***.

Supportive therapy remains the basis of management with attention to the adequacy of the fluid balance and oxygenation are of prime importance and supportive therapy may include inotropic support, assisted ventilation and renal dialysis ***(Mason and*** **Siriwardena,** ***2005).***

Therapeutic endoscopic retrograde cholangio pancreatography (ERCP) with endoscopic sphincterotomy in severe biliary pancreatitis, the use of early antibiotics treatment in necrotizing pancreatitis and the demonstration of enteral feeding are able to decrease the inflammatory response ***(Gurusamy et al, 2005).***

Definitive treatment of patients with gallstone related pancreatitis within four weeks of presentation, availability of intensive care unit, high dependency unit and dynamic CT scanning have reduced the mortality and morbidity of acute pancreatitis ***(Mofidi et al., 2007).***

Aim of the Work

The aim of this work is to review the etiology, pathophysiology, and to have spot light on the updates in management of acute pancreatitis.

Chapter (1)

Anatomy of the Pancreas

Introduction:

The name of Panc is derived from the Gerk "Pan" (all) and "Kreas" (Flesh).It was originally though to act as a cushion for the stomach ***(Satyajet et al., 2008).***

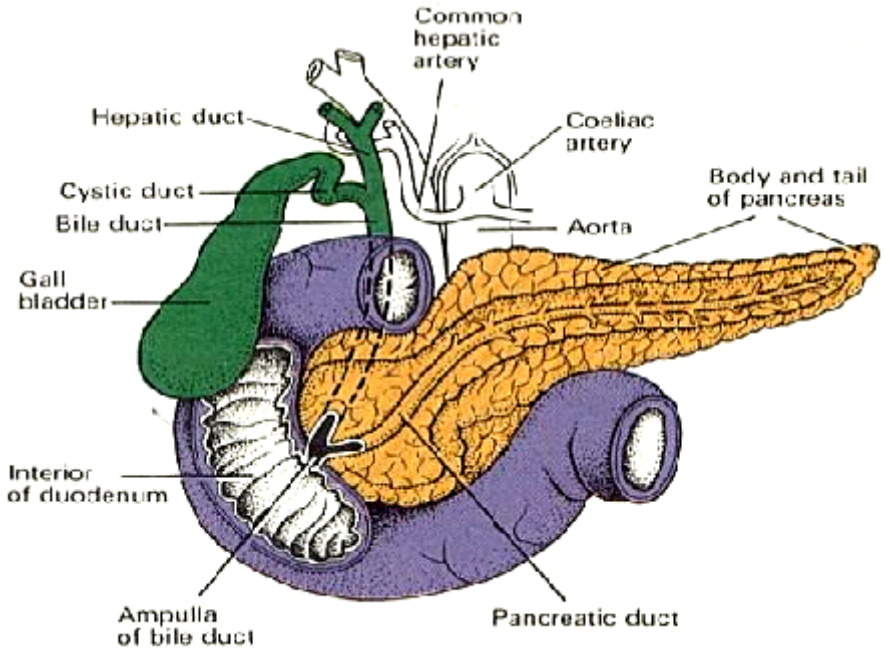

Figure (1): Normal Anatomy of Pancreas ***(Steinberg and tenner., 1994).***

The pancreas is an elongated, yellow-tan, lobulated, solid organ "figure 1" the anatomical segments of the pancreas are the head, uncinate process, neck, body, and tail. The head is encompassed by the duodenum and surround the distal common bile duct. The uncinate process extends from the head posteriorly to lie behind superior mesenteric vein near its union with portal vein. The neck, the narrowest portion of the gland, extends anterior to superior mesenteric vessels and is posterior to the pylorus and first portion of the duodenum. The body contains from the neck obliquely across the retro peritoneum anterior to the first lumbar vertebrae. The body merges into the tail, which ends near the hilum of the spleen ***(Levi et al., 1998).***

In adults the pancreas measures between 12 and 15 cm long and is shaped as a flattened tongue of tissue, thicker at its medial end (head) and thinner towards the lateral end (tail) ***(Harlod et al., 2005).***

Pancreatic duct:

The exocrine pancreatic tissue drains into multiple small lobular ducts, which drain into a single main, and usually a single accessory duct ***(David et al., 2005).***

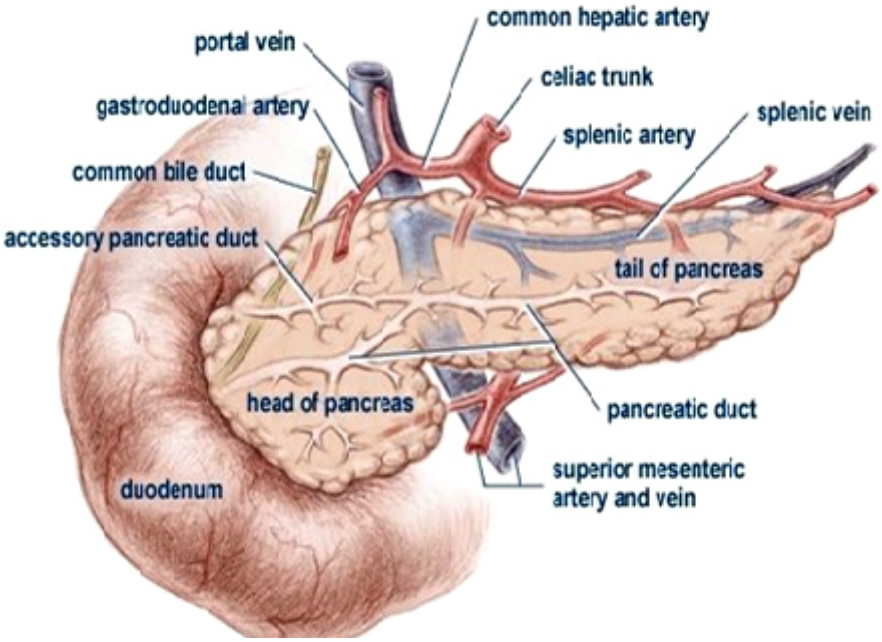

Figure (2): Arterial supply to the Pancreas ***(Neil et al, 2005).***

Arterial supply:

The pancreas is supplied with blood from both the celiac trunk and the superior mesenteric artery "Figure 2". The head of the pancreas and the concave surface of the duodenum are supplied by two pancreaticoduodenal arterial arcades (anterior and posterior). Ligation of both vessels will result in duodenal ischemia and necrosis. All major arteries lie posterior to the ducts ***(Skandalakis et al., 2000).***

The gastroduodenal artery divides to form the anterior superior and posterior superior pancreatico-duodenal arteries. The anterior inferior pancreaticoduodenal arises from the superior mesenteric artery at or above the inferior margin of the pancreatic neck. It may form a common trunk with the posterior inferior artery ***(Skandalakis et al., 2000).***

The splenic artery is located on the posterior surface of the body and tail of the pancreas. From 2 to 10 branches of the splenic artery anastomose with the transverse pancreatic artery. The Lrgest of those, the great pancreatic artery of Von Haller, which is the main blood supply to the tail of the pancreas ***(Skandalakis et al., 2000).***

Venous drainage:

The venous drainage of the pancreas is primarily into the portal system. The head and neck drain primarily via superior and inferior pancreaticoduodenal veins. The body and tail drain mostly via small veins running directly into the splenic vein along the posterior aspect of the gland or occasionally directly into the portal vein. Small venous channels exist between the gland and the retroperitoneal veins, drainage into the lumber veins and these may hypertrophy and become clinically significant in cases of portal hypertension ***(Neil et al, 2005).***

Lymph drainage:

Lymph capillaries commence around the pancreatic acini. The larger lymph vessels follow the arterial supply and drain into the lymph nodes around the pancreas and adjacent node groups. The tail and body lymphatics drain mostly into the pancreaticosplenic nodes although some drain directly to pre aortic nodes, lymphatics from the neck and head drain more widely into nodes along the pancreaticoduodenal, superior mesenteric and hepatic arteries. Drainage also occurs to the pre aortic nodes and celiac axis nodes. There are no lymphatics in the pancreatic islets ***(Neil et al, 2005).***

Nerve supply:

Innervatons of the pancreas occur by the sympathetic division of the autonomic nervous system by the way of the splanchnic nerve and by the parasympathetic division by way of the vagus nerve. These nerves generally follow blood vessels to their destinations ***(Neil et al, 2005).***

Chapter (2)

Etiology of Acute Pancreatitis

Definition:

Acute pancreatitis (AP) is an inflammation of the pancreas secondary to a variety of causes "Table 1". That results in the activation of a number of pancreatic proteolytic enzymes within the organ that can cuminate in digestion of the organ itself. The pathological definition of (AP) is: "A nonbacterial inflammation of the pancreatic gland caused by the activation and the digestion of the gland by its own enzymes" ***(Murray Orbuch, 2004).***

In a collective series of over 1200 patients, Lumsden and Bradly reported gallstone to be the most common etiological factor (34%), alcohol (25%), unrelated surgical treatment (20%), idiopathic (10%), trauma (3%) and post ERCP (8%) ***(Srikanth et al., 2002).***

Gallstone pancreatitis:

Billiary tract stone disease is the most common cause of acute pancreatitis. It accounts for about 30-60% of cases of acute pancreatitis. More women than men are effected and the age of peak incidence is between 50 and 60 years ***(Whitcomb, 2006).***

Because the gallbladder and pancreas share a drainage duct, gallstones usually less than cm that lodge in this duct can prevent the normal flow of pancreatic enzymes leading to high intraductal pressure which could result in ductal disruption with extravasation of activated intraluminal enzymes into the interstitium, where auto digestion of the gland would occur ***(Sakorafas and Tsiotou, 2000).***

Alcohol:

Alcohol is also a common cause of acute pancreatitis. Alcoholic pancreatitis is more common in men and usually occurs in individuals with long standing alcohol abuse. It is responsible for about 30% of all cases of acute pancreatitis. Ethanol is a cellular metabolic poison. It is metabolized in the body to acetaldehyde by the enzyme alcohol dehydrogenase. This occurs primarily in the liver, although may be limited breakdown in the pancreas as well. It is unclear whether the pancreas contains sufficient alcohol dehydrogenase to account for any direct toxicity, although other toxic metabolic products could be produced ***(Matsumoto et al., 1996).***

The mechanism of acetaldehyde toxicity may involve oxygen free radical generation by the enzyme xanthine oxidase. Moreover, alcohol stimulates gastric secretion by direct effect on the mucosa and HCL produced is a potent stimulant for secretin release and could result in an increase in the pancreatic

ductal pressure. In addition, ethanol may cause chemical duodenitis and ampullitis, which could partially obstruct the ampulla of vater and further increase the intraductal pressure in the pancreas which could lead to duct disruption ***(Sakorafas and Tsiotou, 2000).***

Table (1): Etiology of acute pancreatitis.

Mechanical	Gallstones biliary sludge, ascariasis, periampullary or pancreatic cancer, preiampullary diverticulum, ampullary stenosis, duodenal stricture or obstruction
Toxic	Ethanol, methanol, scorpion venom, organophosphate poisoning
Metabolic	Hyperlipidemia (types I, IV, V), hypercalcemia
Drugs	Didanosine, pentamidine, metronidazole, stibogluconate, tetracycline furosemide, thiazides, sulphasalazine, 5-ASA, L-asparagionase, azathioprine, valproic acid, sulindac, salicylates, calcium, estrogen.
Infection	Viruses: mumps, coxsackie, hepatitis B, CMV, varicela-zoster, HSV, HIV Bacteria: mycoplasma, legionella, leptospira, salmonella Fungi: aspergillus Parasites: toxoplasma, cryptosporidium, ascaris
Trauma	Blunt or penetrating abdominal injury, iatrogenic injury during surgery or ERCP (sphincterotomy)
Congenital	Cholodochocelel type V, pancreas divisum
Vascular	Ischemia, atheroembolism, vasculitis (polyarterites nodosa, SLE)
Miscellaneous	Post ERCP, pregnancy, renal transplantation, alpha-1-antitrypsin deficiency
Genetic	CFTR and other genetic mutations

(Steven, 2007)

Chapter (3)

Pathophysiology of Acute Pancreatitis

Introduction:

The pancreas is a gland located in the upper, posterior abdomen and is responsible for insulin production (endocrine pancreas) and the manufacture and secretion of digestive enzymes (exocrine pancreas) leading to carbohydrate, fat, and protein metabolism. Approximately 80% of the gross weight of the pancreas supports exocrine function, while the remaining 20% is involved with endocrine function ***(Timothy and* Gardener *., 2008).***

The principal of the exocrine pancreas is to make food digesting enzymes. The pancreas, comprising only 0.1% of total body weight, has 13 times the protein producing capacity of the liver and the reticuloendothelial system combined, which make up 4% of total body weight. Enzymes are produced within the pancreatic acinar cells, packaged into storage vesicles called zymogens, and then released via the pancreatic ductal cells into the pancreatic duct, where they are secreted into the small intestine to begin the metabolic process ***(Paul Yakshe et al., 2008).***

Normal pancreatic function:

In normal pancreatic function, up to 15 different types of digestive enzymes are manufactured in the rough endoplasmic reticulum, targeted in the golgi apparatus and packaged into zymogens as pro-enzymes. When a meal is ingested, the vegal nerves. VIP, GRP, secretin, CCK, and encephalins stimulate enzymatic release into the pancreatic duct. The pro-enzymes travel to the brush border of the duodenum, where trypsinogen, the proenzyme for trypsin, is activated via hydrolysis of an N-terminal hexapeptide fragment by the brush border enzyme enterokinase. Trypsin then facilitates the conversion of the other pro enzymes to their active form ***(Brian et al., 2008).***

A feedback mechanism exists to limit pancreatic enzyme activation after appropriate metabolism has occurred. It is hypothesized that elevated levels of trypsin, having become unbound from digesting food, lead to decreased CCK and secretin levels, thus limiting further pancreatic secretion ***(Paul Yakshe et al, 2008).***

Mechanism of acute pancreatits:

Premature activation of pancreatic enzymes within the pancreas leads to organ injury and pancreatitis, several mechanisms exist to limit this occurrence. First, proteins are

translated into the inactive pro-enzymes. Later, posttranslational modification of the Golgi cells allows their segregation into the unique subcellular zymogen compartments. The pro-enzymes are packaged in a paracrystalline arrangement with protease inhibitors ***(Timothy* and Gardener., *2008).***

Zymogen granules have an acidic pH and a low calcium concentration, which are factors that guard against premature activation until after secretion occurs and extracellular factors trigger the activation cascade. Under various conditions, these protective mechanisms are disrupted, resulting in intracellular enzyme activation and pancreatic autodigestion, leading to acute pancreatitis ***(Brian et al., 2008).***

Acute pancreatitis may occur when factors involved in maintaining cellular homeostasis are out of balance. The initiating event may be anything that injures the acinar cell and impairs the secretion of zymogen granules, pathophysiologic event triggers the onset of acute pancreatitis. However, it is believed that both extracellular factors (e.g., neural response, vascular response) and intracellular factors (e.g., intracellular digestive enzyme activation, increased calcium signaling, heat shock protein activation) play a role. In addition, acute pancreatitis can develop when ductal cell injury leads to delay or absent enzymatic secretion, ***(Paul Yakshe et al, 2008).***