Zoonotic atypical pneumonia due to \textit{Chlamydophila psittaci}: First reported psittacosis case in Taiwan

Yu-Jen Cheng\textsuperscript{a}, Kun-Yen Lin\textsuperscript{b}, Chun-Chen Chen\textsuperscript{b}, Yen-Lin Huang\textsuperscript{b}, Chun-Eng Liu\textsuperscript{a,*},\dagger, Shu-Ying Li\textsuperscript{b,**},\dagger

\textsuperscript{a}Division of Infectious Diseases, Department of Internal Medicine, Changhua Christian Hospital, Taiwan
\textsuperscript{b}Research and Diagnostic Center, Centers for Disease Control, Taipei 115, Taiwan

Received 3 May 2012; received in revised form 20 August 2012; accepted 26 August 2012

Human psittacosis caused by \textit{Chlamydophila psittaci} is one of the most common zoonotic atypical pneumonias featuring pulmonary as well as extrapulmonary infections. Most of the cases involve avian contact history especially with psittacine birds. Herein we report a 44-year-old male patient displaying atypical pneumonia symptoms of intermittent fever, dry cough, chest pain, dyspnea, headache, hepatitis, and hyponatremia. He had two sick cockatiels, one of which had died a month previously. A microimmunofluorescence test was performed to check the serum antibody levels against \textit{Chlamydophila psittaci}. The serum IgM titer showed positive titer of 1:256, 1:256, and 1:128 on Days 11, 23, and 43 after disease onset, respectively. His fever subsided soon and clinical symptoms improved after minocycline was administrated on Day 12. The psittacosis case was confirmed by history of psittacine bird contact, clinical symptoms, treatment response, and positive IgM titer. To our knowledge, this is the first report of a psittacosis case in Taiwan.

Copyright © 2012, Elsevier Taiwan LLC & Formosan Medical Association. All rights reserved.

\* Corresponding author. Division of Infectious Diseases, Department of Medicine, Changhua Christian Hospital, 135 Nanxiao Street, Changhua City, Changhua County 500, Taiwan.
\** Corresponding author. Research and Diagnostic Center, Centers for Disease Control, 161 Kun-Yang Street, Taipei 115, Taiwan.
E-mail addresses: 63557@cch.org.tw (C.-E. Liu), syl@cdc.gov.tw (S.-Y. Li).
\dagger Chun-Eng Liu and Shu-Ying Li as equally contributing co-corresponding authors

0929-6646/S - see front matter Copyright © 2012, Elsevier Taiwan LLC & Formosan Medical Association. All rights reserved.
http://dx.doi.org/10.1016/j.jfma.2012.08.017
Introduction

Human psittacosis, also known as parrot fever and ornithosis, is a zoonotic infectious disease caused by the obligate intracellular bacterium *Chlamydia psittaci*. Symptoms of psittacosis may include fever, headache, myalgia, chill, nonproductive cough, and respiratory distress. In some serious cases, *C. psittaci* may cause gastrointestinal problems, such as vomiting and diarrhea as well as pneumonia, encephalitis, or myocarditis.

Avian chlamydiosis is particularly common in tropical and subtropical regions in psittacine birds (e.g., cockatiels, parrots, parakeets, and lories), and infections of pigeons, turkeys, canaries, ducks, and wild birds have also been reported. *C. psittaci* is predominantly transmitted through inhalation of contaminated aerosols or dust of dried feces from an infected or asymptomatic animal. Psittacosis has an incubation period of 3 to 10 days in birds, and 5 to 28 days in humans after infection. Individuals with frequent recreational or occupational exposure to birds, such as pet bird owners, bird fair visitors, zoo veterinarians, pet shop workers, avian quarantine workers, and poultry processing plant workers, are at elevated risk for psittacosis. Outbreaks of psittacosis commonly occur in an occupational setting. Community and familial outbreaks have also been reported.

Psittacosis can be diagnosed by isolation of *C. psittaci*, serology, or molecular detection. Isolation of *C. psittaci* requires cell culture. Because of its ease of respiratory dissemination and high mortality, *C. psittaci* is categorized as possible bioterrorism agent and handling of culture should be done with proper biocontainment. For serological diagnosis, three serological tests, complement fixation (CF) test, enzyme-linked immunosorbent assay (ELISA), and microimmunofluorescence (MIF) test, are used to diagnose chlamydial infections. Currently, the MIF is the gold standard for serological diagnosis of chlamydial infections. Nucleic-acid amplification techniques such as PCR targeting outer membrane protein A or 16S rRNA gene provide sensitive and species-specific detection of *C. psittaci*.

In this report, we describe the first human psittacosis case in Taiwan diagnosed based on the history of psittacine bird contact, clinical manifestation, treatment response, and serological MIF assay.

Case report

The patient was a 44-year-old male living in central Taiwan. He had no travel history within one month. He was a nonsmoker, did not use intravenous drugs or street drugs, and did not have alcohol drinking or betel nut chewing habits. He kept two cockatiels (*Nymphicus hollandicus*) at home. One of the cockatiels died one month before the patient was ill, the other died during his hospitalization. Two weeks before the patient’s admission, his mother was also admitted for pneumonia. He had had intermittent fever, severe cough without sputum, headache, and epigastric pain since January 1, 2011 (Day 1). He took medicine in his local clinic but in vain: fever and dyspnea continued. Therefore he was admitted to a medical center on January 9, 2011 (Day 9). On admission, the patient was conscious, ambulatory but very malaise and with a blood pressure of 104/66 mmHg, heart rate of 110 beats/minute, respiratory rate of 20/minute, and temperature of 39.4 °C. Chest examination revealed crackling breathing sounds without wheezing in the left upper lung. He had a supple neck, normal heart sounds without murmur, a soft abdomen without tenderness, and no Murphy’s sign. Laboratory investigations showed a leukocyte count of 10.5 × 10⁹/L, hemoglobin level of 128 g/L, and a platelet count of 368 × 10⁹/L. The biochemistry tests indicated 0.81 mg/dL creatinine, 139 mg/dL glucose, 61 U/L glutamate pyruvate transaminase, 130 mmol/L of sodium, and 2.9 mmol/L potassium. The urinalysis showed microscopic hematuria (17.1 red blood cells/high-power field) without pyuria. The cultures of blood and sputum samples collected on admission were all negative. Results for influenza rapid test, urine Legionella antigen test, HBs Ag and Anti-HCV were all negative. Chest X-ray on Days 9 and 12 showed infiltration of the left upper lung with patchy reticular infiltrates radiating from the left hilum and no pleural effusion was found. He received empirical antibiotic (pipraclillin) therapy for the initial 24 hours. Despite the antibiotic treatment, he showed persistent high fever, progressive dry cough, dyspnea, poor appetite, and headache. After detail review of his animal contact history, travel history, family cluster, and laboratory data, atypical pneumonia was highly suspected. Therefore, he received further survey for psittacosis, endemic typhus, Q fever, and leptospirosis and began empirical antibiotics therapy of minocycline 100 mg every 12 hours intravenously combined.

Figure 1 Chest X-ray taken (A) on Day 12 shows abnormalities with infiltration and patchy lesion on the left upper lung and (B) on Day 24 reveals improvement after minocycline treatment.
with ceftriaxone. His fever subsided with general condition improving after 36 hours of minocycline therapy. His hyponatremia (from initial 130 mM of sodium to 137 mM) and leukocytosis (from initial leukocyte count of 10.5 \times 10^9/L to 8.1 \times 10^9/L) improved at the same time. Based on the above evidence supporting atypical pneumonia, ceftriaxone therapy was ceased 3 days later and minocycline monotherapy continued. He was discharged after 5 days of minocycline therapy and kept on oral minocycline therapy. He received chest X-ray follow-up after 14 days of minocycline therapy in the outpatient department, and his chest image demonstrated improvement (Fig. 1B), so the minocycline therapy was stopped.

**Discussion**

Atypical pneumonias are most commonly caused by three zoonotic pathogens, *C psittaci* (psittacosis), *Francisella tularensis* (tularemia), and *Coxiella burnetii* (Q fever), and three nonzoonotic pathogens, *Chlamydia pneumoniae*, *Mycoplasma pneumoniae*, and Legionella. Atypical pneumonia pathogens cause systemic infections with pulmonary and extrapulmonary involvement such as, hepatitis, headache, hyponatremia, and microscopic hematuria. The patient had typical presentation of pneumonia (fever, dry cough, and dyspnea) with systemic involvement (hepatitis, hyponatremia, headache, microscopic hematuria, and poor appetite). The reviewing of his history of travel, occupation, contact, and cluster, revealed that he had family cluster and pet bird contact history. Because of the obviously sick bird contact history, samples were sent to TW-CDC for laboratory diagnosis of psittacosis, endemic typhus, leptospirosis, and Q fever survey. The serologic studies confirmed psittacosis and excluded endemic typhus, leptospirosis, and Q fever.

For serological diagnosis, CF test, ELISA, and MIF test are used to diagnose chlamydial infections. However, there is no *C psittaci*-specific serological test due to serological cross-reaction between different species of the Chlamydiaceae family, as some of the surface-located antigens, such as the chlamydial lipopolysaccharide (LPS) or the heat shock protein, can cross-react with antibodies to other chlamydial species or bacteria, which makes it difficult to distinguish among *C psittaci*, *C trachomatis*, and *C pneumoniae* antibodies in humans. To circumvent this problem, MIF tests using chlamydial organisms without the LPS were developed. These new methods improve specificity of MIF. In the SeroFIA kit, the LPS, which is genus-specific and cross-reactive antigen for the three species, is not removed from elementary bodies (EB) of all three species. The ANI Labsystems *Chlamydia pneumoniae* IgM/IgG Micro-IF kit also uses the elementary body particles of *C pneumoniae*, *C trachomatis*, and *C psittaci* as diagnostic antigens. In the ANI Labsystems kit, the LPS is removed from EB of *C pneumoniae* and *C trachomatis* but is not removed from EB of *C psittaci*. In this study, the Chlamydia IgM/IgG/IgA SeroFIA test was used to detect *C psittaci*-specific antibody and *Chlamydia pneumoniae* IgM/IgG micro-IF test to exclude cross-reaction between different species of the Chlamydiaceae family in specimens. False-negative results by using MIF in psittacosis patients have been reported. Treatment with antibiotics during the 2 to 3 weeks before testing may lead to negative antibody result. This may explain the negative result of chlamydial IgG and IgA titers in this study.

The antibiotic choice for psittacosis is tetracycline hydrochloride, 500 mg *per os* four times daily, or doxycycline, 100 mg *per os* twice daily, for 10 to 21 days. Most patients will defervesce by 48 hours of treatment with doxycycline. Minocycline, a second generation tetracycline, has been used clinically with success. Minocycline is one of the most active tetracyclines with a 90% minimum inhibitory concentration (MIC90) of 0.06 mg/L. Erythromycin therapy is the alternative treatment but may be less efficacious in severe case and may not protect the fetus when treating pregnant patients. Most patients responded to treatment within 24 hours. Untreated psittacosis could result in 15% to 20% mortality; with treatment, it drops to 1%. For our patient, his high fever, dyspnea, and headache improved dramatically after 36 hours of minocycline therapy. His chest X-ray follow-up after 14 days of minocycline therapy showed improvement (Fig. 1B), so the minocycline therapy was discontinued. When he visited outpatient department 3 months later, his liver function, complete blood count, renal function, and electrolyte were all within normal limits and his chest image showed further improvement.

In this report, a psittacosis case was confirmed by clinical presentation, epidemiological investigation, serological
evidence, and clinical antibiotic response. The sick cockatiels were suspected to be the possible source of C. psittaci infection. To our knowledge, this is the first report of a psittacosis case in Taiwan. Judicious interpretation of the serological reaction profile and integrated evaluation of serological data with clinical, radiographic, and travel, occupation, contact, and cluster information, especially bird contact and recent foreign travel, is paramount for correct and efficient differential diagnosis of human psittacosis.

Acknowledgments

This work was supported by grants DOH99-DC-2011 and DOH100-DC-2025 from the Centers for Disease Control, Department of Health, Taiwan.

References