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How to Deal with Infected Pancreatic Necrosis?

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Introduction

Acute pancreatitis is frequently a mild disease. However, about one in every five patients develops a more severe disease with (peri)pancreatic necrosis. Early organ or multiorgan failure develops in severe disease, usually within the first week of onset, due to systemic inflammatory response syndrome. Late development of organ failure is usually due to sepsis secondary to infection of (peri)pancreatic necrosis. Infected necrotizing pancreatitis is therefore one of the most severe complications of acute pancreatitis and one of the greatest therapeutic challenges in this disease.

Infected (peri)pancreatic necrosis was historically considered an indication for early open necrosectomy [1]. However, this approach was associated with a high rate of complications and death. Because of this, prevention of infection of pancreatic necrosis became the main therapeutic aim in acute necrotizing pancreatitis, and prophylactic administration of antibiotics, mainly imipenem, was included as part of the standard of care of these patients [2,3].

Several landmark studies and publications over the last 15 years have led to a dramatic change in the management of patients with acute necrotizing pancreatitis.

- 1) Several double-blind randomized controlled trials and meta-analyses have shown that prophylactic antibiotics are ineffective for preventing severe complications and death in patients with acute necrotizing pancreatitis [4–9].
- 2) Local complications of acute pancreatitis have been redefined based on scientific evidence and consensus among experts in the so-called revised Atlanta classification [10]. Acute fluid collections and pseudocysts, and acute necrotic collections and walled-off necrosis (WON) are clearly defined as local complications of

acute edematous interstitial pancreatitis and acute necrotizing pancreatitis, respectively.

- 3) A minimally invasive step-up surgical approach using percutaneous drainage and laparoscopic or video-assisted retroperitoneal debridement has been shown to be superior to open necrosectomy for the treatment of infected (peri)pancreatic necrosis [11,12].
- 4) Delaying intervention of infected pancreatic necrosis is associated with better outcomes compared with an early approach [13,14]. Therefore, intervention should be delayed as much as possible, at least four weeks from onset of the disease, when WON with mature wall has developed.
- 5) An endoscopic approach has been established as a valid and probably safer alternative to the minimally invasive surgical approach for the step-up treatment of patients with infected (peri)pancreatic necrosis [15–17].

Prevention of Infection of (Peri)pancreatic Necrosis

Intestinal bacterial translocation is generally accepted as the main source of infection of pancreatic necrosis [18]. In fact, intestinal permeability is increased and splanchnic perfusion is impaired in severe acute pancreatitis [19,20]. In addition, the bacteria infecting pancreatic necrosis are mainly of intestinal origin [21]. Since antibiotic prophylaxis has failed to provide any benefit in acute necrotizing pancreatitis [4–9] and because it is definitely not recommended in clinical practice, avoiding intestinal bacterial translocation is the main aim in the prevention of infection of pancreatic necrosis.

Enteral nutrition is one of the pillars in the management of severe acute pancreatitis. This not only provides nutrients to a severely ill patient, but also maintains

intestinal barrier function. Enteral nutrition improves luminal gut nutrition, enhances splanchnic blood flow, and may stimulate enteral motility, thus reducing the risk of intestinal bacterial overgrowth and bacterial translocation [22,23]. This explains, at least partly, why enteral nutrition is superior to parenteral nutrition in patients with severe acute pancreatitis in terms of infection of pancreatic necrosis, septic complications, and death [24,25].

Enteral nutrition can be delivered through a nasogastric or a nasojejunal tube [26,27]. Based on the similar efficacy and safety of both routes, nasogastric feeding is generally preferred as the first step in clinical practice. Nasojejunal feeding is mainly reserved for patients with gastric outflow obstruction and those with intolerance to gastric feeding.

Early initiation of enteral feeding was generally recommended in clinical practice for patients with predicted severe acute pancreatitis. However, recent clinical trials have shown that early feeding is not associated with a reduction in infection, persistent organ failure, or mortality [28,29]. Based on this, enteral feeding can be delayed and given on demand to patients who are unable to tolerate oral refeeding after 72 hours from onset of acute pancreatitis.

Diagnosis of Infected (Peri)pancreatic Necrosis

The presence of fever early in acute pancreatitis is usually secondary to the release of inflammatory mediators. Later, the development of clinical and laboratory markers of sepsis in the absence of any extrapancreatic infection (respiratory, urinary, venous catheter) is the basis for the diagnosis of infected pancreatic necrosis. The presence of gas within the (peri)pancreatic area on computed tomography (CT) confirms the diagnosis (Figure 14.1). In the absence of pancreatic gas bubbles, which occurs in up to 60% of patients [30], fine needle aspiration (FNA) may be required to confirm the diagnosis of infection within the pancreatic necrosis. However, culture of FNA samples produces false-negative results in about 25% of cases and frequently does not modify the therapeutic approach in patients with sepsis [30]. In our center, FNA for culture and antibiotic resistance testing is only performed once drainage of the necrotic collection has been indicated based on clinical, laboratory, and imaging data.

Finally, serum measurements of procalcitonin may be a valuable tool supporting the diagnosis of infected pancreatic necrosis in patients with acute necrotizing pancreatitis and without extrapancreatic infection [31,32].

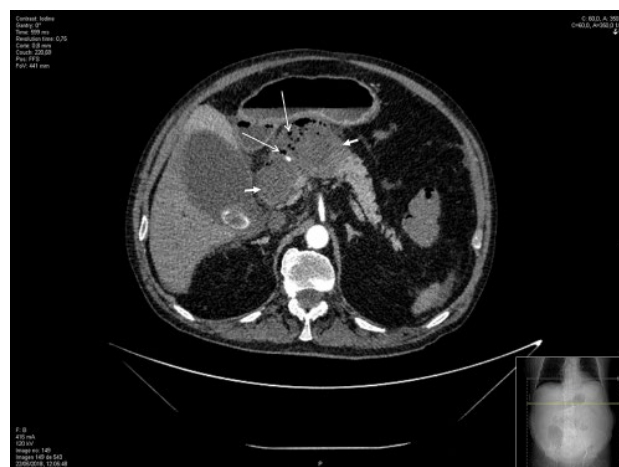


Figure 14.1 CT scan of a patient with walled-off necrosis (short arrows). Presence of gas bubbles indicates the presence of infected (peri)pancreatic necrosis (long arrows). *Source:* courtesy of J.E. Domínguez-Muñoz.

How to Deal with Infected (Peri)pancreatic Necrosis

Infected pancreatic necrosis is associated with a high complication and mortality rate. Optimal management requires a multidisciplinary approach, including at least gastroenterologists, surgeons, interventional radiologists, and specialists in critical care medicine. Based on this approach, patients with severe disease should be transferred to high-volume specialized centers.

Infected pancreatic necrosis is currently managed following a minimally invasive step-up approach. This approach is based on the stepwise use of (i) systemic antibiotics, (ii) endoscopic or percutaneous drainage, and (iii) endoscopic or percutaneous minimally invasive necrosectomy.

Systemic Antibiotics

Intravenous antibiotics, usually carbapenems, are the first step in the treatment of infected pancreatic necrosis. Antifungal agents are not consistently recommended. About 15–30% of patients respond well to this conservative approach and do not require any invasive intervention [33,34]. How long antibiotic therapy should be maintained is an open question that should be evaluated in each individual patient. If clinical and laboratory markers of sepsis do not improve after 48–72 hours of antibiotic therapy, infected WON should be drained.

Endoscopic or Percutaneous Drainage

Pancreatic drainage should be avoided in the early phase of the disease (first two weeks) and should be optimally



Figure 14.2 CT scan of a patient with infected walled-off necrosis after placement of a transgastric lumen apposing metal stent (short arrows) and a 7 Fr tube deep in the collection for local antibiotic infusion (long arrows). *Source:* courtesy of J.E. Domínguez-Muñoz.

delayed for four weeks when a mature wall has developed. Drainage of infected WON is effective in 35–70% of cases without the need for an additional necrosectomy [11,17].

Drainage of infected necrosis can be performed either endoscopically (endoscopic ultrasound guided) or percutaneously (CT guided). If drainage fails to treat infected necrosis, endoscopic drainage is followed by endoscopic necrosectomy, and percutaneous drainage is followed by laparoscopic necrosectomy according to the step-up approach. Both approaches have been shown to be equally effective in terms of major complications or death, although the endoscopic approach is associated with less pancreatic fistulas and shorter hospital stay [17].

Based on a previously reported theoretical approach to local infusion of antibiotics for infected pancreatic necrosis [21], we have recently developed a protocol that combines local antibiotic therapy delivered via a single-pigtail 7–8.5 Fr naso-cystic tube with systemic antibiotics and endoscopic drainage for infected WON (Figure 14.2). This method may reduce the need for necrosectomy by increasing the antibiotic concentration in the necrotic tissue. The efficacy of this approach should be tested in randomized controlled trials.

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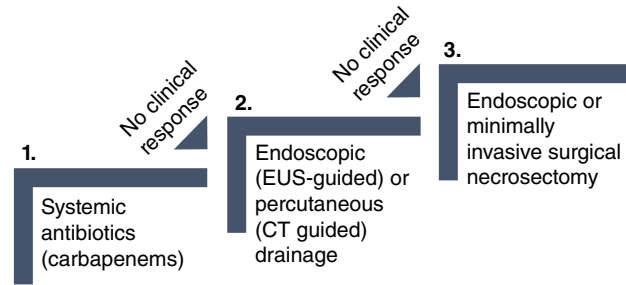


Figure 14.3 Step-up approach for the management of infected pancreatic necrosis. EUS, endoscopic ultrasound.

Although evidence favoring either metal or plastic stents for EUS-guided endoscopic drainage of infected WON is lacking [35], lumen apposing metal stents (LAMS) are generally preferred in order to facilitate endoscopic necrosectomy if needed [36]. LAMS should be removed as soon as the collection resolves in order to minimize the risk of complications, mainly bleeding, migration, and stent occlusion [37].

Together with anatomical factors (location and extent of the necrosis), the decision about whether to drain infected WON endoscopically or percutaneously should be based on clinical expertise. In addition, the combination of percutaneous and endoscopic drainage should be considered for patients with WON that extends into the paracolic gutters and pelvis [36].

Endoscopic or Laparoscopic Necrosectomy

Endoscopic and minimally invasive surgical necrosectomy are safe procedures even in high-risk patients, and significantly safer than open necrosectomy [15]. As previously stated, selection of the endoscopic or minimally invasive surgical approach depends on anatomical features of WON and on clinical expertise. Both endoscopic and minimally invasive surgical procedures are extensively discussed in the following two chapters of this book. Independently of this, patients with infected WON who require any invasive intervention should be managed in high-volume expert centers after a multidisciplinary evaluation. Figure 14.3 summarizes the step-up approach to patients with infected pancreatic necrosis.

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