Infected necrosis complicating acute pancreatitis: experience with 131 cases

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**Objective:** Despite advances in its management, the mortality of infected pancreatic necrosis (IPN) remains high. We report our observations on complications and treatment of IPN. **Methods:** We studied 131 patients with IPN seen over a 20-year period. Infection, suspected clinically, was proved by presence of extraluminal air on CT scan (23 cases), or by guided percutaneous aspiration of fluid or solid necrotic tissue, and bacteriological studies of the aspirate. Apart from organ support, vigorous nutritional support and appropriate antibiotic therapy were instituted. Evacuation of pus and surgical necrosectomy was done. Feeding jejunostomy was done in the majority of patients. **Results:** Postoperative complications included multiple organ dysfunction syndrome (MODS; n=40, in addition to 65 with pre-operative MODS), pancreatic fistula (69), gastrointestinal fistula (24), and severe extra-intestinal bleeding (8 patients). Pancreatic fistula developed in 30 of 63 patients who received octreotide and in 39 of 68 patients who did not (p=ns). Forty-five patients died. Of 35 patients who underwent surgery within 15 days of the onset of acute necrotizing pancreatitis, 21 (60%) died; in comparison, of the 96 patients who underwent surgery more than 15 days after onset, 24 (25%) died (p<0.002). Mortality was higher among those with serum albumin less than 2.5 g/dl than in those with albumin above 2.5 g/dl (20/36 versus 25/95; p=0.002), and in those with MODS (43/105) than in those without (2/26; p=0.001). **Conclusions:** Complications of IPN include MODS (pre- or post-operative), gastrointestinal and pancreatic fistula, and extra-intestinal bleeding. Serum albumin below 2.5 g/dl, development of MODS and need for early surgery appear to be unfavorable features associated with higher mortality. [Indian J Gastroenterol 2003;22:7-10]

**Key words:** Albumin, gastrointestinal bleed, multiple organ dysfunction syndrome, octreotide, pancreatic fistula

Acut necrotizing pancreatitis constitutes approximately 20% of patients with acute pancreatitis, and is associated with a very high mortality, especially if infection develops. We report our data on 131 patients with infected pancreatic necrosis (IPN) seen over the last 20 years.

**Methods**

We analyzed the data of 131 patients (101 men) with IPN complicating acute pancreatitis, managed between 1982 and 2001. Twenty-four patients with pancreatic abscess, defined as an intra-abdominal collection of pus at least 4 weeks after the episode of acute pancreatitis, managed during the same period were excluded.

A majority of patients (n=100) were aged 31-50 years; 11 patients were >60 years. The two common etiological factors were biliary stones (50) and ethanol (52). Four patients developed pancreatitis after ERCP. In two patients each, primary hyperparathyroidism and derangement of lipid profile were present. In 23 patients, no cause could be found.

Ultrasonography (USG) of abdomen was carried out on admission. Contrast-enhanced computed tomography (CECT) was performed 5-10 days after the onset of pancreatitis.

All patients with IPN were treated in an ICU. Fluids (and, if needed, inotropic drugs) were administered according to urine output and central venous pressure measurement or, where indicated, pulmonary artery pressure measurement. Total parenteral nutrition was instituted in all patients as soon as hemodynamic, pulmonary and respiratory stability was established: lipids were administered and serum triglycerides were monitored. Human albumin (20%, 100 mL) was administered for 3-4 days if serum albumin was lower than 2.0 g/dl. In 12 of 22 patients treated during the last 5 years, nasogastrodudenoejunal tube was inserted under radiologic control for feeding as soon as peristalsis returned.

Antibiotics were routinely administered. In the earlier years, i.e., till 1995, the initial antibiotic cover was with a quinolone or third-generation cephalosporin and metronidazole, but later imipenem has been used as the initial antibiotic whenever the patient could afford it. Treatment for organ dysfunction was administered as required. Management of patients with small intestinal fistula depended on individual circumstances. The criteria for diagnosis of pancreatic fistula (PF) was ≥50 mL.
of drainage per day and amylase content of drain fluid of ≥5000 IU per mL.

In 65 patients, dysfunction in two or more organs (multiple organ dysfunction syndrome; MODS) was found prior to surgery for infection: this included lung dysfunction in 65 patients, renal dysfunction in 55, coagulopathy in 15, hepatopathy in 12, and myocardial dysfunction in three.

**Diagnosis of IPN**

Infection was suspected whenever the clinical picture deteriorated or did not improve in spite of vigorous treatment and / or the size and tenderness of a palpable abdominal lump increased. Infection was confirmed by: (1) bacteriologic examination of fluid aspirated percutaneously under USG guidance (24 patients, prior to 1986 when CT was not available); (2) presence of extraluminal air on CECT scan (23 patients, after 1986); (3) bacteriologic examination of aspirate from fluid or solid necrotic tissue obtained under CECT guidance (80 patients).

Aspiration was done from three locations to minimize sampling error. If the initial aspirate was negative for infection and clinical condition did not improve with medical treatment, diagnostic aspiration was repeated four to seven days later.

**Treatment of IPN**

Conventional trans-celiac surgical exploration of the pancreatic and peripancreatic regions was done as soon as possible after the diagnosis of IPN was reached. However, in 11 patients seen during the last 4 years, surgery was delayed as much as possible, provided toxemia and MODS were not severe. During this period, fluid and necrotic material were drained using multiple (10 to 12 F) pigtail drains.

A rooftop or Chevron incision (or bilateral Kocher's incision) was made. A near-total necrectomy using fingers was carried out, total excision being impossible because of dense adhesions between necrosed tissue and vital structures. As much of the pus and fluid as possible was drained out. Following this, in all except six patients, the peritoneum and abdominal muscles were sutured primarily, with drainage of the peritoneal cavity by three to six multiholed, wide-bored (32 or 36 F) Portex tubes (SIMS Portex; Hythe, England). Feeding jejunostomy was done in all patients except the 12 patients in whom a nasojejunal tube had been placed prior to surgery. Open laparostoma (i.e., open packing) was carried out in two patients, and the peritoneum was temporarily closed by polypropylene mesh or polytetrafluoroethylene patch in two patients each; these six patients needed early and repeated surgery (within 24-72 hours).

All patients were mechanically ventilated in the early postoperative period. The preoperative antibiotics were continued. Fluconazole was used wherever fungal infection was proved by culture of pus, necrosed tissue or blood, or empirically in severely ill patients with inadequate clinical response to other measures. Total parenteral nutrition (TPN) was resumed within 24-48 hours as soon as hemodynamic and renal stability was achieved. Jejunostomy feeds were commenced by the 3rd to 6th day when intestinal activity returned, and TPN tapered off when jejunal intake exceeded 1000 calories.

Patients operated on after 1992 routinely received octreotide (100 micrograms subcutaneously thrice a day; n=63).

Every 72 hours, the drainage tubes were shortened in length by 1-2 cm and rotated through 360° in a clockwise and anti-clockwise direction. The amylase content of the drainage fluid was estimated every five days. The drainage tubes were removed when the discharge was less than 30 mL per day and the drainage fluid amylase less than 5000 IU/mL. If necessary, the drain tube was changed after two weeks.

**Statistical analysis**

Chi-squared test was used to compare the frequencies of various complications.

**Results**

In addition to the 65 patients who suffered from MODS preoperatively, 40 developed MODS postoperatively. Fourteen patients developed colonic fistula and five small intestinal fistula. Five patients developed multiple fistulae. In three patients, colonic fistula healed spontaneously, whereas eleven required diversion ileostomy. PF developed in 39 of the 68 patients who did not receive octreotide and 30 of the 63 who did (p<0.05).

With aggressive nutritional support and appropriate antibiotic therapy, PF healed in all patients except two who required distal pancreatectomy with splenectomy. In later years, endoscopic stenting of the main pancreatic duct was resorted to if the PF did not heal in 3 weeks (12 patients); in 7, PF healed within 2-4 weeks. In the remaining 5 patients, attempts at re-stenting failed because of unfavorable local anatomy.

The six patients in whom laparostoma was carried out at initial surgery underwent revision necrectomy and evacuation of pus, every 24-72 hours. In addition, 44 patients had persistent or recurrent infection. In 16 of these 44, pus was drained by one or more 10 or 12 F pigtail catheters inserted under CT guidance. In 28 patients, catheter drainage was not done as on CECT the pus either appeared very thick or formed multiple small pockets. Catheter drainage cleared the infection in 7 of the 16 patients. Thirty-seven patients (25 in whom catheter drainage was not attempted and 9 in whom it failed) underwent revision surgery for infection, including laparostoma in nine patients.
Eight patients developed severe extra-intestinal bleeding (requiring more than six units of blood transfusion in 24 hours). In five of these, angiographic vascular embolization achieved hemostasis; three other patients underwent surgery.

Mortality

Forty-five patients died postoperatively, the most frequent cause of death being multiple organ failure. Twelve of 15 patients who were subjected to laparostomy died. Relationship of mortality rate and to presence of some complications is shown in the Table. Of the 35 patients who were operated on within 15 days of the onset of pancreatitis, 21 (60%) died; in comparison, only 24 (25%) of 96 patients operated on 16–28 days after the onset died (p<0.002; Fig).

Discussion

Infection supervenes within 5 and 25 days from the onset of severe acute pancreatitis. Extraluminal air on CECT, seen in 17.6% of our cases, has been reported in about 20% of patients with infection. In its absence, the only certain method of diagnosis of infection is CECT-guided aspiration of necrotic tissue for bacteriological studies. False-negative results may be minimized by aspiration from multiple sites. Early surgical necrosectomy and drainage has been the treatment of choice for IPN. The ideal goal of total removal of slough is not always feasible, and evacuation of as much pus and necrotic material as possible and placement of multiple peritoneal drains is done. With this method, mortality rate in our patients was 35%; rates of 30% to 60% have been reported by others. Deaths are mainly related to persistent or recurrent infection (developing in 40% of our cases).

Bradley and DeGioia and Schein advocated the Table: Relation of mortality to some complications

<table>
<thead>
<tr>
<th>Factor</th>
<th>No. of cases</th>
<th>No. (% dead)</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative albumin (g/dL)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;2.5</td>
<td>36</td>
<td>20 (55.6)</td>
<td>0.002</td>
</tr>
<tr>
<td>≥2.5</td>
<td>95</td>
<td>25 (26.2)</td>
<td></td>
</tr>
<tr>
<td>Multiple organ dysfunction syndrome</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preoperative</td>
<td>65</td>
<td>29 (44.6)</td>
<td>0.001</td>
</tr>
<tr>
<td>Postoperative</td>
<td>40</td>
<td>14 (35.0)</td>
<td></td>
</tr>
<tr>
<td>No MODS</td>
<td>26</td>
<td>2 (7.7)</td>
<td></td>
</tr>
<tr>
<td>Postoperative pancreatic fistula</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>69</td>
<td>28 (40.6)</td>
<td>0.11</td>
</tr>
<tr>
<td>No</td>
<td>62</td>
<td>17 (27.4)</td>
<td></td>
</tr>
<tr>
<td>Postoperative gastrointestinal fistula</td>
<td></td>
<td></td>
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<tr>
<td>Yes</td>
<td>24</td>
<td>12 (50)</td>
<td>0.74</td>
</tr>
<tr>
<td>No</td>
<td>33</td>
<td>3 (9.1)</td>
<td></td>
</tr>
<tr>
<td>Postoperative extra-intestinal severe bleeding (&gt;4 units blood/day)</td>
<td></td>
<td></td>
<td></td>
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<td>Yes</td>
<td>8</td>
<td>7 (87.5)</td>
<td>0.002</td>
</tr>
<tr>
<td>No</td>
<td>123</td>
<td>38 (30.9)</td>
<td></td>
</tr>
</tbody>
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*χ² test

leaving the peritoneum open, packing the abdomen after necrosectomy; they reported reduction in mortality to around 14% to 21% with this technique. Van Vyve coined the term laparostomy for this technique. In a modification, known as closed packing or semi-open method, the peritoneum may be closed temporarily by inlay polypropylene mesh or polytetrafluoro ethylene patch and reopened as required (albeit with a low threshold of revision surgery); this technique may reduce the loss of fluid, electrolytes and proteins. We observed a high mortality (12 of 15) in our laparostomy patients; this may be related to selection of only severely ill patients for this procedure, i.e., those with MODS and massive necrosis with infection setting in less than two weeks after onset of pancreatitis.

In order to reduce infective complications, we preferred antibiotics that cross the blood-pancreas barrier, including imipenem if patients could afford it. We used octreotide in an attempt to reduce the frequency of PF due to disruption of the main pancreatic duct or its major branches, which is seen in about 50% of cases. However, we found that the rate of PF was similar in patients who received octreotide and those who did not.

The reported mortality rate in patients with IPN is 15% to 40%. Our data is in consonance with this. Almost 80% of deaths are due to infection and consequent MODS. The prognosis is worse in patients with early onset of infection. In a collection of 262 cases, mortality was 32% in 79 cases operated on within 15 days of the onset of pancreatitis and 15% in the 183 cases operated on later. In our patients, the mortality rates were 60% and 24%, respectively. Recently, placement of wide-bore percutaneous drainage and delaying the surgery to around 28 days has been advocated, unless acute septic syndrome forces earlier surgery.

In conclusion, mortality in IPN appears to be higher in patients with a shorter interval between the onset of pancreatitis and the onset of infection. Surgery, which
is frequently inevitable, may lead to development of MODS, pancreato-cutaneous fistula, intestino-cutaneous fistula and severe postoperative infection. Serum albumin below 2.5 g/dL, development of MODS and need for early surgery appear to be unfavorable features associated with higher mortality.

References

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