Acute Pancreatitis: Bacterial Translocation and Pancreatic Infections

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Introduction

Acute pancreatitis ranges from a mild, transitory illness to a severe, rapidly fatal disease. While patients with mild acute pancreatitis can be treated on a regular ward, patients suffering from necrotizing pancreatitis (NP) should be treated in an intensive care unit. Improved intensive care therapy reduces early cardiorespiratory complications and mortality during the initial critical period dominated by severe inflammatory response syndrome (SIRS) [1]. However, during the course of the disease, infected pancreatic necrosis and septic complications are reported to develop in 40%-70% of patients with severe acute pancreatitis, which represents the major cause of morbidity and mortality [2-4]. Sepsis and related multiple organ failure are responsible for mortality in up to 80% of cases. The gut has been suggested as a possible origin of pancreatic infections in several experimental studies [5-10], but the exact route by which a sterile pancreatic necrosis becomes infected has not yet been clearly defined.

Possible Pathways for Pancreatic Infection

There are several hypothetical mechanisms by which bacteria may enter pancreatic and peripancreatic necrosis: (a) the hematogenous pathway via the circulation [5, 11], (b) transmural migration through the colon [9], (c) via colonic translocation of bacteria to the lymphatics [7, 8, 10], (d) via ascites [5, 7, 8], (e) via the biliary duct system [12, 13], and (f) from the duodenum via the main pancreatic duct [9, 14].

Since most pathogens in pancreatic infection are common gastrointestinal flora, the gut seems to be the principle source of pancreatitis-related infections and it is reasonable to postulate that bacterial translocation may be the mechanism of inoculation. Intestinal bacterial translocation may be defined as the passage of bacteria and bacterial products, such as exotoxins, endotoxins, and cell wall fragments, from the intestinal lumen to usually sterile extraintestinal sites. The intestinal mucosa normally provides a functional and anatomical barrier against intestinal organisms. However, this mucosal bar-
rier is not complete and a minimal number of bacteria pass from the gastro-intestinal tract through the mucosal lamina propria [15]. These contaminating organisms are usually cleared by immunocompetent cells in healthy individuals. In stress situations, however, this barrier fails, allowing these organisms to “translocate” to mesenteric lymph nodes, the portal venous circulation, the peritoneal cavity, and abdominal organs, with the resultant super­vening sepsis and critical complications [16, 17]. This translocation is now recognized as a major cause of complicating infections in hospitalized pa­tients, especially in immunocompromised individuals. Although the exact incidence of bacterial translocation in hospitalized patients is difficult to estab­lish, many clinical studies indicate that systemic infections often originate from intestinal flora. Sedman et al. examined 267 general surgical patients by bacterial analysis of intestinal serosa and mesenteric lymph nodes taken at the time of surgery [18]. Excluding patients with distal intestinal obstruction and those with inflammatory bowel disease, in whom translocation was more common, the prevalence of bacterial translocation was 5%. Post-surgical complications were twice as prevalent in these patients.

It is of note that while the majority of complicating infections in animal studies and hospitalized patients is caused by a few species (Escherichia coli, other Enterobacteriaceae, and Enterococcus sp), the normal intestinal flora generally contains more than 400 species of bacteria [19]. In pancreatic infection, these germs also account for the majority of infections.

Numerous investigators have analyzed the clinical conditions which facilitate bacterial translocation, including enteric overgrowth, mesenteric ischemia, hemorrhagic shock, trauma, surgery, liquid alimentation, bowel stasis, and immunosuppression. Based on these animal studies, three potential mechanisms exist for the pathogenesis of bacterial translocation in acute pancreatitis:

1. Altered permeability of the intestinal mucosa: Acute pancreatitis causes severe volume depletion, with a reduction in cardiac output and intestinal blood flow [20, 21]. This probably leads to ischemic injury of the intestinal mucosa, with a consequent failure of mucosal barrier function.

2. Decreased host defense: Impaired phagocytic and reticuloendothelial function, demonstrated by a reduced clearance of E. coli from the circulation, has been noted by Widdison et al. [22], while Gianotti et al. have proven that local and systemic bacterial clearance is impaired in a rat model with acute pancreatitis [23].

3. Disruption of indigenous gut flora: Impairment of intestinal motility may play a pathophysiological role in the development of bacterial overgrowth, resulting in bacterial translocation to mesenteric lymph nodes [8, 24].

Ample animal studies exist to implicate enteric bacterial translocation in the pathogenesis of pancreatic infection. Wang et al. found a significant increase in bacterial translocation from the gut to mesenteric lymph nodes and lungs after 12 h and to the systemic circulation, ascites, and the pancreas at 24 h in rats [25]. These experiments demonstrated that translocation of enteric bacteria occurs during the early stage of acute pancreatitis and that the mesenteric lymph node-thoracic duct-circulation may be a major route for bacteri-