Self-limiting Pneumonia Due to *Chlamydia pneumoniae*

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Abstract

A case of self-limiting pneumonia due to *Chlamydia pneumoniae* is described. A 39-year-old male visited our hospital complaining of a persistent cough. No antibiotics were administered to this patient because of the absence of fever and a mild positive inflammatory response, but an infiltrate on a chest radiograph improved. Finally, a diagnosis of *C. pneumoniae* pneumonia was made by seroconversion of the *C. pneumoniae*-specific antibody and detection of the *C. pneumoniae* gene in bronchoalveolar lavage fluid. Self-limiting *C. pneumoniae* pneumonia is rarely encountered, although self-limiting upper respiratory tract infections due to *C. pneumoniae* are common. Thus, most self-limiting *C. pneumoniae* pneumonia may be missed when symptoms are minimal. (Internal Medicine 44: 870–874, 2005)

Key words: *Chlamydia pneumoniae*, self-limiting, asymptomatic infection, community-acquired pneumonia, antibody response

Introduction

Chlamydia pneumoniae is a major pathogen in a variety of respiratory infections (1). It is involved in a wide spectrum of various respiratory tract infections in both immunocompetent and immunocompromised hosts (1). In several epidemiological studies on pneumonia, *C. pneumoniae* was a relevant cause of community-acquired pneumonia (CAP) with a range of 6% to more than 20% of cases. It also often ranks among the third or fourth most common etiologic pathogen (2, 3). Most *C. pneumoniae* pneumonia is relatively mild, although patients with underlying medical conditions rarely become quite ill (1, 4–8). In addition, some *C. pneumoniae* upper and lower respiratory tract infections appear to be self-limiting (1, 4, 9). Here, we report a case of

self-limiting pneumonia due to *C. pneumoniae*, and discuss the antibody response.

Case Report

A 39-year-old male visited our hospital on April 19, 2002, complaining of a persistent cough and sputum production for one month without fever. He was admitted on the same day because a chest radiograph revealed a homogeneous infiltrate in the right middle and lower lung fields (Figs. 1 and 2). On admission, his temperature was 36.4°C with normal vital findings. The laboratory data revealed a normal white blood cell (WBC) count and mild elevation of C-reactive protein, ESR, ALT and γ -GTP (Table 1). His breath sounds were normal and no abnormal physical findings were observed. No microorganisms were observed in either sputum Gram's stain or culture. Urinary antigen tests for detection of *Streptococcus pneumoniae* and *Legionella* spp. were also negative (Table 2). On April 23, we carried out bronchoscopy, and the transbronchial lung biopsy specimen showed cryptogenic organizing pneumonia. However, no causative microorganisms were observed. We collected paired serum samples for a suspected chlamydial infection because his complement fixation (CF) titer against *Chlamydia* was significantly elevated on admission (Table 2). He was afebrile and had a mild positive inflammatory response, and the infiltrate on chest radiograph improved without antibiotics (Fig. 3). A diagnosis of *C. pneumoniae* pneumonia was made by seroconversion of *C. pneumoniae*-specific antibody between the paired serum samples, and the *C. pneumoniae* gene detected in bronchoalveolar lavage fluid (BALF) by the polymerase chain reaction (PCR). Finally, we did not use antibiotics after diagnosis of *C. pneumoniae* infection, but no relapse was observed for more than one year.

Laboratory tests for *Chlamydia* species

Nasopharyngeal swab and BALF specimens were obtained from the patient for isolation in cell culture and the PCR. These specimens were placed in a sucrose-phosphate-

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Figure 1. Chest radiograph on admission shows a homogeneous infiltrate in the right middle and lower lung fields.

Figure 2. Chest computed tomographic scan on admission demonstrates a homogeneous infiltrate with airbronchogram in the right middle lobe.

inclusions. Inclusion bodies formed in the cells were observed with a Nikon epifluorescence microscope at $\times 200$ or $\times 400$ magnification. The *C. pneumoniae*-specific and genus-specific primers used for PCR were from the DNA base sequence within the 53-kDa protein gene and major outer membrane protein gene, respectively, established in our laboratory. This assay was performed as previously described (10), and it was carried out without prior knowledge of the culture results.

Several serum samples were collected over a period of over six months and stored at -70°C until testing. Informed consent was obtained each time. The microimmunofluorescence (MIF) test was used for titration of IgG and IgM antibodies against *C. pneumoniae* (1), using formalinized elementary bodies of the *C. pneumoniae* TW-183 (purchased from the Washington Research Foundation, Seattle, WA, USA) and KKpn-15, and *C. trachomatis* L2/434/Bu and *C. psittaci* Budgerigar-1 strains as antigens (10). Sera with IgM against *Chlamydia* were retested after absorption with goat anti-human IgG antibody reagent (Gullsorb; Gull Laboratories, Salt Lake City, UT, USA) in order to exclude false-positive reactions.

glutamate transport medium. Culturing for *Chlamydia* was performed in cycloheximide-treated HEP-2 cells grown in a 24-well cell culture plate, as reported previously (10). Following incubation, a genus-specific fluorescein isothiocyanate-conjugated monoclonal antibody (Chlamydia FA Seiken; Denka Seiken, Tokyo, Japan) and *C. pneumoniae* species-specific monoclonal antibodies were used to stain

Discussion

C. pneumoniae has been established as an important cause of both lower and upper acute respiratory illnesses among children and adults (1). Pneumonia and bronchitis are the most frequently recognized illnesses associated with *C. pneumoniae*. On the other hand, asymptomatic or mildly

Table 1. Laboratory Findings on Admission

CBC: RBC	497×10 ⁴ /mm ³	Screening: TP	7.7 g/dl
Hb	14.9 g/dl	Alb	4.0 g/dl
Ht	44.5%	Glu	149 mg/dl
WBC	6,600/mm ³	ChE	371 IU/l
Neut.	74%	AST	27 IU/l
Eosino	6%	ALT	66 IU/dl
Baso.	1%	γ-GTP	185 IU/l
Mono.	3%	LDH	356 IU/l
Lymph.	16%	Bil-T	0.2 mg/dl
Platelets	44.9×10 ⁴ /mm ³	Crn	0.86 mg/dl
ESR:	64 mm•h	BUN	15 mg/dl
CRP:	5.3 mg/dl	UA	5.3 mg/dl
Urinalysis: Protein	(-)	Amy	144 IU/l
Sugar	(-)	Mineral:Na	138 mEq/l
Occult blood	(-)	K	3.8 mEq/l
Sediment WBC	0/HPF	Cl	104 mEq/l
RBC	0/HPF		

Table 2. Microbiological Tests on Admission

Sputum examination; Bacteria:	stain (-), culture normal flora
Mycobacteria:	stain (-), culture (-)
Serological test: <i>Mycoplasma pneumoniae</i>	PA 1 : 40, CF 1 : 16
<i>Chlamydia pneumoniae</i>	Immuno Card (-)
<i>Chlamydia</i> CF	ELISA: IgG 0.34, IgA 0.97
<i>Legionella</i> species	1 : 64
Mycotic examination	<1 : 16
	β-D glucan <6 pg/ml
	Aspergillus Ag, Ab (-)
	Candida Ag (-)
	Cryptococcus Ag (-)
Urinary antigen test: <i>Streptococcus pneumoniae</i>	(-)
<i>Legionella</i>	(-)

symptomatic *C. pneumoniae* infections are also common, since an approximately 50% prevalence of the serum antibodies to this organism have been reported in several countries (1, 4–6, 11). We have also reported the prevalence of asymptomatic infection with *C. pneumoniae* by isolation and the PCR in subjectively healthy persons (12).

Association of *C. pneumoniae* with clinical illnesses was fortunately discovered on routine chest radiographs during an epidemic of mild pneumonia in northern Finland in 1978 (4). In that survey, pneumonic infiltrates were found in 34 persons, and only one-third of the patients had received antibiotics and some patients were completely asymptomatic. In addition, recovery from *C. pneumoniae* pneumonia without effective antibiotics has been also described (13–16). Kauppinen et al (14) and Falguera et al (15) reported that only 36% and 50% of the patients, respectively, were treated with appropriate antibiotics, while the remaining patients were treated with inappropriate antibiotics, such as β-lactams. Lieberman et al (16) also reported that 63% of their patients in whom *C. pneumoniae* was identified as the only

etiologic cause of CAP were treated with appropriate antibiotics. The remaining patients were treated at all stages of their illness only with inappropriate antibiotics but all patients recovered completely (16). In our mouse model of chlamydial pneumonitis, all the infected mice with the *C. psittaci* california 10 strain died within seven days after nasal instillation (10⁵ inclusion forming units [IFU]/mouse) (17, 18), while all those infected with *C. pneumoniae* TWAR strains spontaneously recovered even when the sample size was increased (10⁶–10⁷ IFU/mouse) (19). The above clinical findings and mouse pneumonitis models strongly suggest that some cases of *C. pneumoniae* pneumonia are probably self-limiting. In these self-limiting cases, there is no general consensus that the anti-chlamydial antibiotics should be used.

In the present case, we concluded self-limiting *C. pneumoniae* pneumonia by serological and the PCR methods. Recently, we reviewed 62 cases of *C. pneumoniae* pneumonia collected from three hospitals in Okayama and 15 cases from a multicenter CAP surveillance study throughout

Self-limiting *C. pneumoniae* Pneumonia

Figure 3. Clinical course.

Figure 4. *Chlamydia pneumoniae*-specific IgG and IgM antibody response measured by the microimmunofluorescence test.

Japan (7, 8), however, there were no asymptomatic or self-limiting cases. Therefore, self-limiting pneumonia due to *C. pneumoniae* may be uncommon, although its incidence is unclear. Most self-limiting *C. pneumoniae* pneumonia may

have been missed if asymptomatic pneumonia is common.

Serological test is the most useful for determining the prevalence of *C. pneumoniae* infection in epidemiologic studies because *C. pneumoniae* is quite difficult to cultivate

in a cell culture system. Two patterns of antibody response to acute *C. pneumoniae* infections have been identified (1, 20): one is associated with primary infection and the other is associated with reinfection. In primary *C. pneumoniae* infection, a prompt chlamydial CF antibody response is seen. *C. pneumoniae* MIF IgM antibody appears later, about three weeks after the onset of illness. Antibody in the IgG fraction may not appear until six to eight weeks after onset. In reinfection, CF and IgM antibody may not appear or may appear only at low titers. The IgG antibody titer quickly rises within two weeks, and possibly reaches a titer value of 512 or more. In our case with primary infection, for the first five weeks, antibody responses were characterized by a relatively high-titered IgM antibody with a slowly developing lower-titered IgG antibody (Fig. 4). IgM antibody titers lasted for more than two months, whereas IgG titers rose after five weeks and reached a plateau after about three months. Because of the relatively long period until the development of a serologic response in a primary infection, the antibody response might be missed if convalescent sera were obtained too soon (i.e., earlier than three weeks after the onset of illness). To diagnose a primary infection with *C. pneumoniae* as shown in the present case, paired sera samples should be obtained at least four weeks apart as recommended by the Centers for Disease Control and Prevention (USA) and by the Laboratory Centre for Disease Control (Canada) (20).

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