

Acute Q Fever with Jaundice and Pleuritis Refractory to Doxycycline or Levofloxacin Monotherapy : A Case Report

Po-Lin Chen¹, Nan-Yao Lee¹, and Wen-Chien Ko^{1,2}

¹*Division of Infectious Diseases, Department of Internal Medicine,
National Cheng Kung University Hospital;*

²*Department of Medicine, College of Medicine,
National Cheng Kung University, Tainan, Taiwan*

Abstract

Q fever, caused by *Coxiella burnetii*, is an emergent infectious disease in Taiwan. Major clinical presentations of indigenous cases of acute Q fever were acute febrile illness and hepatitis. Here, we report a case of acute Q fever complicated with mild jaundice and pleuritis. He did not respond well to doxycycline or levofloxacin initially, but recovered subsequently with adjuvant steroid therapy. (J Intern Med Taiwan 2007; 18: 371- 374)

Key Words : Q fever, *Coxiella burnetii*, Hepatitis, Jaundice, Steroid, Doxycycline

Introduction

Q fever is a worldwide zoonotic infection caused by *Coxiella burnetii*. In Taiwan, Q fever is not uncommon and could be viewed as an emerging infectious disease^{1,2}. Major clinical presentations of acute Q fever include febrile illness, pneumonia, and hepatitis³. The diagnosis of Q fever is usually relied on serological immunofluorescence assay (IFA), and an-

tibody is usually detectable three weeks after onset of clinical symptoms³. Drug of choice for Q fever includes doxycycline, newer macrolides, and fluoroquinolones^{4,5}. This report described an unusual case of Q fever with prolonged fever and successfully treated with steroid and antibiotics.

Case Report

A 53 year-old, male presented to emergency

Correspondence and requests for reprints : Dr. Po-Lin Chen

Address : Division of Infectious Diseases, Department of Internal Medicine, National Cheng Kung University of Hospital, No.138, Sheng Li Road, Tainan, 704, Taiwan

room with intermittent high fever about one week. He was healthy previously and denied any systemic disease. He was an onion farmer, and lived in Heng-Chun Town, Pingtung County. He denied recent animal contact or travel. His son and elder brother who lived together with him, had pulmonary tuberculosis, and completed anti-tuberculosis therapy six months ago.

On arrival, relative bradycardia was detected, with a heart rate of 92 beats per minute, in conjunction with high fever of 39 °C. Epigastric tenderness was noted. Initial serum biochemistry profiles revealed AST 138 IU/L, ALT 152 IU/L, alkaline phosphate (ALK-P) 185 IU/L, and total bilirubin (Bil-T) 1.8 mg/dL. Maximal serum level of ALT was 165 IU/L, AST 220 IU/L, Bil-T 2.2 mg/dL and ALK-P 224 IU/L. In addition, thrombocytopenia (platelets 92,000/mm³) and activated partial thrombin time (aPTT) of 50.5 seconds (normal value 30.0 seconds) were detected. White blood cell counts, hemoglobin, and serum creatinine were normal. Chest X-ray was normal. Abdominal computed tomography showed mild fatty liver and thickening of gallbladder wall. Gastroendoscopic examination found gastric ulcer. Blood cultures were sterile.

Empirical antibiotic therapy with intravenous

ceftriaxone (1g per 12 hours) and oral doxycycline (100 mg per 12 hours) were given. Fever subsided on the 4th day, and he insisted discharge next day with the prescription of oral levofloxacin (500 mg per day). However, he was re-admitted five days later due to intermittent fever and left pleuritic pain. Left pleural effusion was recognized (figure 1). Pleural effusion was inflammatory in characteristics (white blood cells 1300/mm³, neutrophil 93%, lymphocyte 4%, and red blood cells 150,000/mm³) and sterile. Coagulopathy was still noted with aPTT of 72.4 seconds (normal value 28.7 seconds). Anticardiolipin antibody and lupus anticoagulant were positive. However, AST, ALT and Bil-T were within normal range. Paired serums of antibodies for leptospirosis, *Orientia tsutsugamushi*, *Rickettsiae typhi* and dengue virus showed negative results. Serological surveys for hepatitis A, B, and C virus infection were all negative. Inflammatory gallium scan did not reveal significant lesions.

After admission, oral doxycycline and intravenous cefpirome were resumed. The latter drug was discontinued 5 days later because of sterile blood cultures. Serum obtained on 16th hospital day showed positive IgG and IgM antibodies for *C. burnetii* (phase

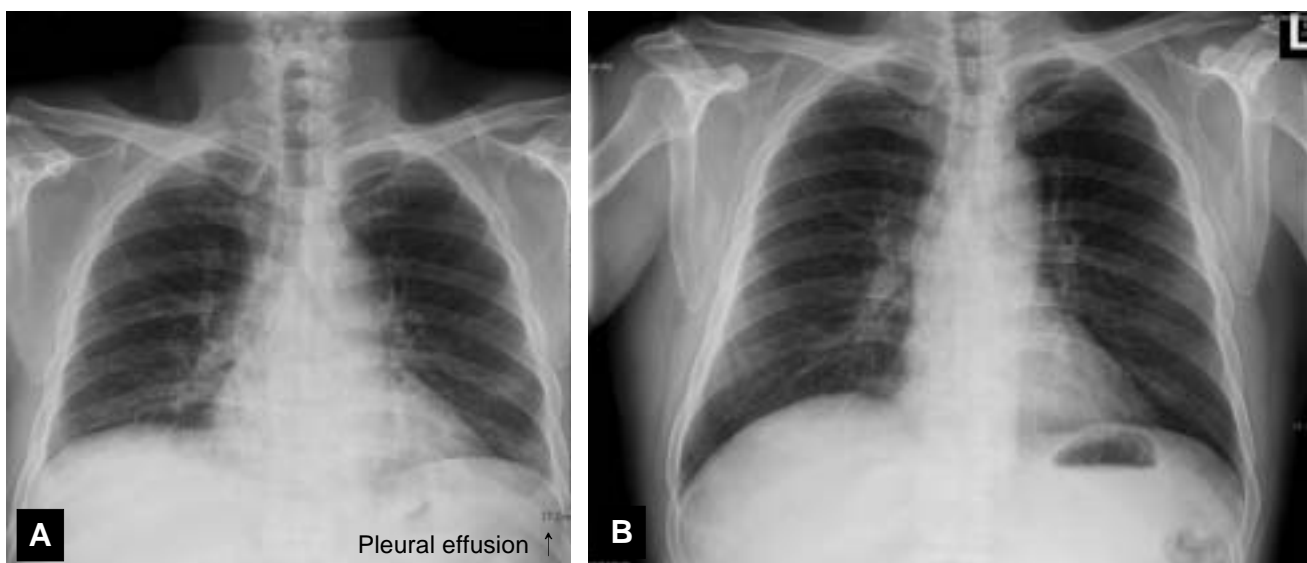


Fig.1. The chest film of a case of acute Q fever: pleuritis with left-side pleural effusion noted on day 21 (A). Left-side pleural effusion in resolution after antibiotic and adjuvant steroid therapy (B).

IgG 1:160; phase II IgG 1:640; phase I and II IgM 1:160). Under the impression of acute Q fever with inadequate clinical response to doxycycline, oral levofloxacin (500 mg per day) and prednisolone (30 mg per day) were initiated. He became afebrile after 20th hospital day. Light-side pleuritis and pleural effusion was also improved. After discharge, he received oral levofloxacin for another two weeks, and was free of relapse in the follow-up for one month.

Discussion

Q fever, caused by *Coxiella burnetii*, is a zoonotic disease, and in human it often had two clinical patterns: acute and chronic forms. Common presentations of acute Q fever included febrile illness, hepatitis, and pneumonia, and varied in regions³.

Acute Q fever can be regarded as an emerging infectious disease in southern Taiwan. Moreover, febrile illness and elevated aminotransferases are the major clinical manifestations^{1,2}. In previous literatures, frank hepatitis with jaundice has been rarely reported³. In a study from southern Taiwan, all 28 patients with acute Q fever had elevated aminotransferases, and five of them developed hyperbilirubinemia⁶. In Chung's study in the same area, eight of 35 patients with elevated aminotransferases developed hyperbilirubinemia (serum total bilirubin \geq 2 mg/dL), and tented to have delayed defervescence

even with presumed effective therapy⁷. Although the definition of hyperbilirubinemia varied between studies, it suggested that a substantial proportion of acute Q fever cases in southern Taiwan will develop hyperbilirubinemia during symptomatic courses of acute Q fever.

Pneumonia is also an acute illness of Q fever, but is rarely reported in Taiwan. Q fever pneumonia often presents with a productive cough and pleuritic chest pain³. However, no obvious symptoms and signs of airway infection were noted in this case, but severe pleuritic chest pain with pleural effusion was detected. After effective antibiotic treatment with adjuvant steroid, pleuritis was improved in the follow-up.

Doxycycline, newer macrolides, and fluoroquinolones are drugs of choice for *C. burnetii* infection^{4,5}. Most cases of acute Q fever became afebrile within three days after initiation of treatment⁴. However, variations of antibiotic responses had been observed in vivo and in vitro^{5,8}. In a study of 113 patients with acute Q fever, earlier defervescence was observed among patients treated with doxycycline than those with newer macrolides⁴. It is unique for this case that his febrile duration lasted for four weeks under therapy with doxycycline or levofloxacin, which was rarely mentioned in the literature. It was not clear whether those with hyperbilirubinemia would have more extensive inflammation, and the latter led to a delayed clinical response to antimicrobial therapy. The present case received antimicrobial drugs and adjuvant prednisolone (0.5 mg/kg/day), and recovered thereafter, as suggested by Crespo et al. that moderate doses of steroids could be beneficial for patients with Q fever hepatitis and suboptimal response to antibiotics⁹. Hypersensitivity mechanism, as evidenced by the presence of autoantibodies (anticardiolipin and lupus anticoagulant in this patient), is a possible explanation for the use of steroid.

In summary, patients present with fever of unknown origin and elevated aminotransferases in endemic areas, *C. burnetii* infection should be includ-

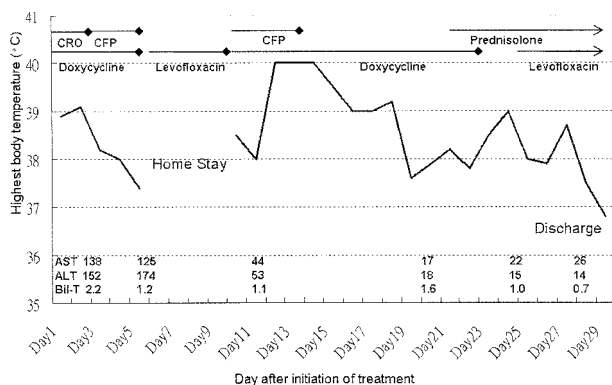


Fig.2. Summary of the clinical course and antimicrobial therapy for a case of acute Q fever with pleurisy and mild jaundice. (CRO, ceftriaxone; CFP, cefpirome).

ed in differential diagnosis. The patients with acute Q fever with slow regression of symptoms under appropriate antibiotic treatment may benefit from steroid.

References

1. Ko WC, Liang CC, Chen HY, Chuang YC. Seroprevalence of *Coxiella burnetii* infection in southern Taiwan. *J Formos Med Assoc* 2000; 99: 33-8.
2. Ko WC, Liu JW, Chuang YC. Acute Q fever as a cause of acute febrile illness of unknown origin in Taiwan: report of seven cases. *J Formos Med Assoc* 1997; 96: 295-7.
3. Parker NR, Barralet JH, Bell AM. Q fever. *Lancet* 2006; 367: 679-88.
4. Gikas A, Kofteridis DP, Manios A, Padiaditis J, Tselentis Y. Newer macrolides as empiric treatment for acute Q fever infection. *Antimicrob Agents Chemother* 2001; 45: 3644-6.
5. Lever MS, Bewley KR, Dowsett B, Lloyd G. In vitro susceptibility of *Coxiella burnetii* to azithromycin, doxycycline, ciprofloxacin and a range of newer fluoroquinolones. *Int J Antimicrob Agents* 2004; 24: 194-6.
6. Lee HC, Ko WC, Lee HL, Chen HY. Clinical manifestations and complications of rickettsiosis in southern Taiwan. *J Formos Med Assoc* 2002; 101: 385-92.
7. Chang K, Yan JJ, Lee HC, Liu KH, Lee NY, Ko WC. Acute hepatitis with or without jaundice: a predominant presentation of acute Q fever in southern Taiwan. *J Microbiol Immunol Infect* 2004; 37: 103-8.
8. Yeaman MR, Mitscher LA, Baca OG. In vitro susceptibility of *Coxiella burnetii* to antibiotics, including several quinolones. *Antimicrob Agents Chemother* 1987; 31: 1079-84.
9. Crespo M, Sopena B, Bordon J, de la Fuente J, Rubianes M, Martinez-Vazquez C. Steroids treatment of granulomatous hepatitis complicating *Coxiella burnetii* acute infection. *Infection* 1999; 27: 132-3.

急性Q熱合併黃疸及肋膜炎且Doxycycline和Levofloxacin治療無效：病例報告

陳柏齡¹ 李南瑤¹ 柯文謙^{1,2}

國立成功大學醫學院附設醫院 ¹內科部感染科

國立成功大學醫學院 ²內科部

摘要

Q熱是由 *Coxiella burnetii* 感染所引起，在台灣地區是一種新興的感染疾病。本土性的個案臨床上的主要表現是以急性發燒和肝炎為主。在此報告一例急性Q熱合併黃疸及肋膜炎的個案，病患住院接受doxycycline及levofloxacin治療但反應不佳，合併類固醇治療後痊癒。