Pancreatology 14 (2014) 450–453

Contents lists available at ScienceDirect

Pancreatology

journal homepage: www.elsevier.com/locate/pan

Original article

Emergence of multidrug resistant infection in patients with severe acute pancreatitis

Ho-Su Lee [a], Sung Koo Lee [a, *], Do Hyun Park [a], Sang Soo Lee [a], Dong-Wan Seo [a], Myung-Hwan Kim [a], Yong Pil Chong [b]

[a] Department of Gastroenterology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea
[b] Department of Infectious Diseases, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea

ARTICLE INFO

Article history:
Available online 18 October 2014

Keywords:
Severe acute pancreatitis
Necrotizing pancreatitis
Infection
Multidrug resistant
Antimicrobial-resistant
Treatment

ABSTRACT

Background/objectives: Infection is the most important risk factor contributing to death in severe acute pancreatitis. Multidrug resistant (MDR) bacterial infections are an emerging problem in severe acute pancreatitis.
Methods: From January 2009 to December 2011 the medical records of 46 patients with infected severe acute pancreatitis were reviewed retrospectively to identify risk factors for the development of MDR bacterial infection and assess the related outcomes.
Results: The mean age of the 46 patients was 55 years; 38 were males. Thirty-six patients (78.3%) had necrotizing pancreatitis and all of enrolled 46 patients had suspected or proven pancreatic infection. MDR microorganisms was found in 29 (63%) of the 46 patients. A total of 51 episodes of MDR infection were collected from 11 cases of infected pancreatic pseudocysts, 36 cases of infected necrosis/infected walled-off necrosis and 4 cases of bacteremia. The most frequent MDR bacteria was methicillin-resistant *Staphylococcus aureus* ($n = 15$). Transferred patients had a higher incidence of MDR infections than primarily admitted patients (72% vs. 35%, $P = .015$). The mean intensive care unit stay was significantly longer in patients with MDR bacterial infections (20 vs. 2 days, $P = .001$). Mortality was not significantly different in the patients with MDR infections vs. those without it (14% vs. 6%, $P = .411$).
Conclusions: Clinicians should be aware of the high incidence of MDR bacterial infections in patients with severe acute pancreatitis, especially referred patients. Empiric therapy directed at these pathogens may be used in patients where severe sepsis persists, until definitive culture results are obtained.

Introduction

Acute pancreatitis is a disease with a wide variety of clinical presentations, ranging from a mild, transitory illness to a severe, rapidly fatal disease [1]. Severe acute pancreatitis (SAP) is a serious type of acute pancreatitis, in which the mortality rate may be up to 30% [2]. The majority of deaths related to SAP are the result of infectious complications. During the natural course of acute pancreatitis, bacterial infection is reported to develop in 40% to 70% of all patients with necrotizing disease [3,4]. Therefore, prevention, diagnosis, and the optimal treatment of infection in SAP have become principal aims in improving the outcome of this disease.

The emergence of multidrug resistant (MDR) microorganisms has been one of the major concerns for physicians involved in the care of critically ill patients in the last decade [5]. Recent investigation suggests that the incidence of infections caused by MDR organisms is increasing in SAP [6]. However, knowledge of the antibiotic resistance pattern of MDR pathogens in SAP, and their clinical effects, is limited. Therefore, we decided to perform a retrospective study aimed at assessing the prevalence, epidemiology, risk factors, and effects on outcome of MDR bacterial infections in SAP.

Methods

Study subjects

We performed a retrospective evaluation of all bacterial and fungal infections occurring in patients with SAP. Between January 1, 2009, and December 31, 2011, one hundred eighty six consecutive

* Corresponding author. Department of Gastroenterology, Asan Medical Center, 88, Olympic-ro 43-gil, Songpa-gu, Seoul 138-736, Republic of Korea. Tel.: +82 2 3010 3186; fax: +82 2 3010 8043.
E-mail address: sklee@amc.seoul.kr (S.K. Lee).

http://dx.doi.org/10.1016/j.pan.2014.10.003
1424-3903/

patients with SAP according to CT findings were seen at the Asan Medical Center. All patients met the criteria for severe disease as proposed by the Atlanta consensus meeting [7,8]. Microorganisms were identified in 51 patients with clinical infection. To identify the infections due to SAP, all the results of culture and the corresponding antibiograms were reviewed by an infectious disease specialist (Y.P.C.). Any discrepancies involving the correlation between infection and SAP were resolved by consensus. Patients who underwent solid organ transplant ($n = 3$), a patient with active Crohn's disease who was taking high dose glucocorticoid ($n = 1$), and a patient with leukemia ($n = 1$) were excluded. A total of 46 patients with infected severe acute pancreatitis were enrolled.

We recorded demographic characteristics, cause, and disease severity assessed by the bedside index for severity in acute pancreatitis (BISAP) [9] at admission and a computed tomography (CT) severity index (CTSI) [10]. CT was performed within 48–72 h of admission in every patient. Organ failure was defined as follows: cardiovascular failure, a mean arterial pressure of <60 mmHg or the need for vasoactive therapy; renal failure, a serum creatinine level of >2.0 mg/dL; pulmonary failure, the need for mechanical ventilation or the presence of acute lung injury or adult respiratory distress syndrome.

In our hospital, all patients were treated medically according to generally accepted principles consisting of withholding oral intake, providing pain relief, and restoring fluid and electrolyte losses intravenously. All patients were given prophylactic antibiotics. The choice of antibiotic was left to the discretion of the attending physician.

Definitions

Isolation of organism was defined as a positive culture obtained from blood, fine-needle aspiration, and the first drainage of the percutaneous procedure only, or surgery. Isolated organisms were tested for antimicrobial susceptibility through minimum inhibitory concentration testing using the VITEK2 system (bioMérieux, Vitek Inc, Hazelwood, MO, United States), according to the recommendations of the Clinical and Laboratory Standards Institute [11]. The following bacteria were considered MDR: methicillin-resistant *Staphylococcus aureus* (MRSA), methicillin-resistant coagulase-negative staphylococci (MRCNS), vancomycin-resistant *Enterococcus* species (VRE), third generation cephalosporin-resistant or β-lactam-esistant *Enterobacteriaceae* [12] (e.g., *Escherichia coli*, *Klebsiella pneumonia*, and *Serratia marcescens*) or MDR gram-negative rods defined as other gram-negative rods not susceptibile to at least one agent in three or more antimicrobial categories (e.g., *Acinetobacter baumanii*, and *Pseudomonas aeruginosa*).

Statistical analysis

Categorical variables are presented as frequencies (percentage) and were compared using the chi-square or Fisher's exact test. Continuous variables are presented as mean ± SD and were compared by Student's *t*-test. Differences were considered significant at the level of 0.05. Data were analyzed with SPSS package, version 18.0 (SPSS Inc., Chicago, IL).

Results

This study included a total of 46 subjects, 29 in the MDR group and 17 in the non-MDR group. Demographic characteristics were similar for the patients with and without MDR bacteria and are summarized in Table 1.The mean age was 53.6 ± 15.7 years and 59.5 ± 17.0 years for the MDR and non-MDR group, respectively. The MDR group consisted of approximately 85.7% males. Among them, 27 (58.7%) were transferred to our center. Disease severity based on BISAP and CTSI and the etiology of SAP were not different. The transferred patients had a higher incidence of MDR bacterial infections than the primarily admitted patients (72% vs. 35%, $P = .015$). Antibiotics, either prophylactic or therapeutic, were administered to all of the patients. The antibiotics used were a third generation cephalosporin (cefotaxime) ± metronidazole or carbapenem. Initial use of carbapenem was higher in patients who had SAP with MDR bacteria, although this difference was not statistically significant (66% vs. 41%, $P = .112$). Also, there was a tendency for initial antibiotic duration to be longer in the MDR group. Polymicrobial infection was significantly higher in the patients with MDR bacterial infections (96.6% vs. 47.1%, $P < 0.001$), whereas the rates of bacteremia and concomitant fungal infection were not significantly different. Of 17 positive blood cultures from 11 patients, 41.2% (7/17) were concordant with the pancreatic cultures obtained.

Infection with MDR microorganisms was found in 29 (63%) of the 46 patients. In total, 131 bacterial ($n = 115$) and fungal ($n = 16$) infections were detected. Microorganisms recovered from the 46 patients are summarized in Table 2. *P. aeruginosa* ($n = 18$) was the main organism identified, followed by *Enterococci* species ($n = 17$), *S. aureus* ($n = 15$), and *Klebsiella pneumoniae* ($n = 12$). We detected 51 episodes of microbiologically confirmed MDR bacteria (11 cases with infected pancreatic pseudocysts, 36 cases with infected necrosis/infected walled-off necrosis and 4 cases with bacteremia), of which 29 (56.9) were MDR gram-negative bacteria and 22 (43.1) were MDR gram-positive bacteria (Table 2). The most common MDR bacterium was MRSA ($n = 15$). Other common pathogens were MDR *P. aeruginosa* ($n = 12$), ESBL-producing *K. pneumoniae* ($n = 7$), MRCNS ($n = 6$), MDR *A. baumanii* ($n = 5$), ESBL-producing *E. coli* ($n = 4$), VRE ($n = 1$) and AmpC β-lactamase- producing *S. marcescens* ($n = 1$).

The 51 isolates were collected from 24 specimens from transmural drainage, 20 from percutaneous drainage, 4 blood specimens, 2 specimens from necrosectomy, and 1 specimen from transpapillary drainage (Table 3). The biliary and percutaneous procedures performed within two weeks before culture did not differ

Table 1
Demographic and clinical characteristics of patients with and patients without multidrug resistant bacterial infection.

Characteristic	MDR ($N = 29$)	Non-MDR($N = 17$)	*P* value
Age (year)	53.6 ± 15.7	59.5 ± 17.0	.249
Age > 60	10 (34.5%)	10 (58.8%)	.112
Male sex (%)	24 (85.7%)	14 (77.8%)	.972
BMI (kg/m^2)	24.4 ± 2.7	23.2 ± 3.4	.233
Transferred	21 (72.4%)	6 (35.3%)	.015
Cause			.419
Alcohol	12 (41.4%)	4 (23.5%)	
Biliary	5 (17.2%)	2 (11.8%)	
After ERCP or operation	6 (20.7%)	4 (23.5%)	
Others	6 (20.7%)	7 (42.2%)	
Organ failure (%)	14 (48.3%)	5 (29.4%)	.215
SIRS (%)	21 (72.4%)	13 (76.5%)	.765
BISAP	1.9 ± 1.1	2.4 ± 1.0	.183
CTSI score	4.7 ± 2.3	4.0 ± 2.0	.298
CRP (mg/dL)	19.2 ± 12.1	15.6 ± 11.6	.328
Initial use of carbapenem	19 (65.5%)	7 (41.2%)	.112
Duration of initial antibiotics	24.2 ± 21.7	16.8 ± 15.4	.255
Bacteremia	8 (27.6%)	3 (17.6%)	.446
Fungal infection	9 (31.0%)	4 (23.5%)	.585
Polymicrobial infection	28 (96.6%)	8 (47.1%)	<.001

Values are reported as means ± SDs. BISAP, Bedside index for severity in acute pancreatitis; BMI, body mass index; CRP, C-reactive protein; CTSI, computed tomography severity index; ERCP, Endoscopic retrograde cholangiopancreatography; MDR, Multidrug resistant.