Severe Community-Acquired Pneumonia with Acute Hypoxemic Respiratory Failure Due to Primary Infection with *Chlamydia pneumoniae* in a Previously Healthy Adult

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Community-acquired pneumonia due to *Chlamydia pneumoniae* is associated with a benign clinical course. Severe, life-threatening pneumonia is rare and occurs only in immunocompromised hosts. We report a case of severe pneumonia complicated by acute hypoxemic respiratory failure due to primary infection with *C. pneumoniae* in a previously healthy 46-year-old woman.

*Chlamydia pneumoniae* is an important pathogen of the respiratory tract. Infection with this strain results in a wide spectrum of clinical manifestations that vary from subclinical infection to severe pneumonia requiring hospitalization, and reinfection is very common [1, 2]. Pneumonia due to *C. pneumoniae* usually has a prolonged but mild clinical course. Severe, life-threatening pneumonia is rare and occurs only in elderly individuals or in patients with chronic disease. Comorbid illness and coinfection with another pathogen appear to be important determinants of disease severity in this group of patients [1–5]. Here, we report an unusually severe case of community-acquired pneumonia (CAP) due to infection with *C. pneumoniae* in a previously healthy adult. Serological testing with a species-specific microimmunofluorescence (MIF) assay established the diagnosis in a timely fashion and revealed that *C. pneumoniae* infection was the primary infection.

A previously healthy 46-year-old white woman was admitted to the hospital because of pneumonia and acute respiratory failure. The patient had been healthy until 12 days earlier, when she developed a common cold-like illness with low-grade fever (temperature, 37.5°C), sore throat, nonproductive cough, and weakness. Two days before hospital admission, her temperature increased to 39.5°C, and her cough became productive, with a mucopurulent expectoration. The patient had not received any antimicrobial treatment. The medical history was unremarkable. She was a nonsmoker, worked as a household cleaner, had no risk factors for HIV infection, had no history of foreign travel, and denied abusing alcohol.

At hospital admission, the patient complained of right-side pleuritic chest pain, and she was pale and in respiratory distress. Her temperature was 39.5°C, her pulse was 100 beats/min, her respiration rate was 30 breaths/min, and her blood pressure was 110–75 mm Hg. Auscultation revealed a few crackles over the left-lower lung field and diffuse crackles over the right-lower and right-middle lung fields. Radiography performed at the time of hospital admission revealed alveolar-type lung infiltrates with nodular opacities in the right-middle, the right-lower, and (less so) the right-upper lung fields (figure 1).

The findings of laboratory studies were remarkable: the WBC count was 32,400 cells/μL (75% neutrophils), and the erythrocyte sedimentation rate (ESR) was 104 mm/h. Arterial blood gas determination with a fraction of inspired oxygen (FiO2) of 21% was compatible with acute hypoxemic respiratory failure (partial pressure of oxygen, arterial [PaO2], 50 mm Hg; partial pressure of carbon dioxide, arterial [PaCO2], 28 mm Hg; pH, 7.53). Bronchoscopy was performed, and a bronchoalveolar lavage (BAL) specimen was obtained from the right-middle lobe 32 h after hospital admission. The mucosa appeared to be edematous and bled easily, especially at the right bronchial tree, and a profuse mucopurulent exudate was observed. Examination of the BAL specimen revealed a WBC count of $19 \times 10^4$ cells/mL (70% macrophages, 13% neutrophils, 11% lymphocytes, and 6% eosinophils). Blood, sputum, and BAL specimens were obtained for bacterial cultures, the results of which were negative. Sputum and blood culture samples were obtained before and BAL culture samples were obtained after the initiation of antimicrobial therapy.

A serum sample obtained on the second hospital day was examined for *C. pneumoniae*-specific IgG and IgM antibodies with use of an MIF assay (MRL Diagnostic), which demonstrated the presence of IgM antibodies only (titer of $\geq 1:16$ after absorption of rheumatoid factor). A second serum sample obtained 3 weeks after hospital admission revealed IgG seroconversion (titer, 1:1024), and IgM antibodies were still pre-

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Figure 1. Chest radiograph obtained at hospital admission showing alveolar-type lung infiltrates, with nodular opacities in the right-middle, right-lower, and (less so) right-upper lung fields.

sent. Paired serum samples were also tested for IgG- and IgM-specific antibodies to Mycoplasma pneumoniae and Chlamydia psittaci by MIF assay (Bios and MRL Diagnostic, respectively) and to Legionella pneumophila, Coxiella burnetti, respiratory syncytial virus, cytomegalovirus, Epstein-Barr virus, influenza viruses A and B, parainfluenza viruses 1, 2, and 3, and adenovirus by ELISA (Serion). The results ruled out infection with these pathogens.

The patient was initially treated with intravenous sodium cefuroxime (750 mg q8h) and erythromycin (1 g q6h) and received oxygen with a Venturi mask (Fio2, 31%). Sodium cefuroxime therapy was discontinued as soon as serological diagnosis was obtained (hospital day 4). On hospital day 8, clinical improvement was evident (Fio2, 21%; PaO2, 65 mm Hg; PaCO2, 36 mm Hg; pH, 7.42; WBC count, 13,000 cells/µL; and ESR, 72 mm; the patient was afebrile for 24 h), and oral azithromycin (500 mg q.d.) was substituted for erythromycin. Two days later, the patient’s temperature increased again to 37.5°C, and her respiratory function deteriorated (Fio2, 21%; PaO2, 55 mm Hg; PaCO2, 29 mm Hg; pH, 7.53). Therefore, azithromycin was replaced with intravenous erythromycin (1 g q8h) for the next 12 days. Chest CT was performed on the 20th day of hospitalization and revealed multiple patchy lung infiltrates in the right-lower and right-middle lung lobes and a large triangular lung infiltrate with airspace consolidation adjacent to the pleura at the right-middle lobe (figure 2). After the patient had been afebrile for 3 days and demonstrated a constant improvement in respiratory function, she received an 8-day course of oral erythromycin (500 mg q6h). One month after hospital admission, the patient was discharged, with respiratory function fully restored to normal. After several months, an in-house PCR assay specific for C. pneumoniae was developed [6]; the frozen BAL specimen was tested with it, and the result was positive.

This previously healthy 46-year-old woman demonstrated the biphasic illness associated with C. pneumoniae pneumonia but developed a strikingly severe disease that is reported to occur only in elderly patients or patients with severe chronic disease. This unusual presentation prompted extensive laboratory testing, and the diagnosis of primary infection with C. pneumoniae was established, although C. pneumoniae DNA was detected in the BAL specimen only retrospectively. Severe pneumonia due to C. pneumoniae has been associated with coinfection with other pathogens [1, 2, 7]. No other pathogen was identified in this case, however, and a likely explanation for this severe pneumonia is the fact that it represented the primary encounter of a host beyond the age of early adulthood with C. pneumoniae. Limited data exist on the interplay between patient age, severity of disease, and primary-versus-secondary encounters with this pathogen [2, 5, 7]. Among patients with CAP, young adults more often have primary infection, whereas reinfection is far more prevalent among older adults and elderly persons. Severe, life-threatening pneumonia occurring in elderly persons or patients with chronic disease is also usually due to reinfection.

Our patient demonstrated a slow response to treatment and had a relapse. She did not tolerate intravenously administered treatment because of thrombophlebitis-associated pain, and erythromycin was replaced by oral azithromycin on the eighth day of hospitalization, because azithromycin is not available for parenteral use in Greece. She was improving clinically but had been afebrile only for 24 h. After 2 days, her condition relapsed. Because of the severe clinical presentation and the relapse, the patient received prolonged antimicrobial treatment. Although the slow clinical response and frequent relapses requiring additional treatment were observed in the early studies of C. pneumoniae pneumonia [8], no controlled trials addressing the issue of treatment duration exist.

To our knowledge, only 3 cases of unusually severe CAP associated with C. pneumoniae in previously healthy adults have been reported in the literature [9–11]. Although definitive laboratory diagnosis, exclusion of coinfection, and exclusion of mere colonization were not established for all of these cases,
the cases illustrate the potential for *C. pneumoniae* to cause severe, life-threatening infection in previously healthy hosts.

Laboratory diagnosis of *C. pneumoniae* infection is difficult to obtain [1, 7]. This fastidious pathogen grows poorly on cell culture, antigen detection methods have low sensitivity, and nucleic acid amplification techniques are not widely available or standardized. The only sensitive and specific test is the species-specific MIF assay, which also allows for the discrimination between primary infection, reinfection, and past exposure. However, this assay is not routinely used, because the results cannot be obtained in a timely fashion [2]. Furthermore, performing the test requires expertise, and the test is expensive and not yet standardized [12].

This case report demonstrates that *C. pneumoniae* can cause severe CAP complicated by acute hypoxemic respiratory failure not only in immunocompromised and/or elderly hosts but also in previously healthy adults. The lack of precise laboratory diagnosis may mean that the full clinical spectrum of *C. pneumoniae* infection has been overlooked. As more-accurate, faster, and standardized methods become available, the spectrum of disease caused by *C. pneumoniae* will be better defined, and patient treatment will be further optimized.

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**References**