Clinical Characteristics of *Chlamydia pneumoniae* Infection as the Sole Cause of Community-Acquired Pneumonia

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The clinical characteristics of 26 patients with community-acquired pneumonia due to *Chlamydia pneumoniae* as the only identified pathogen who required hospitalization were evaluated. Most patients (18) had reinfection based on serological results. The mean age of the patients was 55 years (38 years, patients with primary infection; 63 years, patients with reinfection), and the gender representation was equal. Generally, illness was mild and associated with limited temperature elevation and nonspecific symptoms. The presence of comorbid illnesses and the requirement of supplemental oxygen therapy were the most common criteria for hospital admission.

Prevalent studies have suggested that *Chlamydia pneumoniae* accounts for ~6% to 10% of cases of community-acquired pneumonia (CAP) requiring hospitalization [1, 2]. It has also been suggested that *C. pneumoniae* is often a copathogen of CAP. In a compilation of eight studies of CAP reviewed by Kauppinen and Saikku [2], a total of 176 cases of *C. pneumoniae* pneumonia were identified, of which 68 (39%) represented pneumonia with more than one apparent etiology. The most common associated organism was *Streptococcus pneumoniae*. In such cases, upper or lower respiratory tract infection caused by *C. pneumoniae* may pave the way for invasion by other bacteria such as *S. pneumoniae*. The clinical characteristics of these infections may reflect manifestations of infection with the associated pathogen rather than manifestations of *C. pneumoniae* infection. One previous study found that pneumonia due to dual infection with *C. pneumoniae* and *S. pneumoniae* resulted in a more severe illness than did *C. pneumoniae* infection alone [3].

To further clarify the clinical characteristics of patients with CAP due to *C. pneumoniae* as the sole pathogen who require hospitalization, we evaluated data for patients with pneumonia and a definitive serological diagnosis (fourfold rise in antibody titer) or possible (a static IgG antibody titer) in this study. Patients were categorized as having definite (fourfold rise in antibody titer) or possible (a static IgG antibody titer of $\geq 1:512$ or an IgM antibody titer of $\geq 1:16$) *C. pneumoniae* infection [4]. During the first year of the population-based pneumonia etiology study, definite infection with *C. pneumoniae* was observed in 2.4% of cases, and possible infection was observed in an additional 6.5% [4].

**Methods**

Data analyzed for this report were from a community-based study of the incidence of pneumonia among adults that was conducted in Franklin County and Summit County, Ohio, during 1991–1992 [4]. All patients were 18 years of age or older and had clinical manifestations and a chest radiograph revealing a new infiltrate consistent with pneumonia. All patients (or family members) were interviewed with use of a standardized questionnaire (>100 questions) addressing symptoms and medical history. In addition, charts were reviewed, and information concerning demographic characteristics, underlying health conditions, and results of radiographic and laboratory studies at presentation was collected. Samples of blood, urine, and sputum (if produced) were obtained.

Cultures of sputum for routine bacteria and *Legionella* species were performed in all cases. Specimens for additional cultures (i.e., those for viruses and mycobacteria) were obtained on the basis of the preference of the attending physicians.

In all cases, urine was tested for *Legionella* antigen. Paired serum samples (obtained 4–6 weeks apart) from all patients were tested at the Centers for Disease Control and Prevention for *Legionella* (immunofluorescence), *Mycoplasma pneumoniae* (CF test), and *C. pneumoniae* (microimmunofluorescence). Paired serum samples from patients admitted to the hospital between November and May were also tested for influenza and respiratory syncytial viruses.

The diagnosis of *C. pneumoniae* infection was based on results of serological tests of paired serum samples; neither PCR assay nor culture for *C. pneumoniae* was performed in this study. Patients were categorized as having definite (fourfold rise in antibody titer) or possible (a static IgG antibody titer of $\geq 1:512$ or an IgM antibody titer of $\geq 1:16$) *C. pneumoniae* infection [4]. During the first year of the population-based pneumonia etiology study, definite infection with *C. pneumoniae* was observed in 2.4% of cases, and possible infection was observed in an additional 6.5% [4]. For the
purposes of the present study, we evaluated only patients with a definite serological diagnosis. Serological responses were divided into two patterns, primary infection and reinfection, as previously described [1, 5]. Briefly, primary infection is generally characterized by the early appearance of IgM antibody with a delayed appearance of IgG antibody; in reinfection, IgM antibody is usually absent or present in low titers, and there is an earlier higher rise of IgG antibody titer.

Results

Forty-seven patients with a fourfold rise in titers of antibody to *C. pneumoniae* were identified by microimmunofluorescence. Twenty-one patients had other definite or possible pathogens identified: *S. pneumoniae*, 7 patients (2 of whom were bacteremic); *Haemophilus influenzae*, 3; *Neisseria meningitidis*, 2 (both of whom were bacteremic); *Staphylococcus aureus*, 1; group F streptococcus, 1; gram-negative bacilli, 4 (1 of whom was bacteremic); *Legionella pneumophila*, 2; and *M. pneumoniae*, 1.

Twenty-six patients had no other pathogens identified. Serological responses of these patients were as follows: primary infection, seven patients; and reinfection, 18. The serological response for one patient was undetermined because only IgG antibody titers were measured (IgM antibody titers were not available for analysis). This patient was excluded from the analysis comparing characteristics of primary infection with those of reinfection. The characteristics of the 26 patients with CAP due to *C. pneumoniae* as the sole pathogen who required hospitalization are shown in table 1. Gram staining of sputum from our patients who were able to expectorate appropriate specimens most often showed polymorphonuclear leukocytes without an organism. The most common radiographic finding was a localized segmental infiltrate (13 patients [50%]); other findings were variably described as patchy, interstitial, or mixed.

Clinical characteristics associated with primary infection or reinfection were analyzed separately and were similar except for age and temperature at admission. The mean age for patients with primary infection was significantly less than that for patients with reinfection: 38 vs. 63 years, respectively (0 and 76%, respectively, of these patients were 55 years of age or older; OR, 0.04; 95% CI, 0.00 – 0.04). The mean temperature was higher for patients with primary infection than for those with reinfection: 38.9°C vs. 37.7°C, respectively (86% and 33%, respectively, of these patients had temperatures of >38°C; OR, 12.00; 95% CI, 1.16 –123.0). The following trend was found: the likelihood of a localized segmental infiltrate associated with primary infection (five [83%] of six) was greater than that associated with reinfection (eight [40%] of 20). Wheezing was found during examination in 22% of patients with reinfection but was not found in patients considered to have primary infection.

Discussion

The general perception is that *C. pneumoniae* causes mild, atypical pneumonia. However, this characterization is primar-
ily based on studies using serology for diagnosis that often include patients with a single elevated IgG antibody titer as the sole criterion of diagnosis or patients with infection due to another pathogen. The present evaluation sought to eliminate these concerns as an issue since we included only patients who had a fourfold rise in antibody titer and excluded patients who had a copathogen present. Characteristics of our 26 patients who had definitive CAP due to *C. pneumoniae* without an identified copathogen are consistent with the general perception that *C. pneumoniae* causes mild pneumonia often associated with a limited temperature elevation and nonspecific symptoms. However, since acute- and convalescent-phase serum samples from our patients were required for inclusion in the study, it is possible that we missed cases associated with severe disease (and possible death). Severe pneumonia due to *C. pneumoniae* has been previously described [5].

Although no signs or symptoms appear to be unique to pneumonia due to *C. pneumoniae*, several comments may be made from our results as well as those of previous studies [1–3]. A subacute course is common in most patients who have symptoms for 1 week before admission. Cough is common but is often nonproductive. Fever is usually low grade. Kuo et al. [5] indicated that symptoms of sinus infection are common and that sore throat, sometimes with hoarseness, is often present early in the course of illness—often before the onset of pneumonia. We found that sore throat and hoarseness were common symptoms in our patients (42% and 36%, respectively).

The clinical characteristics associated with primary infection may be difficult to distinguish from those of reinfection because of the confounding effect of comorbid conditions on age. However, one study conducted in Finland during an epidemic in military conscripts compared the symptoms of primary infection with those of reinfection in young adults [6]. Those patients with primary infection were more often hospitalized and more often had fever, an elevated sedimentation rate, rales, and chest pain. We found fever to be more commonly associated with primary infection than reinfection, whereas chest pain was found equally in our two groups of patients.

In conclusion, the results of our evaluation suggest that patients with CAP due to *C. pneumoniae* as the sole cause who require hospitalization (based on a fourfold rise in antibody titer) have characteristics similar to those of patients with pneumonia caused by other etiologies. The severity of illness in patients who had antibody titers in acute- and convalescent-phase serum samples was relatively mild, however, and the presence of comorbid illnesses and the requirement of supplemental oxygen therapy were the most common criteria for hospital admission.

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