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Original Article

# The etiology and bacteriology of healthcare-associated empyema are quite different from those of community-acquired empyema

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#### ABSTRACT

*Objects:* Changes in patients' background and life environment could contribute to increase healthcareassociated (HCA) empyema. There are no guidelines and statements for HCA empyema.

*Methods:* We retrospectively reviewed all patients with empyema who were admitted to the Aichi Medical University Hospital, Japan between 2008 and 2015. We evaluated patients' characteristics, microbial profiles, treatment and outcomes, and analyzed prognostic factors for 90-day mortality.

*Results*: A total of 48 patients were enrolled in this study. They were categorized into communityacquired (CA) empyema (16 patients) and healthcare-associated (HCA) empyema (32 patients). HCA empyema patients had higher Charlson comorbidity index (CCI) scores, and poorer performance status (PS) than CA empyema patients. Potentially-drug resistant (PDR) pathogens were seen more frequently in HCA empyema than in CA empyema.

Compared with survival and death groups, the death group showed higher CCI scores and poorer PSs than the survival group. The death group had more malignancy than the survival group. PDR pathogens were detected more frequently in the death group than in the survival group. Multivariate analysis showed that emergence of PDR pathogens and malignancies were independent poor prognostic factors for 90-days mortality among empyema.

*Conclusion:* The etiology and bacteriology of HCA empyema are quite different from those of CA empyema. Especially, the mortality of HCA empyema was higher than the one of CA empyema. Emergence of PDR pathogens in the pleural fluid detected by culture, pulmonary disease and malignancies were independent poor prognostic factors among CA and HCA empyema by multivariate logistic regression analysis.

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#### 1. Introduction

Advances of antimicrobial agents and wide-spread use of chest tube drainage have contributed to improving the mortality of empyema [1–3]. Nevertheless, its mortality rate remains high, accounting for 10–20% [4–6]. With the advent of antibiotics, the incidence of empyema was dramatically reduced. However, recent studies demonstrated the increase of pleural infection [3,6,7]. As the aging circumstances advances in recent days, patients living in nursing homes, or requiring homecare are increasing year by year worldwide. We sometimes encounter empyema patients who live in a nursing home, or receive hemodialysis or chemotherapy. While these patients should be categorized as having healthcare-associated infections, there is no evidence-based standard guide-line for healthcare-associated empyema for nursing home patients, patients who receive hemodialysis, or those who receive

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chemotherapy [8–10]. In fact, healthcare-associated empyema patients are generally considered and treated as a community-acquired infection.

Healthcare-associated pneumonia (HCAP) is a new category of respiratory infections documented in 2005 ATS/IDSA guideline [11]. Patients with HCAP are described as an independent group of patients with pneumonia who are excluded from the CAP category because the epidemiologic pattern is similar to that of hospital-acquired pneumonia (HAP). Likewise, we hypothesized whether the etiology and bacteriology of healthcare-associated empyema could be quite different from those of community-acquired empyema. Thus, we conducted this retrospective study to evaluate the difference between community-acquired (CA) empyema and healthcare-associated (HCA) empyema. There are some reports documenting HCA empyema [12]. To the best of our knowledge, this is the second report about the etiology and bacteriology of HCA empyema, and is the first report showing a prognostic factor among CA and HCA empyema.

## 2. Methods

We retrospectively reviewed the medical and microbiological records of all patients with empyema who were admitted to Aichi Medical University hospital, an 800-bed teaching hospital located in Aichi Prefecture, Japan, from 2008 to 2015. The patients were categorized into either community-acquired empyema (CA empyema) or healthcare-associated empyema (HCA empyema) groups. For the purpose of evaluating the clinical features, bacteriology and prognostic factors for empyema, we compared the baseline characteristics, laboratory findings, characteristics of pleural effusion including pH and glucose and lactate dehydrogenase (LDH), identified pathogens, treatment (antibiotics used, drainage or surgical procedure, and usage of urokinase), and clinical outcomes in each group. This study was approved by the Institutional Review Board of Aichi Medical University Hospital.

As for a diagnosis of empyema, patients were included if they met the following criteria: 1) pleural fluid by thoracentesis was purulent, 2) microscopic examination of the pleural effusion revealed an elevation of WBC counts with neutrophil predominance, 3) microorganisms were identified by microscopic examination or were isolated by culture, and 4) clinical evidence of infection, including fever, cough, sputum, and elevated white blood cells (WBC) and/or C-reactive protein (CRP) were confirmed [13].

The severity of empyema was categorized according to the guideline by The American College of Chest Physicians (ACCP) [14]. Patients were excluded if a diagnosis of thoracic empyema with or without a bronchopleural fistula was established before admission, or if thoracic empyema had been caused by trauma, surgery, or any invasive procedure involving the pleural cavity. Patients with tuberculous pleurisy, carcinomatous pleuritis were excluded. Hospital-acquired infection was excluded in this study.

# 2.1. Definition of type of empyema

CA empyema and HA empyema were defined based on ATS/IDSA guideline [11]. CA empyema was defined as a diagnosis of empyema in patients who did not meet any of the criteria for HCAP, i.e. the following patients: (a) reside in their own homes and not in a nursing home or in a hospital; (b) receive no care (i.e. no clinic visits, infusion or hemodialysis); and (c) were not admitted to a hospital within the preceding 90 days. In contrast, HCAP included patients with any of the following: (a) hospitalization for two days in the preceding 90 days; (b) residing in a nursing home or extended care facility; (c) receiving home infusion therapy (including antibiotics); (d) on long-term dialysis (including

hemodialysis and peritoneal dialysis) within the 30 days prior to enlistment into the study; and (e) received home wound care [11].

## 2.2. Evaluation of comorbidities

Comorbidities were evaluated by the Charlson comorbidity index. This predicts the ten-year mortality for a patient who may have a range of comorbid conditions such as heart disease. AIDS, or cancer (a total of 22 conditions). Each condition is assigned with a score of 1, 2, 3 or 6 depending on the risk of dying associated with this condition. Then the scores are summed up and given a total score which predicts mortality. There are many variations of the Charlson comorbidity index including the Charlson/Deyo, Charlson/ Romano, Charlson/Manitoba, and Charlson/DHoores adaptations of the Charlson comorbidity index. The clinical conditions and scores are as follows: 1 each: Myocardial infarct, congestive heart failure, peripheral vascular diseases, dementia, cerebrovascular diseases, chronic lung diseases, connective tissue diseases, ulcer, chronic liver diseases. 2 each: Hemiplegia, moderate or severe kidney diseases, diabetes, diabetes with complications, tumor, leukemia, lymphoma. 3 each: Moderate or severe liver disease. 6 each: malignant tumor, metastasis, AIDS. For a physician, it is helpful to decide how aggressively to treat a condition. For example, a patient may have cancer, but also have a heart disease and diabetes so severe that the costs and risks of the treatment outweigh the shortterm benefit from the treatment of the cancer. Since patients often do not know how severe their conditions are, the indexing nurses were originally supposed to go through the patients chart and determine whether the patient had a particular condition in order to calculate the index [15].

The treatment was considered to be appropriate if in vitro susceptibility of the pathogens isolated by effusion fluid culture was consistent with the antibiotics used. In the present study, antimicrobial susceptibility testing was performed using broth microdilution and interpreted according to the guidelines set by Clinical Laboratory Standard Institute (CLSI), which was published in May 2008.

# 2.3. Factors of analysis

Clinical data were collected by a review of electronic medical records. All of the patients were examined at the time of admission to our institute. Twenty-seven candidate predictors were chosen from published clinical studies as potential prognostic factors [1,5,16,17].

Continuous variables of the factors were divided into two categories as follows: age ( $\geq$ 71, <71 years); PS ( $\geq$ 2,  $\leq$ 1); BMI ( $\geq$ 18.5, <18.5 kg/m<sup>2</sup>); body temperature (BT) ( $\geq$ 37.1, <37.1 °C); oxygen saturation (SpO<sub>2</sub>: <90%,  $\geq$ 91%); systemic blood pressure (<90,  $\geq$ 90 mmHg); CCI ( $\geq$ 3, <3); WBC ( $\geq$ 15,200, <15,200/µL); CRP ( $\geq$ 18.5, <18.5 mg/dL); blood urea nitrogen (BUN) ( $\geq$ 23, <23 mg/ dL); albumin (Alb) (<2.8,  $\geq$ 2.8 g/dL); pH in pleural effusion (<7.3,  $\geq$ 7.3); glucose in pleural effusion (<22,  $\geq$ 22 mg/dL); LDH in pleural effusion ( $\geq$ 1887, <1887 IU). The cut-off points for BT, SpO<sub>2</sub> and BP were set at the value that demarcated the normal and abnormal ranges, whereas age, BMI, WBC, CRP, BUN, Alb, characteristics of pleural effusion (pH, glucose and LDH) and CCI score were based on the median values.

#### 2.4. Statistical analysis

To identify factors associated with death within 90 days from admission, the Fisher's exact or  $\chi^2$  statistic test were performed using the 33 parameters among empyema patients. Factors showing *p*-value <0.1, were considered candidate predictors

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