ORIGINAL ARTICLE 10.1111/j.1469-0691.2012.03765.x

Community-acquired pneumonia in immunocompromised older patients: incidence, causative organisms and outcome

D. Sousa[1], I. Justo[1], A. Domínguez[2,3], A. Manzur[4], C. Izquierdo[5], L. Ruiz[5], M. Nebot[3,6], J.-M. Bayas[7], J.-M. Celorrio[8], W. Varona[9], P. Llinares[1], E. Miguez[1], E. Sánchez[1] and J. Carratalá[4]

1) *Department of Infectious Diseases. Complejo Hospitalario Universitario A Coruña, A Coruña,* 2) *Department of Public Health, University of Barcelona, Barcelona,* 3) *CIBER Epidemiología y Salud Pública (CIBERERSP),* 4) *Department of Infectious Diseases. Hospital Universitario de Bellvitge, Barcelona,* 5) *Department of Health, Generalitat of Catalonia, Barcelona,* 6) *Public Health Agency of Barcelona, Barcelona,* 7) *Department of Preventive Medicine and Epidemiology, Hospital Clinic, Barcelona,* 8) *Department of Preventive Medicine, Hospital Ernest Lluch, Calatayud and* 9) *Department of Preventive Medicine, Hospital Royo Villanova, Zaragoza, Spain*

Abstract

The number of elderly patients in the community with immunosuppressive conditions has increased progressively over recent decades. We sought to determine the incidence, causative organisms and outcome of community-acquired pneumonia (CAP) occurring in immunocompromised older patients. We prospectively compared cases of CAP in immunocompromised and non-immunocompromised patients admitted to five public hospitals in three Spanish regions. Of 320 cases studied, 115 (36%) occurred in immunocompromised patients, including: solid or hematological malignancy (97), corticosteroids or other immunosuppressive drugs (44), solid organ or stem cell transplant (five), and other conditions (eight). The etiology was established in 44% of immunocompromised patients vs. 32% of non-immunocompromised patients (p 0.03). *Streptococcus pneumoniae* was the most common causative organism in both groups (29% vs. 21%; p 0.08), followed by *Legionella pneumophila* (3% vs. 6%; p 0.01). Gram-negative bacilli were more frequent among immunocompromised patients (5% vs. 0.5%; p <0.01), particularly *Pseudomonas aeruginosa* (3% vs. 0%; p 0.04). Nocardiosis was only observed in immunocompromised patients (two cases). Bacteremia occurred similarly in the two groups. No significant differences were found with respect to ICU admission (8%, in both groups) or the length of stay (12.5 vs. 10.4 days). The early (<48 h) (3.5 vs. 0.5%; p 0.04) and overall case-fatality rates (12% vs. 3%; p <0.01) were higher in immunocompromised patients. In conclusion, a substantial number of older patients hospitalized for CAP are immunocompromised. Although relatively uncommon, CAP due to gram-negative bacilli, including *P. aeruginosa*, is more frequent among these patients. CAP occurring in immunocompromised patients causes significant morbidity and mortality.

Keywords: CAP, community-acquired pneumonia, elderly, immunocompromised, immunosuppression
Original Submission: 8 November 2011; **Revised Submission:** 28 December 2011; **Accepted:** 5 January 2012
Editor: G. Pappas

Clin Microbiol Infect

Corresponding author: D. Sousa, Unidad de E. Infecciosas. Complejo Hospitalario Universitario A Coruña. Xubias de arriba 84, 15006. A Coruña. Spain
E-mail: dsoureg@sergas.es

Introduction

Community-acquired pneumonia (CAP) is the third-most-frequent hospital diagnosis among patients aged ≥65 years and the sixth leading cause of death in developed countries. In Spain, the incidence of CAP in adults is 2–10 cases/1000 inhabitants/year; but increases to 25–35 cases/1000 inhabitants in people aged >70 years. At least 20% of patients with CAP require hospitalization. The mortality is 10–25%, and is particularly high in the elderly [1] and patients requiring intensive care unit (ICU) admission [2].

The number of elderly patients in the community with immunosuppressive conditions has increased progressively over recent decades [3]. Even though the clinical aspects of nosocomial pneumonia in immunosuppressed patients are well documented, there are few studies of CAP in patients

aged ≥65 years. Moreover, immunocompromised patients have been systematically excluded from prospective CAP studies. In addition, the Infectious Diseases Society of America and the American Thoracic Society consensus guidelines on the management of CAP in adults do not include recommendations for immunocompromised patients [4].

We sought to determine the incidence, causative organisms and outcome of CAP in immunocompromised older patients.

Methods

Setting, participants, and study design

A prospective, observational, multicenter study was conducted in patients aged ≥65 years hospitalized with CAP through the emergency departments of five public hospitals (providing universal free care to the whole population) in three Spanish regions (Aragon, Catalonia, and Galicia) between May 1, 2005 and January 31, 2007. Exclusion criteria were permanent nursing home residence, patients with nosocomial pneumonia (onset ≥2 days after hospital admission), patients whose initial diagnosis of pneumonia was not confirmed during the hospital stay, and CAP due to fungal or mycobacterial etiology.

We compared causative organisms and outcomes in cases of CAP in immunocompromised and non-immunocompromised patients. Outcomes variables analyzed were ICU admission, length of stay, and early and overall case-fatality rates. The ethics committee of each participating hospital approved the study. Oral consent was obtained from all participants or a close relative.

Clinical assessment, antibiotic therapy, and follow-up

At the initial visit, before starting empirical antibiotic therapy, participants underwent a complete clinical history and physical examination. Basic chemistry and hematologic tests, arterial blood gas determinations, and chest radiography were performed. There was not an established protocol for microbiological work up in the study. The microbiological tests were those routinely used in clinical practice at each center. Microbiological studies mainly included two sets of blood cultures and sputum Gram stain and culture when available. Urinary antigen detection for *S. pneumoniae* was performed as indicated by attending physician. Participants were stratified into risk classes and the validated prediction rule calculated according to the Pneumonia Severity Index (PSI) score, as previously described [5].

Empirical antibiotic therapy was administered according to individual hospital guidelines. One or more study investigators saw participants daily during their hospital stay and recorded clinical and microbiological data. The investigators made no decisions about ICU admission or hospital discharge, which were always made by attending physicians. A long-term follow-up visit was made *c.* 1 month after hospital discharge. All assessments were made using a standard protocol form with a checklist of items.

Definitions

Hospitalization criteria have been previously described [6]. Pneumonia was defined as a new infiltrate on chest X-ray and one or more of the following symptoms or signs of acute lower respiratory tract infection: cough, chest pain, fever >38°C, temperature <35°C, and dyspnea within the previous 24 h [7]. Immunosuppression was considered to be present when ≥1 of the following conditions were documented: underlying solid or hematological malignancy, solid organ or stem cell transplant, seropositivity for human immunodeficiency virus (HIV), splenectomy, radiotherapy, administration of corticosteroids (≥20 mg/day during 2 weeks in the last month) and other immunosuppressive drugs, and congenital or acquired immune deficiency disorder. The immunocompromised state had to be active at the time of patient's inclusion. A neoplastic disease was defined as active if it required medical or surgical intervention within the last year or if no-treatable metastases were present at time of the inclusion into the study. Radiotherapy was considered within the last 3 months and chemotherapy or corticosteroids within 1 month.

Length of stay (LOS) was measured in days and was calculated as the time from admission to the date of hospital discharge. The early case fatality-rate was defined as death from any cause ≤48 h after hospitalization. The overall case-fatality rate was defined as death from any cause within 30 days of hospitalization.

Microbiological studies

Pathogens in blood, normally sterile fluids, sputum and other samples were investigated using standard microbiological procedures. Isolation of *Legionella* was attempted in sputum and other respiratory samples by using selective media (buffered charcoal-yeast extract agar). *S. pneumoniae* antigen in urine was detected using rapid immunochromatography (NOW assay, Binax, Inc., Portland, ME, USA). *L. pneumophila* serogroup 1 antigen in urine was detected using immunochromatography (NOW *Legionella* Urinary Antigen, Binax, Inc.). Standard serological methods were used to determine antibodies against the following pathogens: *Mycoplasma pneumoniae* (indirect agglutination), *Chlamydia psittaci* [immunofluorescence (IF)], *Chlamydia pneumoniae* (micro-IF), *Coxiella*