

Pancreas Injury in Shock

Kovács Judit¹, Jung J², Gurzu Simona², Azamfirei L¹, Copotoiu Sanda-Maria¹, Copotoiu Ruxandra¹, Szederjesi J¹

¹ Department of Anesthesia and Intensive Care, University of Medicine and Pharmacy, Tîrgu Mureş, Romania

² Department of Morphotology, University of Medicine and Pharmacy, Tîrgu Mureş, Romania

Background: The causes of acute pancreatitis are well known, and although enzymatic injury is the main factor in its development, pancreatic ischemia due to profound hypoperfusion in cardiogenic or hypovolemic shock patients can be an important etiological factor. The aim of our study was to analyse the histological alterations of the pancreas in patients dying after shock, to study the presence and severity of pancreatic injury.

Material and methods: We studied the morphological alteration of the pancreas, in patients who died after cardiogenic or hypovolemic shock, hospitalized in intensive care units in the County Emergency Hospital Tîrgu Mureş, between 2007–2009.

Results: We examined the structure of the pancreas of 117 patients, 20 showed acute hemorrhagic pancreatic necrosis on autopsy. None of the patients showed typical clinical and laboratory signs for acute pancreatitis. The common findings in these patients were prolonged and severe hypotension, leucocytosis, hyperglycemia and hypocalcemia.

Conclusions: Pancreatitis can occur in patients with shock, due to ischemic injury of the pancreas. It is difficult to diagnose it because clinical signs are altered by the severity of the underlying disease or by analgo-sedation commonly used in intensive care units. We therefore recommend to consider the possible development of acute pancreatitis in patients with shock, in patients with prolonged hypotension, leucocytosis, hypocalcemia, even in the absence of characteristic clinical symptoms and hyperamylasemia.

Keywords: necrotising pancreatitis, hypoperfusion, inflammation, analgo-sedation

Introduction

The pancreas with its microvascular structure is highly vulnerable to ischemic injury. Warsaw and O'Hara observed the alteration of pancreas structure in patients dying after hypovolemic shock [1]. Other authors [2] described the presence of pancreatic injuries in patients who had experienced severe and prolonged hypotension. In experimental studies Reilly et al. demonstrated the role of renin-angiotensin in selective pancreatic vasoconstriction in cardiogenic shock, leading to pancreatic ischemia [3]. These data suggest that circulatory shock, due to severe splanchnic hypoperfusion could be an important cause of acute pancreatitis.

The aim of our study was to examine the presence and severity of pancreatic injury in patients who died after cardiogenic and hypovolemic shock. We also analyse the correlation between the severity of pancreatic lesions and the clinical and paraclinical signs, the need for vasoconstrictor agents, in order to determine some parameters which could predict the development of acute pancreatitis in patients with shock.

Material and methods

We reviewed the autopsy cases of patients who died after cardiogenic or hypovolemic shock, who were admitted to the intensive care unit of the County Emergency Hospital Tîrgu Mureş, between 2007–2009, and we studied the morphological and histological alterations of the pancreas. The pieces collected were stained with hematoxylin-eosin. In patients with pancreatic injury we reviewed the hospital records to assess the clinical signs and laboratory findings.

Results

In the studied interval there were 117 cases autopsied after cardiogenic or hypovolemic shock. In 20 cases we found

acute hemorrhagic pancreatic necrosis on autopsy. On histological studies we observed necrosis of the pancreas and peripancreatic tissue (figures 1 and 2).

The mean age of patients with acute pancreatitis was 59.64 ± 16.7 years (ranging from 1.7 to 78 years), 9 were female and 11 male. Fourteen patients had cardiogenic shock after acute myocardial infarction (4), pericardial tamponade (1) or open heart surgery (9), and 6 died after hemorrhagic shock caused by upper gastro-intestinal bleeding (4) and ruptured aortic aneurysm (2).

None of the patients were diagnosed with acute pancreatitis during life, due to the absence of characteristic symptoms. The digestive complaints were diffuse abdominal pain, signs of mild ileus and in some cases upper gastro-intestinal bleeding, caused by erosive gastritis (demonstrated and treated by gastroscopy) (Table I). Some patients complained of nausea and vomiting, but most of them had nasogastric tube with continuous suction, which could relieve these symptoms.

Eight patients had fever above 38°C . Other clinical signs were connected to shock, postoperative state or other organ dysfunctions, which developed during the admission period. Sixteen patients had associated acute kidney injury with oliguria and elevated serum urea and creatinine, 7 patients presented clinical, laboratory and radiological signs

Table I. Gastrointestinal symptoms in patients with acute pancreatitis

Gastrointestinal symptoms	Nr. of patients
Diffuse abdominal pain	8
Upper abdominal bleeding (erosive gastritis on gastroscopy)	8
Ileus	7
Nausea, vomiting	6

Table II. Laboratory findings in patients with acute pancreatitis

Laboratory findings	No. of patients	Mean values	Range
Serum amylase (U/L)	10	152±29.9	123–216
Glycemia (mg/dL)	20	241± 54.36	151–321
Nr. leucocytes (/mm ³)	20	16,463± 3278	11,300–23,450
Ionized calcium (mg/dL)	18	0.98± 0.13	0.8–1.2
LDH (UI)	17	1121±820	325–3250
CK (UI)	17	389.5±370	95–1221
GOT (UI)	13	312±263.8	56–712
GPT (UI)	13	516.2±315.4	78–1126

of acute respiratory distress syndrome (ARDS), 7 developed bronchopneumonia and in 3 patients disseminated intravascular coagulopathy was noted. Neurological dysfunction could not be evaluated in all patients, because 10 were on continuous perfusion with analgo-sedatives, the others received intermittent boluses.

Laboratory findings were not conclusive (Table II). Most of the patients had hyperglycemia, hypocalcemia and leucocytosis. Serum amylase was ordered only in a few patients because of the absence of clinical signs suggestive for acute pancreatitis, and showed only a mild elevation. Transaminase level (GOT, GPT), lactate dehydrogenase (LDH) and creatinine kinase (CK) were elevated in almost all patients.

In 4 patients hemodynamic stabilization was achieved with volume resuscitation, 2 patients could be stabilized with a combination of inotropics (dobutamine, dopamine), 14 patients received high doses of inotropics associated with epinephrine, in vasoconstrictor doses, in 6 cases norepinephrine had to be associated.

Discussions

Acute pancreatitis is difficult to diagnose in patients with shock, due to their severe clinical condition, the analgesia/analgo-sedation needed for pain relief and to tolerate mechanical ventilation, and the daily interruption of sedation

wasn't long enough to allow the recurrence of pain. Moreover, the morphine used to relieve pain, could potentially worsen the pancreatic injury because it causes spasm of the sphincter of Oddi [4]. The unspecific abdominal pain and the other gastro-intestinal symptoms can occur after surgery, anesthetics, enteral feeding, and in the absence of reliable biochemical markers, acute pancreatitis could not be suspected.

Signs of systemic inflammatory syndrome were present in 8 patients, but they are common after a major surgical intervention and in shock, due to activation of inflammatory mediators in response to tissue hypoxia or mechanical injury [5,6,7].

In acute pancreatitis serum amylase rises within 6–12 hours after the onset of injury and is rapidly cleared from the blood [8], so if it is measured later in the course of the pancreatitis, it could be normal, even in the presence of acute pancreatitis. The sensitivity and specificity of serum amylase for detecting acute pancreatitis is low, because it can be elevated in trauma cases, in renal failure or intestinal diseases [8]. In patients with shock, due to the increased level of lactic acid, hyperamylasemia can be caused by the elevation of salivary isoamylase [9].

In acute pancreatitis leucocytosis, hyperglycemia and hypocalcemia are usually present and they have prognostic values [10]. Leucocytosis indicates a severe inflammation in response to tissue necrosis. Hypocalcemia is due to Ca "soap" formation, secondary to excessive free fatty acids generation by pancreatic lipase [11]. These laboratory findings were present in all of our patients who developed necrotising pancreatitis. Hirano et al. demonstrated that in acute pancreatitis there is an impaired hepatic metabolism, related to increased hepatic lysosomal and mitochondrial fragility caused by proteases derived from the pancreas [12], so elevation of serum transaminases could reflect liver dysfunction caused directly by acute pancreatitis, but also by hepatic ischemia from shock.

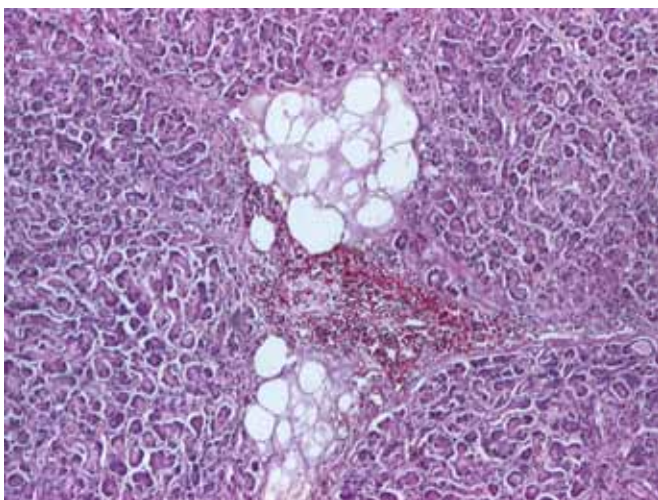


Fig. 1. Focal pancreatic necrosis and areas of hemorrhage seen in the pancreas of a 46 year old patient with aortic dissection (HE, ob. 4x)

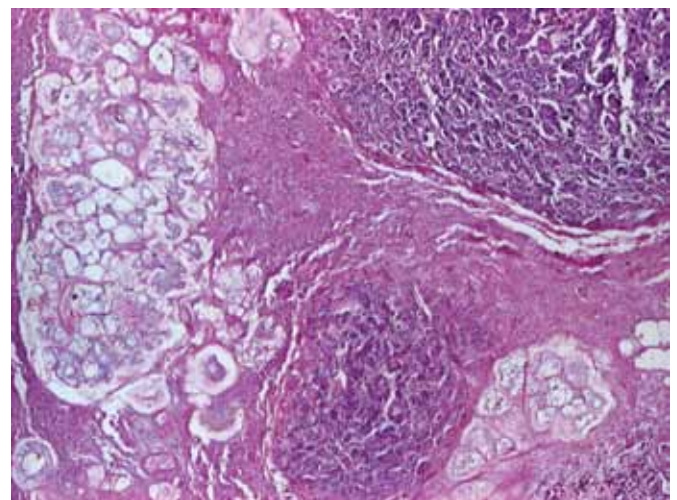


Fig. 2. Inflammatory infiltrates rich in neutrophils around pancreatic steatonecrosis, after correction of congenital heart disease in a 1.7 year old girl (HE, ob. 4x)

Abdominal ultrasound could confirm the diagnosis of acute pancreatitis, but in most of our patients the examination was difficult because of bowel gas, that obscured ultrasonographic images. CT-scan is one of the most important tests to diagnose acute pancreatitis and its complications, but our patients couldn't be transported to CT-scan due to their bad condition.

In our study, acute pancreatitis was associated with multiple organ dysfunction (MODS), which can develop after prolonged and severe organ hypoperfusion, and pancreatic injury can be one of its consequences, but MODS can be due to activation of inflammatory response caused by pancreatic cell injury [13].

In all patients severe hypotension due to blood loss or low cardiac output syndrome was common, which could lead to severe splanchnic hypoperfusion and pancreas ischemia. The pancreas is highly susceptible to ischemic injury. This had been demonstrated in experimental studies [14,15] and in clinical settings after hemorrhagic shock [16], in cardiac surgery [17,18], and pancreas transplantation [19]. The use of vasoconstrictor agents to maintain blood pressure can alter the already existent ischemic pancreatic injury [20].

Ischemic injury to the pancreas was observed in patients after open heart surgery. During cardiopulmonary bypass splanchnic hypoperfusion can lead to pancreas ischemia [20]. Other authors suggested that the systemic inflammatory response activated by cardiopulmonary bypass has the ability to induce endothelial dysfunction, increasing vasomotor tone in the splanchnic territory, causing pancreatic ischemia [21]. Aortic dissection can cause ischemic injury when the emergence of mesenteric vessels is involved or can lead to severe hypoperfusion in case of rupture of the aortic wall into the pericardial, pleural or retroperitoneal space.

Conclusions

Acute pancreatitis can develop in patients with shock, due to hypoperfusion and inflammatory mediator activation. Once present, may alter the prognosis of these patients. It is difficult to recognise it, because clinical and paraclinical findings are often altered by the underlying disease or because of analgo-sedation commonly used in intensive care. We found that the most constant signs in our patients were prolonged hypotension, leucocytosis, hyperglycemia and hypocalcemia, and severe pancreas necrosis was present even in the absence of hyperamylasemia.

Early recognition and intervention in acute pancreatitis is essential for improving outcome, therefore we recommend to consider the possible development of pancreatitis in patients with shock, for prompt and efficient treatment.

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