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Original article

A comparative study of bacteremic and non-bacteremic pneumococcal pneumonia

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Abstract

Background: Few attempts have been made to compare bacteremic and non-bacteremic pneumococcal pneumonia, mainly because it is difficult to gain agreement on which cases represent non-bacteremic pneumococcal pneumonia. Recently, an immunochromatographic assay for the detection of *Streptococcus pneumoniae* urinary antigen has been successfully evaluated for the diagnosis of pneumococcal pneumonia. The aim of our study was to examine and compare clinical and radiological features, risk factors, and outcome associated with bacteremic and non-bacteremic groups.
Methods: A retrospective study (1995–2003) analyzing the clinical records of patients diagnosed with pneumococcal pneumonia in our institution was performed. *S. pneumoniae* were identified by blood cultures (bacteremic group) and detection of urinary antigen (non-bacteremic group).
Results: There were 82 patients (57 bacteremic and 25 non-bacteremic). In seven non-bacteremic cases, another etiology was detected, i.e., *Legionella* ($n=1$) and *Chlamydia pneumoniae* ($n=6$). Bacteremic patients were significantly younger ($p=<0.001$), more likely to have liver disease ($p=0.028$), current smokers ($p=0.024$), alcohol and intravenous drug abusers ($p=0.014$ and $p<0.001$, respectively), and infected with HIV ($p<0.001$). Non-bacteremic patients were more likely to have congestive heart failure ($p=0.004$), chronic obstructive pulmonary disease ($p=0.033$) and to be former smokers ($p=0.004$). Bacteremic cases needed more prolonged intravenous antibiotic treatment (6 days vs. 4.5 days; $p=0.006$) than non-bacteremic cases and their length of stay was also longer.
Conclusion: In our study, smoking was the leading risk factor for pneumococcal pneumonia. However, current smokers have an increased risk of bacteremic forms and former smokers and patients with COPD developed non-bacteremic forms more frequently. Bacteremic patients need more prolonged intravenous antibiotic treatment than non-bacteremic patients.

Keywords: Community-acquired pneumonia; *Streptococcus pneumoniae*; Bacteremia; Antibiotic treatment

1. Introduction

Community-acquired pneumonia (CAP) is a common disease, representing the most frequent cause of hospital admission and mortality of infectious origin. *Streptococcus pneumoniae* is the leading cause of CAP and is responsible for 30–40% of CAP where the etiology can be established following a routine diagnostic work-up. However, *S. pneumoniae* may be underdiagnosed, and it is thought that it could be responsible for at least one of three episodes of CAP without an etiological diagnosis [1]. The reason for this underdiagnosis could be the limitations of conventional diagnostic tests. The diagnosis of pneumococcal pneumonia

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is challenging and complicated by the lack of a highly sensitive and specific diagnostic gold standard method. The isolation of *S. pneumoniae* from blood or pleural fluid is highly specific, but lacks sensitivity, being positive in only about one-fourth of cases. Prior antibiotic therapy significantly reduces its sensitivity.

Diagnosis based only on sputum culture is controversial due to both nasopharyngeal carriage of pneumococci in healthy individuals and inadequate sputum specimen collection. Invasive methods, such as bronchoalveolar lavage or transthoracic needle aspiration, are generally considered to be the most reliable, but they require specialist training and may have side effects.

Based on data accumulated in the pre-antibiotic era, it is believed that non-bacteremic cases account for 70–80% of pneumonia caused by *S pneumoniae* [2]. Thus, new diagnostic tests, such as polymerase chain reaction (PCR) and urine antigen assays, are promising in detecting these cases.

Detection of *S. pneumoniae* antigens in the urine of patients with pneumonia was first described in 1917 [3]. Recently, a rapid immunochromatographic membrane test, the NOW *Streptococcus pneumoniae* urinary antigen test (Binax, USA), has become available and can detect *S. pneumoniae* antigen in urine samples [4]. The test is simple to perform and detects the *S. pneumoniae* C-polysaccharide, which is found in the cell wall and is common to all serotypes, providing results within 15 min. In previous studies, the overall sensitivity and specificity of the test ranged from 70% to 80% and from 70% to 100%, respectively [1,2,4–8].

Few studies have been designed to compare bacteremic and non-bacteremic pneumococcal pneumonia, perhaps because it has been difficult to identify non-bacteremic cases. The aim of this study was to compare clinical, radiological, microbiological, and epidemiological features of bacteremic and non-bacteremic pneumonia due to *S. pneumoniae*.

2. Methods

2.1. Design

We undertook a retrospective study from January 1995 through February 2003 of patients diagnosed with pneumococcal pneumonia in Hospital Clínico de San Juan (Alicante, Spain), a 350-bed, university-affiliated teaching hospital.

2.1.1. Patients

Patients were included in this study if they met the following criteria:

- *Patients with community-acquired pneumonia* (*CAP*)*:* A case of CAP was defined as an illness occurring in a patient older than 18 years presenting with symptoms of a lower respiratory tract infection, an infiltrate on chest radiography, and non-hospitalization of the patient in the preceding 72 h.
- *Bacteremic pneumococcal pneumonia:* Patients with CAP and one or more blood cultures yielding *S. pneumoniae*.
- *Non-bacteremic pneumococcal pneumonia:* Criteria for inclusion in this group were stringent in order to identify a group of patients in whom the diagnosis of non-bacteremic pneumococcal pneumonia could be regarded as unquestionable. This group included patients with CAP and detection of *S. pneumoniae* antigen in urine using a commercially available immunochromatographic assay (Binax NOW *Streptococcus pneumoniae* urinary antigen test; Binax) and at least three negative blood cultures, with the blood having been obtained before antibiotic therapy was begun. Because the Binax NOW *Streptococcus pneumoniae* urinary antigen test was available only after September 2002, all non-bacteremic cases were collected from this date through February 2003.

2.1.2. Baseline data

Patients' sociodemographic and clinical characteristics and laboratory findings were collected by medical record review and included:

1) Predisposing factors such as current smoker (currently or up until 6 months before admission), former smoker (>6 months), severe alcohol or drug abuse, homelessness, nursing home residents, diabetes mellitus, renal or hepatic chronic disease, human immunodeficiency virus (HIV) infection, chronic obstructive pulmonary disease (COPD), solid or hematological malignancy, coronary artery disease, number of hospital admissions in the previous year, congestive heart failure, neurological disease (stroke, dementia), prolonged use of glucocorticosteroids or other immunosuppressive drugs, asthma, neutropenia, and functional or anatomic asplenia.
2) Hematological and chemical tests, including renal and hepatic function, albumin, arterial oxygen saturation, pH, and bilirubin, were performed.
3) Chest radiographs from the time of admission were reviewed and radiological findings compatible with pneumonia were also collected. The type of infiltrate was classified as segmental (≤1 segment within 1 lobe), lobar (≥2 segments within 1 lobe), or multilobar. The presence or absence of pleural effusion was also determined.
4) Microbiological investigations included a total of three blood samples for aerobic and anaerobic culture, a urine sample for detection of *S. pneumoniae* urinary antigen and *Legionella pneumophila* serotype 1 urinary antigen (when available), and serum samples (obtained during the acute stage of illness and 2–4 weeks later) for serological testing. A complement fixation test was performed to detect antibodies against *Mycoplasma pneumoniae, C. pneumoniae, Chlamydia psittaci,* and *Coxiella burnetii.* An indirect immunofluorescence test was used to detect antibodies against *L. pneumophila.*

The presence of pneumococcal C-polysaccharide in urine was determined using a commercially available immunochromatographic assay (Binax NOW *Streptococcus pneumoniae*