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Abstract: Acute pancreatitis is an inflammatory disease of the pancreas. Pancreatic necrosis is the most severe local complication because it is frequently associated with pancreatic infections. Alcohol abuse is the second most frequent cause of acute pancreatitis. Ethanol directly sensitis es acinar cells to cholecystokinin stimulations. Acute pancreatitis develops in 10% of chronic alcohol abusers. Two cases are illustrative for the association of chronic alcohol abuse and acute pancreatitis with rapid fatal evolution.

Key words: chronic alcohol abuse, acute pancreatitis, death

Acute pancreatitis is an inflammatory disease of the pancreas. Acute abdominal pain is the most common symptom and increased concentration of serum amylase and lipase conform the diagnosis. Pancreatic injury is mild in 80% of patients, who recover without complications [1]. Alcohol abuses the most frequent causes of pancreatitis in adults; alcohol abuse is less frequent in women than in in men [4,7].

The incidence of acute pancreatitis has increased in the past two decades [2,3]. Between 1994 and 2000, the incidence of first-time attack in California, increased from 33 to 44 per 100 000 adults [4], and at present acute pancreatitis accounts for more than 200 000 hospital admissions every year in the USA [5]. Such increase is also seen in European countries. In up to 20% acute pancreatitis is complicated by substantial morbidity and mortality [6]. However, the frequency of severe pancreatitis remained stable over time in the USA [4], and European countries [5].

In California, from 1994 to 2001, about 4% of patients died within 92 days after admission half of whom did so within 14 days [4]. Although controversial, most investigators believe that acute pancreatitis is caused by the unregulated activation of trypsin within pancreatic acinar cells. Enzyme activation within the pancreas leads to the autodigestion of the gland and local inflammation. The main factors that trigger acute disease are pancreatic hyperstimulation (mainly seen in experimental models), gallstones, and alcohol abuse.

Acute pancreatitis arises when intracellular protective mechanisms to prevent trypsinogen activation or reduce trypsin activity are overwhelmed. These protective mechanisms include the synthesis of trypsin as inactive enzyme trypsinogen, autolysis of activated trypsin, enzyme compartmentalisation, synthesis of specific trypsin inhibitors such as serine protease inhibitor Kazal type1 (SPINK1), and low intracellular ionised Ca²⁺ concentrations [1].

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Alter activation of trypsinogen into active trypsin within acinar cells, several enzymes, such as elastase and phospholipase A₂, and the complement and kinin pathways are activated [8]. Additionally, inflammation is initiated with local production of mediators such as interleukin-1 (IL-1), interleukin-6 (IL-6), and interleukin-8 (IL-8) from neutrophils, macrophages, and lymphocytes. Tumour necrosis factor α (TNF-α) is also released by local macrophages within pancreatic tissue and its production correlates with severity of the experimental disease [9]. Anti-inflammatory cytokines, such as interleukin 10 [IL-10] decrease the severity of experimental pancreatitis [10].

**Cases reports**

**Case 1.** A 51-year-old woman was admitted in a hospital in a state of profound coma (GCS 3) after sustaining a severe head injury (accidental fall). The personal history revealed a chronic alcohol abuse. The initial investigations revealed thrombocytopenia, toxic hepatitis, metabolic acidosis. Blood alcohol concentration was 0.35g‰ and urine alcohol concentration 0.40g‰. Four days after admission the patient died. Forensic autopsy evidenced subdural haemorrhages with brain injury, ponto-mezencephalic and right occipital haemorrhages, and right apical fibro-nodular pulmonary tuberculosis. The histopathological examination evidenced an acute haemorrhagic and necrotising pancreatitis (fig. 1, 2).

**Case 2.** A 49-year-old man was hospitalised for severe metabolic acidosis of unknown etiology, hypokalemia, hyponatremia, diabetes mellitus type II, chronic alcohol abuse. An acute pancreatitis was suspected. The patient died after 3 days. The main autopsy findings were obesity gr. I, cardiomegaly (460 g), hepatomegaly (2520 g), splenomegaly (180 g), pancreatic fibrosis, atrophy, and disseminated necrosis foci (acute pancreatitis with citosteatonecrosis and thrombosis) (fig. 3, 4, 5).
Discussion

Pancreatic necrosis is the most severe local complication because it is frequently associated with pancreatic infections. The diffuse or local area of non-viable parenchyma is initially sterile and can become infected by bacteria of gut origin. Mortality in sterile and infected necrosis is 10% and 25%, respectively. Pseudocyst is a collection of pancreatic juice endorsed by a wall of granulation tissue that results from pancreatic duct leakage. Pancreatic abscess consists of a circumscribed collection of pus that arises around a restricted area of pancreatic necrosis [1].

Early diagnosis of severe disease is important because it prompts an aggressive treatment, whereas mild attack might be expected in the absence of severity. Several scoring systems have been used to help to identify patients at risk for adverse outcome, such as the Ranson criteria [13], acute physiology, and chronic health evaluation (APACHE II) [14], and SOFE scores [12]. These scores assess injury in extrapancreatic organs; the greater the number of organ injured, to greater to score. Large variation exists between these scores in the ability to predict severe diseases [15]. During the first week of admission, organ dysfunction usually resolves, whereas worsening of organ dysfunction is associated with high mortality rate [16]. Another important factor that can contribute to severity is obesity [17]. Early CT severity score correlates well with the occurrence of complications, sepsis, mortality rate, and need for admission to intensive care units [18].

Besides markers included in severity score, serum concentrations of additional
mediators on admission, such as C-reactive protein (C-RP), cytokines, phospholipase A2, antiproteinas, and procalcitonin have been correlated with disease development [11,19]. Serum concentrations of the trypsinogen activation peptide (TAP) and anionic trypsinogen-2 might also predict severity [20,21]. In healthy individuals, trypsinogen is cleaved by a duodenal enterokinase into active trypsin and TAP, whereas during acute pancreatitis inappropriate activation of trypsinogen within acinar cells results in systemic release of TAP and trypsin. However, markers other than C-RP are not used in routine clinical practice [1].

Many causes for acute pancreatitis exist, and in 75-85% of patients the cause is easily identified. In developed countries, observations of the common bile duct by stones (38%) and alcohol abuse (36%) are the most frequent causes of acute pancreatitis [22]. Alcohol abuse is the second most frequent cause of acute pancreatitis, but the correlation between alcohol and pancreatitis is not completely understood. In experimental models, Gorelick [23] showed that ethanol directly sensitises acinar cells to cholecystokinin stimulation. Acute pancreatitis developed in 10% of chronic alcohol abusers (>80 g daily intake). The development of pancreatitis is affected by both genetic and environmental factors [24]. Thus, failure to inhibit trypsin activity (gene mutation and absence of function of SPINKA1) or failure to wash active trypsin intro pancreatic ducts (gene mutation with dysfunction of the cystic fibrosis transmembrane conductance regulator gene - CFTR) might promote alcoholic pancreatitis [1, 24].

References