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Introductory Chapter: Current Challenges in the Management of Patients with Acute and Chronic Pancreatitis

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1. Introduction

As part of medical science, pancreatology reflects the level of technological progress and modern achievements in the natural sciences. Over the past five centuries, since A. Vesalius first described the pancreas and its topography, tremendous work has been done to determine the physiological role of the pancreas in the process of digestion, to study the causes and patterns characteristic of pancreatic diseases, and to find the ways of treatment. In this regard, the current challenges in modern pancreatology include the development and implementation of methods for early and accurate diagnosis and selection of the optimal tactics for treating patients with acute and chronic pancreatitis.

2. Acute pancreatitis

Acute pancreatitis is an acute surgical disease of the pancreas, which consists of primary edema or aseptic necrosis of pancreatic parenchyma with the possible infection of the pancreas and retroperitoneal tissue. Acute pancreatitis is one of the most common causes of acute abdomen, ranking third after acute appendicitis and acute cholecystitis. Along with an increase in the number of patients with acute pancreatitis in recent years, there has been a tendency to an increase in the incidence of its destructive forms [1].

Despite the progress achieved in improving the diagnostics of acute pancreatitis, pathogenetically substantiated intensive therapy, antibiotic therapy, and minimally invasive surgical treatment, mortality in acute pancreatitis has remained at the same level over the past decades. Moreover, while the overall mortality is within 3–6%, depending on the fluctuation of destructive pancreatitis incidence, the mortality rate is 15–30% in pancreatic necrosis, is 85% in infected pancreatic necrosis, and reaches 100% in fulminant acute pancreatitis [2].

Currently, the immediate prescription of antibiotics in severe forms of acute pancreatitis is no longer debatable. However, there are still different opinions on the effectiveness of existing methods of delivering antibacterial drugs to the site of pancreatic destruction. The situation is aggravated by the increasing polyresistance of microorganisms to most antimicrobial chemotherapeutic agents [3]. According to modern conception, immune disorders are considered as a factor that largely determines the course of acute pancreatitis, helps maintain the inflammatory

process, and reduces the effectiveness of reparative mechanisms [4]. In this regard, an urgent problem is the early prevention of infection in severe pancreatitis, timely detection and correction of immunological deficiency, and timely diagnosis and treatment of septic complications including systemic inflammatory response, multiple organ failure, and sepsis [5].

At present, some certainty has been achieved in approaches to the management of patients with acute pancreatitis. Nevertheless, one of the most important problems is to choose the tactics of surgical treatment. Mild pancreatitis does not require surgery and quickly disappears after using standard conservative treatment and eliminating the etiological factor. However, in 10–20% of patients, surgeons encounter severe pancreatic necrosis, which is essentially a hypermetabolic syndrome of multiple organ failure. While the questions about the indications and the most favorable time period for surgical treatment are mostly answered in severe pancreatitis, it is still not obvious what the most appropriate techniques and type of surgery are. Along with experience in minimally invasive interventions, it becomes clear that their active implementation does not solve all the problems of acute pancreatitis treatment and requires further research [6].

Thus, the most important objective in improving treatment results in acute pancreatitis is the use of standardized approaches to diagnostics and treatment of various forms of the disease and its complications, taking into account the modern generally accepted international classification [7].

3. Chronic pancreatitis

Chronic pancreatitis is characterized by inflammation of the pancreas, which is replaced by fibrosis and progressing pancreatic tissue destruction. According to the M-ANNHEIM classification, the following etiological causes are involved in the pathogenesis of chronic pancreatitis: alcohol consumption, nicotine consumption, nutrition factors, hereditary factors, efferent duct factors, immunological risk factors, and miscellaneous (tropical chronic pancreatitis, primary hypercalcemia, hyperparathyroidism, hyperlipidemia) [8]. Clinically, at an early stage of the disease, abdominal pain or recurrent episodes of acute pancreatitis usually prevail, whereas, at a late stage, symptoms are associated with exocrine and/or endocrine insufficiency. Consequently, the three main clinical signs of chronic pancreatitis are pain, maldigestion, and diabetes. The incidence is estimated at 2–10/100000 and tends to increase [9]. In addition, there are many patients with characteristic symptoms but with undiagnosed chronic pancreatitis.

Chronic pancreatitis is not only an urgent medical problem but also a significant economic burden that has a profound effect on social life and the structure of employment [10]. In the United States in 2000, there were 327,000 hospitalizations and 532,000 visits to doctors due to chronic pancreatitis, which cost \$2.5 billion [11].

Diagnostics and follow-up of patients with chronic pancreatitis are based on both the clinical picture and imaging methods, and the diagnosis of chronic pancreatitis at an early stage is a clinical problem. Historically, diagnostic methods included ultrasound imaging of the abdominal organs, endoscopic ultrasound (EUS), ultrasound with contrast enhancement (CEUS), endoscopic retrograde cholangiopancreatography (ERCP), magnetic resonance imaging (MRI), and computed tomography (CT). While ultrasound is considered the least accurate, and EUS is one of the most sensitive methods [12], ERCP is no longer a diagnostic test for chronic pancreatitis [13]. EUS is highly accurate in assessing the parenchyma and ductal system of the pancreas and is also very useful in identifying

complication characteristic of chronic pancreatitis [14]. CEUS helps diagnose cystic and solid lesions of the pancreas, which are associated with chronic pancreatitis. It was convincing in 90% of cases, so it may be considered as a first-line method of visualization [15]. MRI makes it possible to accurately determine the morphological and functional changes of the pancreas and is a recognized method for detecting calculi in pancreatic ducts [16]. At the same time, the calcinates may be determined by means of portal-phase contrast-enhanced CT with moderate sensitivity and very high specificity (close to 100%) [17].

The degree of exocrine and endocrine pancreatic insufficiency is also important to determine when diagnosing chronic pancreatitis. The so-called direct or invasive methods for detecting exocrine insufficiency, such as the Lund test, are a thing of the past. Currently, the “gold standard” is 3-day fecal fat quantification and determination of the coefficient of fat absorption. Due to the cumbersomeness and unpleasantness of the method for both patient and laboratory personnel, it is very rarely used in everyday clinical practice. Other methods for diagnosing exocrine pancreatic insufficiency include measuring the concentration of fecal elastase 1, the ^{13}C -mixed triglycerides (^{13}C -MTG) breath test, a test based on analysis of pancreatic juice after secretin/erulein stimulation, and others [18].

In the absence of complications, the main goal of treating chronic pancreatitis is the effective correction of its main manifestations: pain, maldigestion, and diabetes. Abdominal pain is usually severe and often occurs after a meal, which, despite adequate enzyme replacement therapy, leads to malnutrition. Although pain may be associated with strictures and stones in the main pancreatic duct, new investigations have questioned the importance of micro- and macrostructural pathological changes. Currently, the neurogenic causes of pain are widely discussed, which should be taken into account when choosing the method of pain relief for patients [19]. Malnutrition that is related to a lack of enzymes leads not only to weight loss but also to a certain deficiency of vitamins and nutrients that are necessary for normal physiological functioning. Malnutrition in chronic pancreatitis is often overlooked. It is very important that gastroenterologists consider this fact while making a differential diagnosis in patients with weight loss [20]. Diabetes of the exocrine pancreas is a form of diabetes that occurs due to pancreatic disease. It is more common than previously thought. A recent study found that in 1.8% of adults with diabetes, it should be classified as diabetes of the exocrine pancreas. However, in most cases, it is referred to as type 2 diabetes. Patients with diabetes of the exocrine pancreas have varying degrees of exocrine and endocrine dysfunction. Damage to the islets of Langerhans affects the secretion of hormones by the pancreatic polypeptide, β -, and α -cells. Polypeptides and a low concentration of insulin and glucagon promote sharp fluctuations in the glucose level. This form of “fragile diabetes” in patients with diabetes of the exocrine pancreas may lead to worse glycemic control in comparison with type 2 diabetes [21].

If conservative therapy is not effective, it is possible to apply the endoscopic treatment, conduction anesthesia or neurolysis, or surgical techniques. Endoscopic methods are usually required for the elimination of the main pancreatic duct obstruction caused by a stricture or stone. In addition, endoscopy is the first-choice treatment of pancreatic pseudocysts [22]. Celiac plexus block is useful for eliminating pain. It is performed via a gastric approach using EUS guidance and has high success rates and relatively low complication rates [23]. Surgical treatment of chronic pancreatitis is aimed primarily at relieving pain, improving the patient's quality of life, and treating complications. Surgical operations include decompression (drainage) of the main pancreatic duct, various types of pancreatic resections, their combination, and neuroablation [24].

In recent years, important advances have been made in understanding the pathogenesis of chronic pancreatitis. Although the disease is still difficult to treat, the development of new approaches has reduced the severity of clinical manifestations and improved the life quality of patients with chronic pancreatitis.

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