
Chlamydia pneumoniae Community-Acquired Pneumonia: A Review of 62 Hospitalized Adult Patients

Summary: In a prospective study, Chlamydia pneumoniae was identified as the etiological agent in 62 (17.9%) of 346 adult patients hospitalized over the course of one year for community-acquired pneumonia at the Soroka Medical Center in Beer-Sheva, Israel. The diagnosis of C. pneumoniae infection was based on serological testing of antibodies by the MIF technique. In 43 of these patients (69.4%), at least one other etiological agent, in addition to C. pneumoniae for community-acquired pneumonia was identified. Streptococcus pneumoniae was identified in 34 patients with C. pneumoniae (54.8%), as an additional causative factor in infection. Community-acquired pneumonia patients with C. pneumoniae were significantly older than non-C. pneumoniae patients (p=0.03), had a higher APACHE II score on admission (p<0.05), a higher rate of positive blood cultures (p=0.02), and longer periods of hospitalization (p=0.022). Seven patients with pure C. pneumoniae infection recovered, despite treatment which is not considered to be specific for C. pneumoniae. It was concluded that C. pneumoniae is a common etiological agent for community-acquired pneumonia in our region, particularly in the elderly, and is characterized by a high rate of concomitant infections with other pulmonary pathogens. No specific clinical or radiological pattern was discerned that could distinguish between C. pneumoniae community-acquired pneumonia and non-C. pneumoniae community-acquired pneumonia.

Introduction

Chlamydia pneumoniae has been identified in recent years as a significant pathogen for community-acquired pneumonia (CAP). Its prevalence according to various studies ranges from 1.3–13% of all hospitalized adult CAP patients [1–3].

Three hundred and forty six adult patients hospitalized with CAP were included in a prospective study conducted over the course of one year in the Soroka Medical Center in Beer-Sheva, Israel. Serological evidence for C. pneumoniae as the etiological agent of CAP was found in 62 (17.9%) patients. This etiology was the third most common prevailing one (25.5%) among patients over the age of 55 years.

The aim of the present study was to analyze and describe the epidemiological, clinical, laboratory, radiological and therapeutic features of this group of 62 patients with C. pneumoniae CAP. The Soroka Medical Center is located in a city of 150,000 residents in the south of Israel. The center serves a population of 300,000 inhabitants of the Negev, a semi-arid region at sea level, in which the mean temperatures during the study year ranged from 27°C in the summer to 9°C in the winter. The mean annual precipitation (rain falls only during the winter) is approximately 200 mm.

Patients and Methods

Patients: We conducted a prospective study on the etiology of CAP in all 346 adult patients who were hospitalized with this diagnosis at the Soroka Medical Center over a period of one year between 1 November 1991 and 31 October 1992. The study was approved by the review board for human research (the Helsinki committee) of the Soroka Medical Center, and all patients gave their informed consent to participate.

The mean age of the patients was 49.3±19.5 years (SD, range: 17–94). One hundred and eighty seven patients (54%) were men. Sixteen patients (4.6%) died in the hospital. All other patients were alive at least 6 weeks after admission to the hospital. During the course of their hospitalization the patients were diagnosed and treated by the medical staff of the internal medicine wards, without intervention by the investigators. Upon discharge, the patients were referred to the investigators at the pulmonary disease clinic of the hospital for clinical and radiological follow-up.

CAP was diagnosed in the presence of an acute febrile disease, with an acute pulmonary infiltrate on chest X-ray, and a clinical and radiological course that confirmed the diagnosis. Exclusion criteria included patients with positive blood tests for HIV, patients with pulmonary malignancies, and patients who were discharged from the hospital less than 21 days before their current hospitalization with pneumonia.

In addition to routine hospital blood tests (complete blood

Received: 27 July 1995/Revision accepted: 27 November 1995

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Table 1: Frequency distribution of etiologies of community-acquired pneumonia in 346 patients.

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Number of patients (%)</th>
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<tbody>
<tr>
<td><em>Streptococcus pneumonia</em></td>
<td>148 (42.8)</td>
</tr>
<tr>
<td><em>Mycoplasma pneumoniae</em></td>
<td>101 (29.2)</td>
</tr>
<tr>
<td><em>Chlamydia pneumoniae</em></td>
<td>62 (17.9)</td>
</tr>
<tr>
<td><em>Legionella sp.</em></td>
<td>56 (16.2)</td>
</tr>
<tr>
<td><em>Viruses</em></td>
<td>35 (10.1)</td>
</tr>
<tr>
<td><em>Coxiella burnetii</em></td>
<td>20 (5.8)</td>
</tr>
<tr>
<td><em>Haemophilus influenzae</em></td>
<td>19 (5.5)</td>
</tr>
<tr>
<td><em>Other</em></td>
<td>21 (6.1)</td>
</tr>
<tr>
<td><em>Unknown etiology</em></td>
<td>67 (19.4)</td>
</tr>
</tbody>
</table>

*Including *Moraxella catarrhalis* (7), active pulmonary tuberculosis (7), non-pneumoniae *Streptococcus* (4), *Staphylococcus aureus* (1), *Acinetobacter* spp. (1), and *Pseudomonas aeruginosa* (1).

count, biochemistry and blood cultures), we drew blood within the first 48 h of admission for serological testing. A second (convalescent) serum was obtained from 308 patients (89%), usually at the follow-up appointment in the pulmonary clinic. The mean interval between the two serum samples was 31.7±12.1 days (range: 17–45). All sera were separated immediately and stored at −70°C until serum testing was performed.

Microbiological and serological testing and diagnoses: *C. pneumoniae* pneumonia was diagnosed using a micro-IF method utilizing *C. pneumoniae* elementary bodies (Washington Research Foundation, USA, and Kajaani 6, Finland) as antigen to detect IgG, IgA and IgM antibodies specific to *C. pneumoniae*. All IgM-positive sera were retested after treatment with Gull sorb (Gull Laboratories, USA), which removes IgG antibodies, thus avoiding false-positive IgM findings due to the presence of rheumatoid factor. A 4-fold or greater increase in titer for any immunoglobulin class between paired sera, an IgG titer ≥ 512, an IgA titer ≥ 64, or an IgM titer ≥ 16 in any serum was considered to be diagnostic of *C. pneumoniae* pneumonia.

Pneumococcal etiology was diagnosed by standard blood cultures and by two serological techniques. IgG antibodies to pneumococcal protein toxin, pneumolysin, were measured by EIA utilizing pneumolysin produced in *Bacillus subtilis* as antigen [1]. A rise in antibody titer equal to or more than two-fold between paired sera was considered diagnostic for pneumococcal infection [1, 2]. Pneumococcus-specific immune complexes were determined in all 654 (paired and unpaired) sera by measuring antibodies to pneumolysin and to the mixture of 23 capsular polysaccharides present in vaccine from precipitated and redissolved immune complexes [3, 4]. The cut-off value for the presence of pneumococcal immune complexes was based on testing of serum samples from 40 healthy elderly people. CAP was considered to be of pneumococcal etiology if there was a positive culture for pneumococcus (blood or pleural fluid), or at least one positive serological test.

Total antibodies to unencapsulated *Haemophilus influenzae* [5] and *Moraxella catarrhalis* [6, 7] were measured by EIA using whole bacterial cells of respective bacteria as antigens. A rise in antibody titer of ≥ 3 between paired sera was considered to be diagnostic [5].

*Mycoplasma pneumoniae* etiology was determined with two different commercial serological kits. The antibody titer was determined by microplate agglutination using the commercial kit Serodia-Myco II (Fujirebio, Japan). In this method, patients were positive for *M. pneumoniae* if they had a 4-fold increase in antibodies in the paired sera, and/or an antibody titer of at least 160 in at least one serum sample as described by Echevarria et al. [8]. The antibody titer for *M. pneumoniae* was also determined by the antibody capture enzyme immunoassay method using the commercial kit Sero *M. pneumoniae* test kit (Diatech Diagnostics, Israel). With this method, a patient was positive if IgM antibodies were present in at least one serum sample or if there was evidence of seroconversion or a significant increase in IgG titer between the two sera. *M. pneumoniae* was considered the etiologic agent for CAP in patients who were positive for *M. pneumoniae* in at least one of the two serological tests.

Serological testing for *Coxiella burnetii* was performed using a commercial kit for indirect immunofluorescence (INDX, Integrated Diagnostics Inc., Baltimore, MD). *C. burnetii* was considered to be the etiological agent in the presence of a four-fold or greater increase in IgG titers between the first and the second serum samples, or a positive test for IgM in a single dilution of 1:80.

Antibodies to 21 different serogroups of *Legionella* spp. were detected using the indirect immunofluorescence test. Formalin fixed *Legionella* bacteria served as antigens. *Legionella* spp. were considered to be the etiological cause of CAP in the presence of a four-fold or greater increase in IgG or if the IgM titer was ≥ 64.

Viral etiologies for CAP were assessed by complement fixation for influenza A, influenza B, adenovirus, respiratory syncytial virus (RSV), parainfluenza 1 and parainfluenza 3, six common respiratory viruses. Testing was carried out with commercial antigens (Virion Ltd, Cham, Switzerland). A viral etiology for CAP was determined if there was evidence for a four-fold or greater increase in antibody titers for a specific viral agent between paired sera.

Data analysis: The χ² test was used to determine the significance of differences in proportions between groups. Student's t-test was used to determine whether the means of continuous variables were significantly different. A p-value < 0.05 was considered to be statistically significant.

Results

Table 1 shows the frequency of various etiological agents for CAP among the 346 patients hospitalized with this diagnosis. In all, 532 etiologies were identified in 279 patients. In 146 patients (42.2%), one causative agent for CAP was identified, while in 133 patients (38.4%), more than one causative agent was found.

*M. pneumoniae* was identified as the etiologic agent in 54.8% of patients (54.8%), a significantly high rate (p=0.03) when compared with the 114 patients (40.1%) with this diagnosis among the 284 patients in the non-*C. pneumoniae* group. There were no statistically significant differences in relation to other etiological agents. Figure 1