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The Evolving Management of Infected Pancreatic Necrosis

GRAHAM DONALD, M.D., TIMOTHY DONAHUE, M.D., HOWARD A. REBER, M.D., and O. JOE HINES, M.D.

Department of Surgery, David Geffen School of Medicine at UCLA, Los Angeles, California

Abstract

Management of infected pancreatic necrosis (IPN) has for decades been based on early operative débridement. This approach is associated with mortality rates as high as 58 per cent. Recently, the care of these patients has evolved and emphasizes delayed operation and early intervention with percutaneous drainage. In 2002, we began to incorporate these new principles for the treatment of IPN and herein characterize the recent UCLA experience with management of IPN. A retrospective review of patients with IPN treated at UCLA between 2002 and 2011 was conducted. Mean patient age was 53.4 years. Mean Ranson's score was 3.3 ± 2.3 and average number of concurrent comorbidities 3.2 ± 2.5 . All patients were treated with intravenous antibiotics. Thirteen of 18 patients (72.2%) had percutaneous drainage catheters placed (mean 1.1 drains per patient). Two patients were treated with percutaneous drainage alone. Sixteen of 18 (88.9%) eventually underwent surgical débridement. Of the operative patients, mean time from diagnosis to surgery was 28.4 days. The mortality in this group was 16.7 per cent. In conclusion, antibiotics and percutaneous drainage is an acceptable and possibly preferable initial therapeutic strategy for patients with IPN. Delayed operation and early intervention with percutaneous drainage appears to improve mortality for these patients.

Acute pancreatitis is a common medical and surgical disease with the overall incidence ranging from 4.5 to 35 per 100,000 people.¹ The disease can be classified into two categories based on severity.² Mild acute pancreatitis generally has few complications and can be treated by withholding oral intake and implementing resuscitative measures until symptoms and laboratory values normalize. Mild and moderate cases of acute pancreatitis have a mortality rate of approximately 3 per cent. Severe acute pancreatitis, however, which occurs in approximately 20 per cent of cases, can lead to a pancreatic necrosis, systemic inflammatory response, multiorgan failure, and death in a significant portion of patients.³ A recent review cited the mortality for sterile and infected necrosis to be 12 and 30 per cent, respectively.⁴

Traditionally, the gold standard treatment for the most severe cases of pancreatitis, namely those in which the inflammation has progressed to the point at which the pancreatic parenchyma undergoes necrosis with subsequent infection, has been open necrosectomy to débride the nonviable, infected tissue with closed drainage.⁵ Although reports vary, this is a highly morbid operation with complication and mortality rates as high as 92 and 58 per cent, respectively.^{6,7} Recent clinical trials, however, have challenged this paradigm and have advocated for a "step-up" approach in managing infected pancreatic necrosis with favorable results.^{8,9} The premise behind the step-up approach is to avoid the morbidity and

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Address correspondence and reprint requests to O. Joe Hines, M.D., Department of Surgery, UCLA School of Medicine, 10833 Le Conte Avenue, Los Angeles, CA 90095-6904. joehines@mednet.ucla.edu.

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complications that follow an open pancreatic débridement and instead initially manage patients by more minimally invasive means, namely percutaneous or endoscopic drainage, or through video-assisted or laparoscopic drainage with the goal of controlling the infection.

We sought to characterize the experience at our institution in regard to the evolving management of the disease and the effect of this evolution on overall mortality.

Methods

Patient Selection

One hundred nine consecutive patients between 2002 and 2011 evaluated by the surgical service for pancreatitis with suspicion for infected necrosis were retrospectively reviewed. Inclusion criteria included 1) the presence of gas on computed tomography in the setting of a portion of hypo-enhancing pancreas (Fig. 1); or 2) positive pancreatic cultures from the first intervention (drainage or surgery) in the setting of a hypo-enhancing pancreas on imaging. Exclusion criteria included: 1) chronic pancreatitis; 2) a pseudocyst that subsequently grew a positive culture; 3) radiographic evidence of pancreatic necrosis without positive cultures or gas on imaging; and 4) prior exploratory laparotomy for pancreatic necrosis at our institution or at an outside hospital.

Study Oversight

The Institutional Review Board at UCLA granted approval for review of our department's surgical database with a waiver for informed consent.

Comorbidities

Comorbidities included coronary artery disease, chronic obstructive pulmonary disease, chronic kidney disease, obesity, smoking, diabetes mellitus, structural heart disease, autoimmune disorders, inflammatory bowel disease, and history of stroke or myocardial infarction. One patient was had received a prior kidney transplantation.

Computed Tomography

A computed tomography (CT) scan of the abdomen and pelvis after a pancreatic protocol was performed on a Siemens 64 multirow-detector scanner. Non-contrast 5-mm axial images through the abdomen were obtained. After the intravenous injection of 120 mL of Omnipaque 350, 2- to 3-mm axial images through the abdomen were obtained during pancreatic phase and 5-mm axial images through the abdomen and pelvis were obtained during the venous phase. Coronal and sagittal reformations were performed.

Percutaneous Drainage

Drainage was performed under CT or ultrasound guidance by an experienced radiologist. The decision to perform one-time drainage *versus* placement of an indwelling catheter for longer-term drainage as well as the number of drainage tubes was made in consultation between the surgeon and radiologist. Cultures were sent from the drain fluid.

Surgery

Surgery was indicated in cases in which the patient was unstable at initial presentation or became unstable or failed to clinically improve after initial attempts at drainage. Open laparotomy was performed through a midline or chevron incision. Necrosectomy and lavage were carried out. The one laparoscopic procedure was performed with one optical trocar and three working trocars. Large-bore drains were placed in each surgical procedure. The drains were irrigated postoperatively with saline twice daily.

Statistical Analysis

Descriptive statistics were applied to all demographic data including comorbidities as well as to number of drainage procedures, time to surgery from initial presentation, complications including hemodialysis and mechanical ventilation, use of antibiotics, presence of positive pancreatic fluid culture, and length of stay. Ranson's criteria were collected as defined at initial presentation to a hospital (whether it be to our own or an outside hospital) and 48 hours thereafter. The primary end point was mortality with secondary end points being organ failure as judged by the need for hemodialysis at any time during their hospitalization or mechanical ventilation for greater than 24 hours.

Results

Baseline patient characteristics are summarized in Table 1. Eighteen patients, 13 men and five women, were chosen who met criteria for infected pancreatic necrosis. Mean age of participants was 53.4 years. Thirteen patients were transferred from an outside hospital to our own institution for a higher level of care (72.2%). Mean Ranson's score and number of comorbidities were 3.3 ± 2.3 and 3.2 ± 2.5 , respectively. The etiology of each patient's pancreatitis differed with one resulting from alcohol (5.6%), nine resulting from gallstones (50%), two resulting from hypertriglyceridemia (11.1%), and six classified as idiopathic pancreatitis (33.3%).

Results are summarized in Table 2. Thirteen of 19 patients (72.2%) had percutaneous drainage procedures (mean, 1.1 per patient; range, 0 to 4). Sixteen (88.9%) eventually underwent surgical intervention (15 open, one laparoscopic débridements). The mean number of surgeries in the operative group was 1.3 (range, 1 to 4) with one patient having four separate débridements and two patients each having two operations. Of the operative patients, mean time from admission to surgery was 28.4 days (range, 1 to 86 days). Mean time from admission to drainage and from drainage to surgery were 16.2 days (range, 0 to 45 days) and 19.6 days (range, 1 to 75 days), respectively. Mean length of stay was 67.8 ± 38.5 days.

Two patients had percutaneous drainage alone with three and four separate drainage procedures, respectively. One of those patients was discharged home without complications, and the other patient died. Overall mortality irrespective of management was 16.7 per cent with three patients dying.

With regard to complications, 12 of 18 patients required mechanical ventilation (66.6%) and six of 18 patients required hemodialysis (33.3%). Six patients required both forms of support (33.3%).

Seventeen of 18 patients had positive cultures (94.4%) with the most common culture being *Enterococcus* (seven of 18 patients). Five patients grew *Candida*, three grew *Enterobacter*, two grew *Escherichia coli*, and two grew *Klebsiella*. All patients received intravenous antibiotics with imipenem as the most common antibiotic used.

Conclusions

Open débridement of infected pancreatic necrosis is associated with a high mortality and complication rates. These patients are often on the brink or already have a significant systemic inflammatory response and some demonstrate organ failure. It has been theorized that the laparotomy in these settings induces an even more profound systemic inflammatory response as the result of the infected, necrotic tissue débridement.¹⁰ Even patients who appear stable preoperatively can quickly deteriorate during and after the procedure.

Although we ultimately operated on most of our patients with confirmed infected pancreatic necrosis, we delayed surgical intervention in our operative group for an average of 28.4 days by implementing early percutaneous drainage. Rodriguez et al.¹¹ recently described a series of 167 consecutive patients with infected pancreatic necrosis treated with open necrosectomy. They reported a significantly higher mortality rate in patients operated on before 28 days as compared with those undergoing operation after the 28-day mark (20.3 vs 5.1%; $P = 0.002$). This underscores the importance of delaying definitive surgical treatment for as long as possible while administering aggressive medical care in an intensive care unit setting.¹² Approaching our patients in this delayed fashion resulted in a lower mortality rate than historical reports and this included a population of patients who was very ill as judged by the number of comorbidities and Ranson scores.

An important randomized clinical trial recently conducted by the Dutch Pancreatitis Study Group further bolsters the case for early drainage.⁸ They randomized 88 patients into either an open necrosectomy group or a “step-up” group. This latter group underwent percutaneous drainage with escalation of care if the patients did not improve to minimally invasive laparoscopic retroperitoneal débridement. They found that complications were far less in the “step-up” group, whereas mortality was no different. Importantly, 35 per cent of patients were treated with percutaneous drainage alone. Prior studies have also demonstrated that it is possible to manage these patients with drainage alone, albeit with less sick patient populations.¹³ Our series comprised particularly sick patients with an mean Ranson score above 3, possibly explaining the need for more frequent operative strategies.

Our treatment algorithm is summarized in Figure 2. When presented with a patient with severe acute pancreatitis, CT should be obtained to judge whether there is an infected fluid collection. If there is no evidence of infection (i.e., sterile necrosis), continued medical management is recommended. If there is radiographic evidence of infection, and the patient is stable, percutaneous drainage should be attempted. If there is no clinical improvement after drainage, repeat imaging should be obtained to assess for any fluid collections not drained, at which point the decision to repeat drainage procedures or not can be made. If at any point along the decision tree the patient becomes unstable, prompt surgical intervention should be undertaken. Whether that surgical intervention is laparoscopic débridement, video-assisted retroperitoneal débridement, or open surgical débridement is dependent on the experience and comfort level of the consulting surgeon.

The number of patients in this study was limited, and this resulted in a lack of separation between a significant operative and nonoperative group. Although far more than 18 patients were evaluated by the surgical service for severe pancreatitis with necrotic features during the study period, our inclusion criteria for infected pancreatic necrosis were stringent. Although many other studies evaluating management of infected pancreatic necrosis include patients in whom infection of pancreatic tissue was not proven but merely clinically suspected, and thus possibly included many patients with sterile necrosis, we elected to only include those with a positive culture or gas on CT scan. In fact, 17 of 18 patients had positive cultures in our study. The one patient without a positive culture demonstrated gas in the necrotic pancreas on CT. The reason for our strict criteria was that sterile necrosis, even in the setting of severe acute pancreatitis, has a different prognosis than infected necrosis and the treatment algorithm branches between those two entities. Furthermore, we excluded many patients who had encapsulated pseudocysts that subsequently became infected, a problem for which we are routinely called to evaluate. It was our belief that this disease process is entirely different than a case of severe acute pancreatitis with a systemic inflammatory response and organ failure that frequently happens in infected necrosis and to include the patients with infected pseudocysts would give falsely low rates of mortality.

Although infected pancreatic necrosis remains highly lethal, the evolving management of disease toward early drainage and delay of surgery is helping to lower mortality rates and improve outcomes for our patients. What is traditionally a surgical disease has become one in which aggressive critical care and minimally invasive drainage procedures are proving to be preferable and in the best interest of the patient. More randomized controlled trials need to be conducted to further solidify this management strategy as the standard of care in the treatment of infected pancreatic necrosis.

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Fig. 1.
Infected pancreatic necrosis. Gas bubbles are present within the hypo-enhancing, necrotic body of the pancreas.

Fig. 2.
Treatment algorithm.

Table 1

Baseline Patient Characteristics

Characteristic	n = 18
Age (years)	53.4 ± 18.7
Male (%)	13 (72.2)
Etiology	
Alcohol	1/18 (5.6)
Gallstones	9/18 (50)
Hypertriglyceridemia	2/18 (11.1)
Idiopathic	6/18 (33.3)
Comorbidities	3.3 ± 2.5
Ranson score	3.2 ± 2.3
Antibiotics (%)	18/18 (100)
Transfer from outside facility (%)	13/18 (72.2)

Table 2**Results Summary**

Outcome	Patients
Operations (%)	16/18 (88.9)
Open necrosectomy	15
Laparoscopic necrosectomy	1
Mortality (%)	3/18 (16.7)
Organ failure (%)	
Hemodialysis	6/18 (33.3)
Mechanical ventilation	12/18 (66.6)
Both	6/18 (33.3)
Positive culture (%)	17/18 (94.4)
Length of stay (days)	67.8 ± 38.5
Admission to surgery, operative (days)	28.4
Drainage (%)	13/18 (72.2)
Number of drainages	
0	5
1	9
2	2
3	1
4	1