Review Article **OPEN ACCESS**

Acute pancreatitis

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Abstract

Background: Acute pancreatitis continues to be a serious illness, and the patients with acute pancreatitis are at risk to develop different complications from ongoing pancreatic inflammation. **Aims**: The present review is to highlight the classification, treatment and prognosis of acute pancreatitis. **Material & Methods**: We reviewed the English-language literature (Medline) addressing pancreatitis. **Results**: Acute pancreatitis is frequently caused by gallstone disease or excess alcohol ingestion. There are a number of important issues regarding clinical highlights in the classification, treatment and prognosis of acute pancreatitis, and treatment options for complications of acute pancreatitis including pancreatic pseudocysts. **Conclusions**: Multidisciplinary approach should be used for the management of the patient with acute pancreatitis.

Keywords: Pancreatitis, acute, gallstone disease, alcohol ingestion, classification,

Introduction

Acute pancreatitis is a common disease with a high mortality[1] , and frequently caused by gallstone disease [1] or excess alcohol ingestion [2]. The diagnosis of acute pancreatitis is supported by an elevation of the serum amylase and lipase levels. The amylase level becomes elevated within hours of the development of pain and may remain elevated for 3 to 5 days. Serum lipase has higher specificity for pancreatic disease, but its level may be elevated in other conditions as well. Laboratory abnormalities encountered in acute pancreatitis include hyperglycemia, hypocalcemia, leukocytosis, and mild elevations of liver function test results. Ultrasound and magnetic resonance cholangiopancreatography are potentially valuable tests in the evaluation of acute pancreatitis, and are helpful in detecting stones in the common bile duct and directly assessing the pancreatic parenchyma.

In the following review, we highlight the classification, treatment and prognosis of acute pancreatitis, and treatment options for complications of acute pancreatitis.

Classification of acute pancreatitis

The first attempt to classify the severity of acute pancreatitis was made by Fitz in 1889, and until the most recent Atlanta symposium in 1992, a morphological component has always been included [3]. Whereas Fitz believed that the morphological features of severe disease were evidence of pancreatic haemorrhage and disseminated fat necrosis, the morphological features of severe disease in the original Atlanta classification were pancreatic necrosis, abscess, and pseudocyst [4].

As stated by Petrov [4], there is an ongoing effort to revise the 1992 Atlanta classification of acute pancreatitis in the light of emerging evidence. From clinician's view, persistent organ failure is predictive of death in acute pancreatitis. Local complications without organ failure are associated with morbidity, prolonged hospital stay but low mortality. However, the categorization of the severity of acute pancreatitis is one of the key elements of the classification [4].

A three category classification of severity of acute pancreatitis were recently designed. Hammel et al concluded that three new category classification of severity of acute pancreatitis identifies patients with high morbidity and mortality (severe acute pancreatitis), high morbidity without mortality (moderate acute pancreatitis) and low morbidity without mortality (mild acute

pancreatitis) [5]. The entity of moderately severe acute pancreatitis is characterized by local complications without organ failure. Mortality in moderately severe acute pancreatitis is similar to that in mild pancreatitis but hospitalization prolonged like in severe pancreatitis. Local complications are defined as pancreatic necrosis or fluid collections [6].

Histopathology of acute pancreatitis

Patients with pancreatic infection may have infected necrosis, pancreatic abscess, and/or infected pseudocysts [7]. The microbes most frequently involved are gram-negative organisms including *Escherichia coli, Enterococcus, and Klebsiella* [8]. On the other hand, for the earliest histopathological changes of acute pancreatitis, Kovalska and co-worker [9] investigated intraoperative pancreatic tissue samples, and attempted to find possibility to reparation of pancreatic tissue in nearest after severe acute pancreatitis. Their study demonstrated that the most severe damages take place in exocrine part of the pancreas. Nerves and stroma appeared to be resistant to pancreatitis associated damage. Stromal construction put on some limitation to extension of the inflammation. Pancreatic intralobular ducts have shown resistance to inflammation, which has been proportional to their diameter. Langerhans islands also have relative stability to inflammation [9].

Distinguish between infected and sterile pancreatic necrosis is always challenging for clinical practice, therefore, needle aspiration may be required [8, 10].

Pathophysiology of pancreatic acinar cell in pancreatitis

Pancreatic duct obstruction rapidly changes the physiological response of the exocrine pancreas to a Ca^{2+}-signaling pattern that has been associated with premature digestive enzyme activation and the onset of pancreatitis [11]. The pancreatitis starts with Ca^{2+} signal that are generated by stimulation with cholecystokinin (CCK) and acetylcholine. It is known that CCK stimulate also the mitochondria. A single local cytosolic Ca^{2+} last for only a short while and probably a prolonged increase of the spikes are the basis for pathological states leasing to inflammation. Toxic CCK concentration elicts sustained calcium elevations, which induces post-exocytic endocytic vaculoe formation. Trypsin is activated in these vacuoles.
Alcohol induces Ca^{2+} dependent intracellular trypsinogen activation in the apical granular area via non-oxidative metabolites, such as fatty acid ethyl esters and fatty acids [12**]**. Intracellular trypsinogen activation is a crucial initiating event in the development of acute pancreatitis, but the specific organelle in which this process takes place has been unknown [13]. Recent data demonstrate that the Ca^{2+} dependent trypsinogen activation occurs in postexocytotic endocytic vacuoles [12**]**. These vacuoles are acid due to a bafilomycin-sensitive vacuolar H^{+} ATPase and have a very Ca^{2+} permeable membrane. Acid endocytic structures, together with lysosomes, zymogen granules and elements of the endoplasmic reticulum, also play an important role in the physiological Ca^{2+} signal generation that normally regulates enzyme and fluid secretion from the exocrine pancreas [12**]** .

The pathogenic mechanisms underlying acute pancreatitis are involved in two key pathologic acinar cell responses of this disease: vacuole accumulation and trypsinogen activation [14]. An increase in intracellular calcium is the basis for activation of trypsinogen, via a co-localization of enzyms (cathepsin B), inducing the inflammation. There are three ways to die: necrosis, apoptosis and autophagy. Without autophagy there is very little active trypsin, but with autophagy there is shown a lot of cytosolic cathepsin B, as part of the caspace activation. Caerulein stimulation causes caspace 3 activation, just as exogenous cathepsin B causes caspace 3 activation in permeable rat acinar cells [15]. However, heat shock proteins protects against caerulin-induced pancreatitis, and has effects on pancreatic cancer. Heat shock proteins are chaperone proteins that protect living cells against injury-inducing stimuli [16].

Possible strategies for early treatment of acute pancreatitis

A genetic study suggested that polymorphisms in toll-like receptor-4 might affect the risk of developing infections in acute pancreatitis [17]. Studies of chronic pancreatitis have shown that specific neural receptors, transient receptor potential vanilloid subtype 1, mediate pain responses in a model of chronic pancreatitis [18].

The pancreatic zymogen, chymotrypsin C, can degrade pathologically activated trypsin in the acinar cell. Inactivating mutations in chymotrypsin C have been reported to predispose to the development of chronic pancreatitis, especially in those who are prone to alcohol abuse [18]. In the early stage of the inflammation, not only the enzymes changes but some special characters are happened: such as increased permeability (local and/or systemic), nerve stimulation, decreased blood flow, and acid environment.

Acute pancreatitis is a drastically dynamic disease in several organs, including cardiovascular system, pulmonary, renal, pancreatic necrosis or infarction, and gut injury (bacterial translocation). Patients with severe acute pancreatitis typically develop vascular leak syndrome, resulting in hemoconcentration, hypotension, pulmonary edema and renal insufficiency. Angiopoietin-1 and 2 are autocrine peptides that reduce or increase endothelial permeability, respectively. it was concluded that serum angiopoietin-2 levels are strongly associated with severe acute pancreatitis and persistent organ failure. Admission angiopoietin-2 levels accurately predict organ failure [19].

Clinically, gallstone disease is still a common cause of acute pancreatitis. To prevent recurrence of acute pancreatitis, cholecystectomy is recommended after first

episode of gallstone pancreatitis and after two bouts of idiopathic acute pancreatitis. However, cholecystectomy fails to prevent recurrence in acute pancreatitis without gallbladder stones and sludge. These results do not support the recommendation for cholecystectomy in idiopathic pancreatitis [20].

Management of pancreatic necrosis

Sterile pancreatic necrosis is typically managed conservatively without drainage. It may be challenging to distinguish between sterile and infected pancreatic necrosis, and therefore, some study suggested CT-guided fine-needle aspiration as a diagnose of the infected pancreatic necrosis. However, fine-needle aspiration is associated with significant risks, and patients with extensive pancreatic necrosis and low C-reactive protein should be observed. CT-guided fine-needle aspiration is indicated only when there is clinical suspicion of infection and CRP >55 mg/L [21].

Timing for debridement of severe acute pancreatitis may take place in proper demarcation of viable tissues enabling an easier and safer debridement. Severe organ failure within the first week after attack, however, is closely linked to infection making postponing of intervention dangerous.

Surgical intervention consisted of open or laparoscopic surgery. Early surgery was accompanied with relatively small number of specific local complications, including bleeding, intestinal fistulas and pancreatic fistulas [22]. One study compared the results of traditional necrosectomy with minimally invasive procedures. Among 2571 patients, 81 percent were treated conservatively and 19 percent underwent surgery. 183 (38 %) patients underwent traditional necrosectomy. In this series of 162 (33 %) patients with organized fluid collections, had resolution of sepsis without ”open” surgery. Large-bore catheters were placed by percutaneous puncture associated with laparoscopy, or through the extraperitoneal translumbar approach. Hospital and postoperative mortality rate was 6 percent and 33 percent in the group of patients who underwent traditional open surgery and 5 percent and 24 percent respectively in the drainage group [23].

There are two peaks of lethality in acute pancreatitis: the first during the first 7-8 days from the disease onset, connected with early dysfunction of organs; the second peak onsets from the second week of the disease and is connected with infected centre’s of necrosis and liquid clumps [24].

Walled-off necrosis in necrotising pancreatitis is established by a thickened wall without epithelial living between the necrosis and the adjacent surviving tissue. For decompression of this fluid collection, it is recommended to implant at least two 10F drains with nasocysticus drain for continuous lavage. The most common complication is occlusion of the drains with debris. Therefore, lavage to get rid of debris and infected materials is a option, and thorough supplementary treatment with tailored antibiotics and jejunal feeding is mandatory [25].

Pancreatitis-induced inflammatory exudates can get to a spleen immediately. Clinical and radiological changes in the spleen were estimated mostly by computer tomography or ultrasonography. Spleen damages can be categorised as infarct, subcapsular fluid collections, subcapsular hematoma and abscess. The spleen changes in acute pancreatitis are transgent, and thus primary conservative treatment can be the strategy in most patients [26].

Conclusion

Acute pancreatitis is a common disease frequently caused by choledocholithiasis or excess alcohol ingestion. A three category classification of severity of acute pancreatitis were recently designed. The management of acute pancreatitis is frequently challenging, and multidisciplinary approach should be used for the management of the patient with acute pancreatitis.

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