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# *Chlamydomphila pneumoniae* Infection Induced Nodular Vasculitis

H. Sakuma S. Niiyama Y. Amoh K. Katsuoka

Department of Dermatology, Kitasato University School of Medicine,  
Sagamihara, Japan

## Key Words

*Chlamydia pneumoniae* · Erythema induratum · Erythema nodosum

## Abstract

We present the case history of a 48-year-old male patient with *Chlamydomphila (Chlamydia) pneumoniae* who developed a nodular vasculitis. He developed a cutaneous vasculitis with the onset of respiratory symptoms. The diagnosis of *Chlamydomphila pneumoniae* infection was based on serology. Since this infection is very common in our population, although often asymptomatic, it should be systematically considered as a causative agent of nodular vasculitis.

## Introduction

Erythema nodosum is the most common type of panniculitis; it may be due to a variety of underlying infectious or otherwise antigenic stimuli. Nodular vasculitis (erythema induratum) is a related but distinctly different clinicopathologic reaction pattern of the subcutaneous fat. It is classically caused by an antigenic stimulus from *Mycobacterium tuberculosis* but may be associated with several other underlying disorders. To our knowledge, there are only a few previous case reports of manifestations of nodular vasculitis in connection with *Chlamydomphila (Chlamydia) pneumoniae* infection.

## Case Report

A 48-year-old Japanese man with diabetes mellitus and sleep apnea syndrome presented with skin eruptions on his extremities that he first noticed 2 weeks prior to his admission to our hospital. A week after the appearance of the eruptions, he developed generalized malaise and a further week after that, he developed fever. He was diagnosed as having bacterial pneumonia by another hospital and treated with  $\beta$ -lactam antimicrobial agents, including cefdinir and ceftazidime for about 10 days,

but without effect. Thus, he visited the department of internal medicine of our hospital about 5 days before admission to our department.

Laboratory data on that day were as follows. Urine *Legionella* antigen and *Streptococcus pneumoniae* antigen were negative. Serum *Mycoplasma* antibody was negative (complement-fixation test). Anti-*C. pneumoniae* IgA 1.61 C.O.I. (negative <0.90), anti-*C. pneumoniae* IgG 2.85 C.O.I. (negative <0.90). On admission (day 1), body temperature was 37.4°C, blood pressure was 114/75 mm Hg, and pulse was regular, 101 beats/min. Laboratory results: hemoglobin 11.8 g/dl, WBC count  $10 \times 10^3/\mu\text{l}$  (neutrophil 71.0%), and PLT count  $37.6 \times 10^4/\mu\text{l}$ . CRP 6.87 mg/dl, total bilirubin 0.4 mg/dl, AST 12 IU/l, ALT 9 IU/l, creatinine 0.58 mg/dl, and albumin 3.4 g/dl. ANA and RF were negative. MPO-ANCA and PR3-ANCA were negative. Chest computed tomography (CT) showed interstitial pneumonia and alveolar pneumonia was intermingled.

Physical examination revealed crops of tender, violaceous nodules on his extremities, and their sizes ranged from 5 to 10 mm in diameter (fig. 1). Histopathological examination shows diffuse septolobular panniculitis of nearby vessels (fig. 2). Perivascular infiltrates with neutrophils, extravasation of red blood cells, and fibrinoid degeneration were identified (fig. 3). A direct immunofluorescent study showed no immunoglobulin deposition. He was diagnosed with *C. pneumoniae* infection, and this infection induced nodular vasculitis.

From the 2nd to the 17th day, he was treated with pazufloxacin, 1 g daily. The serum CRP fell gradually to become 0.57 mg/dl on the 16th day, and return to normal range by one month. After the 20th day, the indurated erythema began to improve, and seemed to run parallel with the improvement of the serum CRP. We measured it again 40 days after the first time: anti-*C. pneumoniae* IgA 0.95 C.O.I., anti-*C. pneumoniae* IgG 3.18 C.O.I.

## Discussion

Summarizing the case, our patient presented with the signs/symptoms of pneumonia with an interstitial shadow and an infiltrating shadow on chest CT. Cephems were ineffective, whereas the newer quinolones were effective. Changes in the blood antibody titers in addition to these observations and results suggested *C. pneumoniae* infection. Nodular vasculitis subsided along with improvement of the pneumonia following antibiotic administration, suggesting that it was caused by *C. pneumoniae* infection.

Several studies showed that *C. pneumoniae* infection could be involved in the pathogenesis of MPO-ANCA-associated glomerulonephritis, reactive arthritis, SLE, and adult onset of Still's disease [1]. Much less is known about the role of *C. pneumoniae* in the pathogenesis of systemic diseases. One explanation is molecular mimicry [2]. Immune responses and/or antibodies against it are unknown. *C. pneumoniae* antigen might cross-react with several body tissues such as the kidney, blood vessels, skin, joint, and muscle. Alternatively, *C. pneumoniae* can survive and replicate within the epithelial cells, macrophages, and neutrophils. *C. pneumoniae*-infected cells may then trigger abnormal signal transduction, resulting in changes of the cytokine profiles and activation and/or deactivation of immunocytes such as B cells, T cells, macrophages, and NK cells [3].

Nodular vasculitis has been associated with infectious tuberculosis and/or nontuberculous and noninfectious disorders. Infectious nontuberculous cases have been associated with *Nocardia*, *Pseudomonas*, and *Fusarium* [4]. There may also be an association with hepatitis B virus and hepatitis C virus [5]. Noninfectious associations may include previous episodes of superficial thrombophlebitis of the lower legs,

hypothyroidism, chronic lymphocytic leukemia, rheumatoid arthritis, and Crohn's disease [5].

Some reports in the past have shown that all cases of exanthema caused by *C. pneumoniae* are of the erythema nodosum type [6–12] (table 1). However, the histopathological findings in 3 [6, 11, 12] of the 7 exanthema cases have been reported previously, and these 3 cases showed features of vasculitis. Although omitted in those papers, the other 4 cases may also have been histopathologically found to show findings of vasculitis. It is therefore possible that the eruption reported as erythema nodosum is actually nodular vasculitis.

### Disclosure Statement

We have no conflict of interest in relation to the publication of this paper.

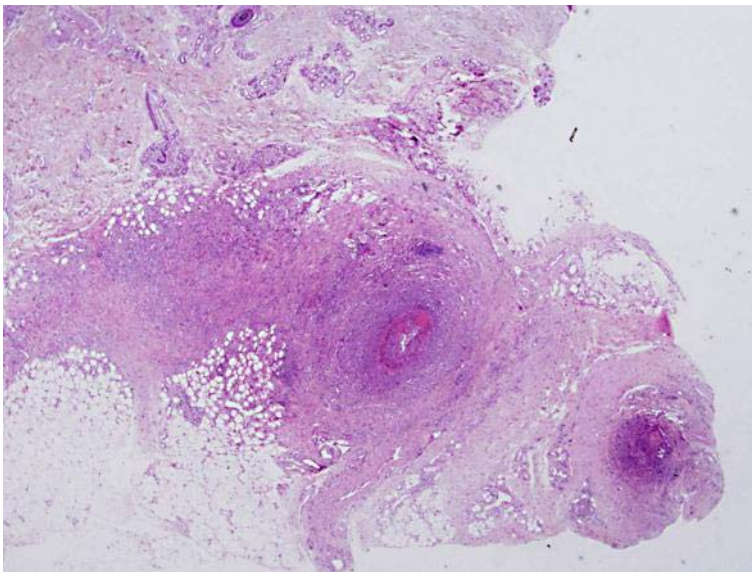
**Table 1.** Review of the literature concerning the association of *C. pneumoniae* infection with erythema nodosum

Reference number	Age/sex	Type of infection	Associated disease(s)	Diagnostic criteria of <i>Chlamydomphila</i> infection	Other findings
[6]	48/F	Lower respiratory	Episcleritis	CF	Histology: vasculitis
[7]	17/M 11/F	Lower respiratory Lower respiratory	None None	MIF MIF	
[8]	37/M	Lower respiratory	Myocarditis, reactive arthritis	MIF	
[9]	37/M	Meningitis	Hepatitis, iritis	MIF	Clinical diagnosis: atypical erythema nodosum or vasculitis
[10]	Not specified		Löfgren's syndrome	MIF	
[11]	45/M	Upper and lower respiratory	Reactive arthritis, conjunctivitis	MIF	Histology: vasculitis
[12]	42/F	None	None		Histology: infiltrations around the vessels
Present study	48/M	Lower respiratory	None		Histology: vasculitis

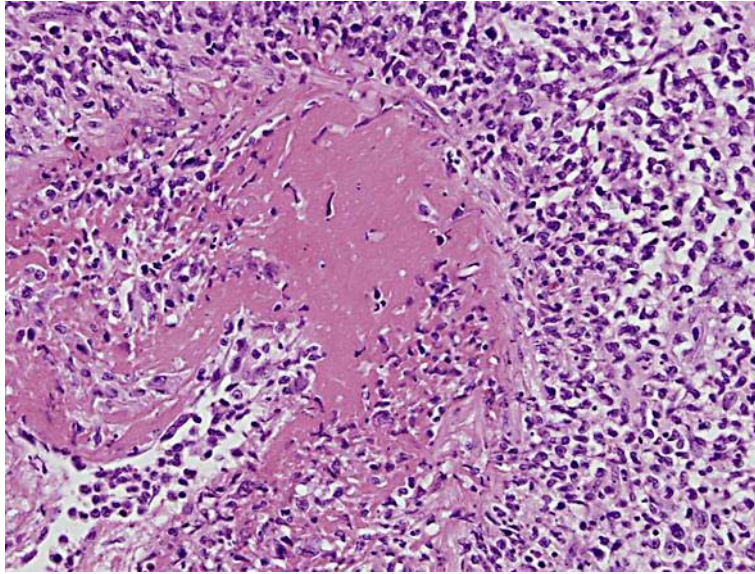
CF = Complement fixation; MIF = micro-immunofluorescence.



**Fig. 1.** Several indurated erythema on the patient's thigh.



**Fig. 2.** Diffuse septolobular panniculitis of nearby vessels.



**Fig. 3.** Necrotizing vasculitis in the lower dermis.

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