J Infect Chemother 20 (2014) 436–442

Contents lists available at ScienceDirect

Journal of Infection and Chemotherapy

journal homepage: http://www.elsevier.com/locate/jic

Original article

Clinical features and outcomes of aspiration pneumonia compared with non-aspiration pneumonia: A retrospective cohort study

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ARTICLE INFO

Article history:
Received 14 January 2014
Received in revised form
4 April 2014
Accepted 8 April 2014

Keywords:
Aspiration pneumonia
Community-acquired pneumonia
Elderly patients
Healthcare-associated pneumonia
Recurrence
Prognosis

ABSTRACT

Pneumonia is a leading cause of death among elderly patients. Although aspiration pneumonia (AP) commonly occurs with aging, its clinical features and outcomes are still uncertain. The aims of this study were to describe the clinical features and outcomes of AP and to assess whether presence of AP affects clinical outcomes in patients with community-acquired pneumonia (CAP) and healthcare-associated pneumonia (HCAP). We retrospectively analyzed patients with CAP and HCAP hospitalized in our institution in Japan from October 2010 to March 2012. We compared clinical features and outcomes between AP and non-AP, and investigated risk factors for recurrence of pneumonia and death. Of 214 consecutive patients, 100 (46.7%) were diagnosed as having aspiration pneumonia. These patients were older and had lower body mass index, more comorbidities, and poorer Eastern Cooperative Oncology Group performance status (ECOG PS) than the patients with non-AP. Patients with AP had more severe disease, required longer hospital stays, and had a frequent recurrence rate of pneumonia and higher mortality. In multivariate analyses, AP, age, and ECOG PS were related to recurrence of pneumonia, and the prognostic factors were CURB-65 score and ECOG PS. AP was not a significant indicator for prognosis but was the strongest risk factor for recurrence of pneumonia. Clinical background and outcomes including recurrence and mortality of AP were obviously different from those of non-AP; therefore AP should be considered as a distinct subtype of pneumonia, and it is important to prevent the recurrence of pneumonia in the patients with AP.

1. Introduction

Pneumonia is a major cause of death, and mortality from pneumonia increases with aging [1]. Particularly in Japan, pneumonia is the third leading cause of death and 96.5% of patients dying from pneumonia are older than 65 years [2]. The frequency of aspiration due to dysphagia also increases with aging in the elderly complicated with comorbidities such as cerebrovascular or degenerative diseases and dementia [3–5]. As a consequence of dysphagia, the incidence of aspiration pneumonia (AP) increases in elderly patients with both community-acquired pneumonia (CAP) and healthcare-associated pneumonia (HCAP) [5–8]. Patients with dysphagia are likely to have pneumonia at a rate 1.6 to 11.9 times greater than patients without dysphagia [5,9–11], and AP accounts for 10.3%–66.8% of hospitalized patients with pneumonia [6,12]. Several recent studies revealed that AP or pneumonia with dysphagia is common in elderly patients, who have a different clinical background, greater disease severity, and poorer prognosis than patients with non-AP [9,13,14]. Almirall and colleagues [10] reported a general prevalence of oropharyngeal dysphagia among CAP patients over 70 years old of 75.0%. Taylor and colleagues [9] revealed that 30-day mortality from pneumonia in patients at risk for aspiration was 17.2% compared with 7.7% in patients not at risk. Because of its frequent prevalence and poor prognosis, AP is an important etiology of pneumonia in elderly patients. Certainly, dysphagia is a risk factor for pneumonia and a prognostic factor in elderly patients [8–11], but data on the clinical features and outcomes of AP are still limited [9,13]. Thus, we conducted this study to

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http://dx.doi.org/10.1016/j.jiac.2014.04.002
1341-321X/

describe the clinical features and outcomes of patients with AP compared with those of patients with non-AP and to determine whether AP affects recurrence of pneumonia and mortality.

2. Patients and methods

2.1. Patients and study design

In this retrospective cohort study, we analyzed patients aged ≥15 years old who were diagnosed as having CAP or HCAP when admitted between October 2010 and March 2012 to the Emergency Department or the Division of Respiratory Medicine at Showa University Fujigaoka Hospital, a 584-bed urban teaching hospital serving a large community and referral population in Yokohama, Japan. The patients were followed until death or through March 2013. Patients who drowned, took a drug overdose, had hospital-acquired pneumonia, or had lung cancer were excluded. We classified the pneumonia as AP or non-AP, compared their clinical features and outcomes, and investigated risk factors for recurrence of pneumonia and death. The study protocol was approved by the Institutional Ethics Committee of Showa University.

2.2. Data collection

All clinical data were collected from medical records and included age, sex, comorbidities, concomitant drugs, Eastern Cooperative Oncology Group performance status (ECOG PS) at 2 weeks before admission, body mass index (BMI), categories of pneumonia (CAP or HCAP, AP or non-AP), physical signs and symptoms, laboratory data, existence of respiratory failure, chest roentgenogram or computed tomography, microbiological examinations, use of antibacterial agents, and clinical outcomes. Microbiological examinations included endotracheal aspirate specimens or sputum (presence of >25 leukocytes and ≤25 squamous cells per low-power-field with Gram stain), blood cultures, urinary antigen tests (BinaxNOW *Streptococcus pneumoniae* and BinaxNOW *Legionella*; Alere Medical Co., Ltd., Tokyo, Japan), serum antibody tests: *Mycoplasma pneumoniae* PA tests and *Chlamydophila pneumoniae* ELISA tests, and rapid influenza diagnostic test. All clinical data were obtained when the patients came to the hospital or immediately after admission. Comorbidities were scored by Charlson comorbidity index (CCI) [15], and risk for drug-resistant pathogens (DRP) was evaluated by counting the number of Shindo's six risk factors for CAP—DRP (prior hospitalization, immunosuppression, previous use of antibiotics, acid-suppressing drugs, tube feeding, and nonambulatory status) [16]. Severity of pneumonia was evaluated by the pneumonia severity index (PSI) [17] and CURB-65 (confusion, blood urea nitrogen >19 mg/dl, respiratory rate ≥30 breaths/min, low blood pressure, age ≥65 years) severity scores. Clinical outcomes were evaluated by time to clinical stability, length of hospital stay, initial treatment failure, in-hospital mortality during hospitalization, and recurrences of pneumonia or deaths during follow-up.

2.3. Definitions

Diagnosis of pneumonia was established by radiographic evidence of pulmonary infiltration plus acute onset of symptoms of lower respiratory tract infection. AP was defined as pneumonia with radiographic evidence of infiltration in the posterior segments of the upper lobes or the apical or basal segments of the lower lobes occurring in the patients with a history of vomiting or witnessed aspiration, or with risks for aspiration. Radiologic findings were evaluated by two expert pulmonologists blinded to the patients' clinical information. We defined risks for aspiration according to previous reports as follows [9,12,13,18]: dementia, cerebrovascular diseases, neuromuscular diseases, pharyngolaryngeal dysfunction, esophageal dysfunction or mechanical obstruction, tube feeding, gastroesophageal reflux, and poor swallowing previously confirmed. We considered patients not meeting the above criteria to be non-AP patients. CAP and HCAP were defined according to the American Thoracic Society/Infectious Diseases Society guidelines [19,20]. HCAP was defined as a diagnosis of pneumonia in patients meeting at least one of following criteria: recent hospitalization for ≥2 days within 90 days; residence in a nursing home or long-term care facility; recent history of home infusion therapy, home wound care, or long-term dialysis during the preceding 30 days. Microbiological diagnosis was made if there was heavy bacterial growth in semi-quantitative culture from endotracheal aspirate specimen or sputum, positive blood culture, positive urinary antigen test for *S. pneumoniae* and *Legionella pneumophila*, or elevated serum antibody titer against *M. pneumoniae* (≥1:320- or ≥4-fold increase) or *C. pneumoniae* (IgA-ID increase ≥1.0 or IgG-ID increase ≥1.35). The definition of a multidrug-resistant (MDR) pathogen conforms to the consensus statement of the European Centre for Disease Prevention and Control and the Centers for Disease Control and Prevention [21]. Initial treatment failure was defined as death during initial treatment or change from the initial antibiotic agents due to the physician's clinical evaluation of treatment ineffectiveness. Changes due to adverse effects of antibacterial agents or transfer to another hospital during initial treatment were considered as unknown data. Inappropriate therapy was defined when pathogens were resistant to initial antibiotic agents. Time to clinical stability was the number of days from admission to the first day that all of the following criteria were achieved simultaneously [22,23]: temperature ≤37.2 °C, heart rate ≤100 beats/min, systolic blood pressure ≥90 mmHg, respiratory rate ≤24 breaths/min, and oxygen saturation ≥92% on room air. Patients discharged from hospital for any cause before achievement of these criteria were considered as having unknown data. Recurrence of pneumonia was defined as the first episode of pneumonia after ≥3 days of completion of treatment for pneumonia in an enrolled patient.

2.4. Statistical analysis

We summarized and compared characteristics of patients at admission, frequency of MDR pathogens, use of antibiotic agents, and clinical outcomes between AP and non-AP using the Mann—Whitney *U*-test or chi-square test in accordance with continuous and nominal variables, respectively. The Kaplan—Meier method and log-rank test were used to detect differences in recurrence rates of pneumonia and mortality between AP and non-AP. To investigate risk factors for recurrence of pneumonia and death, we performed multivariate Cox regression analyses with forced entry method. We chose variables previously recognized to be significant effectors for recurrence of pneumonia (AP, age, ECOG PS, CCI, serum albumin, chronic pulmonary diseases, and administration of acid-suppressing agents) and mortality (AP, HCAP, CURB-65 score, ECOG PS, CCI, and serum albumin) [9–11,24–28]. To evaluate clinical effects of MDR pathogens and inappropriate initial therapy, we performed multivariate Cox regression analyses for recurrence and mortality in patients whose microbiological diagnosis was established. Entered variables were MDR pathogen isolation, inappropriate initial therapy, and others as indicated in the above-described models. To avoid overfitting, the backward stepwise method was used to enter the models. A P value of <0.05 was considered to be statistically significant in all analyses. All data were analyzed with IBM SPSS Statistics version 21.0 (IBM Japan Inc., Tokyo, Japan).