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Original article

Spectrum of microorganisms in infected walled-off pancreatic necrosis – Impact on organ failure and mortality

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ABSTRACT

Objective: Data on the microbial spectrum in infected pancreatic necrosis are scarce. Only few studies have addressed this issue in a larger, consecutive group of patients treated by a standardized algorithm. Since 2005 endoscopic, transmural drainage and necrosectomy (ETDN) has been the treatment of choice for walled-off necrosis in our centre. The present study evaluated the microbial spectrum of infected pancreatic necrosis and the possible relationship between infected necrosis, organ failure, and mortality. Furthermore, we investigated whether the aetiology of pancreatitis, use of external drainage, and antibiotic treatment influenced the microbial findings.

Methods: Retrospective review of medical charts on 78 patients who underwent ETDN in our tertiary referral centre between November 2005 and November 2011.

Results: Twenty-four patients (31%) developed one or more organ failures, 23 (29%) needed treatment in the intensive care unit (ICU), and 9 (11%) died during hospital admission. The prevailing microbial findings at the index endoscopy were enterococci (45%), enterobacteriaceae (42%), and fungi (22%). There was a significant association between the development of organ failure ($p < 0.001$), need of treatment in ICU ($p < 0.002$), in-hospital mortality ($p = 0.039$) and infected necrosis at the time of index endoscopy. Enterococci ($p < 0.0001$) and fungi ($p = 0.01$) were found more frequently in patients who died during admission as compared to survivors.

Conclusion: Different microbes in pancreatic necrosis may influence the prognosis. We believe that a detailed knowledge on the microbial spectrum in necrotizing pancreatitis may be utilized in the treatment to improve the outcome.

Introduction

The early phase of severe acute pancreatitis (SAP) is characterized by an extensive systemic inflammatory response syndrome, which is the major cause of organ failure and death in this phase [1]. Later follows an anti-inflammatory state characterized by inhibition of the immune system and an increased susceptibility to infectious complications, both bacteraemia and infected pancreatic necrosis. Infected necrosis is a major cause of death in the late phase of severe pancreatitis [2,3].

However, data on the microbial spectrum of infected pancreatic necrosis are scarce. It has been suggested that Gram-negative bacteria are the predominant microbial finding [4], but only few studies have addressed this issue in a larger, consecutive group of patients treated by a standardized algorithm [5]. Recently, a shift from a Gram-negative to a Gram-positive microbial flora has been reported [6]. Furthermore, to our knowledge, no studies have directly addressed the issue of microbial findings in the late phase of necrotizing pancreatitis with development of walled-off pancreatic and peripancreatic necrosis (WON). The aim of the present retrospective, single-centre study was to evaluate the microbial spectrum of infected pancreatic necrosis in patients undergoing endoscopic, transmural drainage and necrosectomy (ETDN) for WON, and to evaluate the possible relationship between infected necrosis, organ failure and in-hospital mortality. Furthermore, we aimed to investigate whether the microbial spectrum

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changes during the course of ETDN treatment, and whether the aetiology of pancreatitis, the use of external drainage, and antibiotic treatment influenced the microbial findings.

Methods

We retrospectively reviewed the medical charts on all patients who underwent ETDN in our tertiary referral centre between November 2005 and November 2011. Concomitantly, we retrieved the charts from the referring hospitals in order to obtain information on the patients' previous health status, disease course, microbiological findings, and antibiotic treatment.

All patients had a well documented episode of acute pancreatitis based on the Atlanta criteria leading to WON [7]. The indication for endoscopic intervention was persistently symptomatic collections despite either optimal conservative treatment, percutaneous drainage, or in few cases also surgical treatment. Symptoms included infection, pain, gastric outlet obstruction, bile duct obstruction, and leakage (e.g. ascites).

Endoscopic procedure

Endosonography-guided, transgastric or transduodenal drainage was performed using a curve-linear echoendoscope (Olympus GF-UCT140-AL5/Aloka SSD-5000) by: 1) needle puncture (ECHO-19; Cook Medical), 2) fluid aspiration for microbiological diagnostics, 3) insertion of a guidewire (0.035 ″ Dreamwire; Boston Scientific) through the needle, 4) needle knife incision over the wire (Huibregtse Triple Lumen; Cook Medical), 5) balloon dilatation of the tract (CRE Wireguided 12–20 mm; Boston Scientific), 6) placement of two double pigtail stents (Zimmon 7 Fr/6 cm, Cook Medical) and a nasocystic catheter (7-Fr nasal biliary drainage set; Cook Medical) for subsequent irrigation of the cavity, and 7) endoscopic debridement of loose necrotic material using a therapeutic gastroscope (Olympus GIF-1TQ160/XTQ160) and either tripod, stone retrieval basket, or polypectomy snare (used in most cases).

A small dilatation balloon diameter was usually chosen at the index procedure and when there was an increased risk of bleeding from collaterals e.g. in cases with splenic vein thrombosis. Endoscopic necrosectomy was usually not performed during the index procedure. Additional placement of percutaneous catheters was done in cases of widely expanding peripancreatic collections that were not accessible by endoscopic route alone. All endoscopies were performed with CO_2 insufflation.

Irrigation of the collections through nasocystic and/or percutaneous catheters was done 3–6 times a day. The irrigation volume depended on the size of the collection, usually 100–250 mL per procedure. The endoscopic sessions with redilatation of the transmural tract and debridement were repeated at weekly intervals until the necrotic cavity was free of debris and vital granulation tissue was seen. At that time the nasocystic and/or percutaneous catheters were removed.

As a part of the endoscopic treatment, fluid from the collections was aspirated for microbiological diagnostics before further endoscopic intervention. The fluid was cultured both for aerobic, anaerobic, and fungal organisms.

The occurrence of organ failure was noted using the following definitions: 1) Circulatory failure: need for inotropic support or temporal pacemaker, 2) respiratory failure: need for mechanical ventilation, 3) renal failure: need for haemofiltration, and 4) gastrointestinal failure: absence of bowel sounds and intestinal paralysis on diagnostic imaging.

The severity of the disease at the time of index endoscopy was assessed by Sequential Organ Failure Assessment (SOFA) [8] and both Computed Tomography Severity Index (CTSI) [9], and modified CTSI [10].

Statistics

All data are expressed as median and interquartile ranges (IQR). Chi-square test was used to analyse categorical data.

Differences were judged as statistically significant if the p value was less than 0.05.

Univariate and multivariate regression was used to evaluate predictors of in-hospital mortality, development of organ failure and need for ICU. The results of the regression analysis are presented as odds ratios (OR) with 95% confidence intervals (CI).

Results

Base-line characteristics and severity assessment

Base-line data at the time of index endoscopy are presented in Table 1.

Twenty-four (31%) patients developed one or more organ failures. Twenty-three (29%) patients needed treatment in the ICU. Nine patients (11%) died during hospital admission.

Procedure-related complications were seen in 10 patients (12%) and included one procedure-related death due to development of peri-procedural septic shock and multi-organ failure. Despite aggressive fluid resuscitation, administration of broad-spectrum antibiotics and inotropics in the ICU, the patient died the day after the index endoscopy. Four patients experienced bleeding from the necrosis cavity managed by embolization, four experienced pneumoperitoneum without need of intervention or treated with needle aspiration, and one patient bleeding from the transmural tract treated with epinephrine injection and red blood cell transfusion.

Microbial assessment at the index endoscopy

Culture proven infected necrosis was demonstrated at the index endoscopy in 55 out of 78 (71%) patients. A single microbial species was found in 27 patients (49%), two species were found in 21

Table 1
The base-line data of 78 patients with walled-off necrosis treated by endoscopic, transmural drainage and necrosectomy.

	Total $N = 78$	Sterile necrosis $N = 23$	Infected necrosis $N = 55$	p-value
Gender, males/females	49/29	13/10	36/19	0.458
Age, median (IQR[a])	54 (40–63)	44 (38–57)	55 (41–65)	0.035
BMI, median (IQR)	27 (24–30)	27 (24–30)	27 (24–31)	0.927
Etiology, *n*				0.779
- alcohol	26	8	18	
- gallstone	33	8	25	
- other	19	7	12	
Time from onset of symptoms to index endoscopy, days, median (IQR)	44 (29–61)	49 (24–85)	44 (29–54)	0.683
Antibiotic treatment prior to index endoscopy, *n*	54	14	40	0.301
External drainage and/or fine-needle aspiration prior to index endoscopy, *n*	40	10	30	0.373
CTSI[b], median (IQR)	7 (5–9)	7 (5–8)	7.5 (5–9)	0.40
Modified CTSI, median (IQR)	9 (8–10)	10 (8–10)	8 (8–10)	0.663
SOFA[c]-score, median (IQR)	3 (0–9)	1 (0–3)	4 (2–10)	0.0004

[a] IQR = interquartile range.
[b] CTSI = computed tomography severity index.
[c] SOFA = sequential organ failure assessment.