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Severe Human Psittacosis Requiring Artificial Ventilation: Case Report and Review

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Severe respiratory failure is an uncommon manifestation of psittacosis. We describe a patient with psittacosis who developed severe respiratory failure and required artificial ventilation. We also review 11 cases reported in the English-language literature over the past 30 years. A history of exposure to birds was reported in 10 of 12 cases and remains the most significant risk factor. Severe hypoxemia or renal impairment was associated with a poor prognosis. Eight patients died of psittacosis or related complications of the infection. Diagnostic aspects, clinical manifestations, and management options are discussed.

The clinical presentation of human psittacosis can vary from an asymptomatic infection to overwhelming illness involving multiple organ systems [1, 2]. We describe an unusually severe case of psittacosis that resulted in respiratory failure, and we review other case reports of severe psittacosis requiring respiratory support that have been published in the English-language literature during the past 30 years [3–7].

Case Report

A 46-year-old man was admitted to our hospital with fever and chills, a productive cough, and myalgias, all of 10 days' duration. At first the family doctor suspected a flu-like illness, but because the fever persisted, empirical antimicrobial therapy with oral amoxicillin/clavulanic acid (500 mg/125 mg every 8 hours) was initiated. The patient had a complex medical history that was remarkable for splenectomy, sarcoidosis, ulcerative colitis, a stomach ulcer, insulin-dependent diabetes mellitus, and chronic relapsing pancreatitis. The patient was receiving insulin, and his medications consisted of prednisone (10 mg), famotidine (20 mg), and loperamide (2 mg), each taken once daily. Diffuse bilateral pulmonary infiltrates were apparent on a chest roentgenogram. The leukocyte count was $13.2 \times 10^9/L$ (92% neutrophils, 7% lymphocytes, and 1% monocytes), and the erythrocyte sedimentation rate was 75 mm/h. A gram stain of purulent sputum showed leukocytes (>25 per high-power field; magnifica-

tion, $\times 1,000$) but no microorganisms were found, and cultures remained negative. The patient's antimicrobial therapy was changed to erythromycin (1 g iv every 6 hours) and rifampin (600 mg iv every 12 hours); however, the development of respiratory failure prompted transfer to the intensive care unit where he was intubated and artificial ventilation was started. Bronchoalveolar lavage (BAL) was performed, but cultures of the fluid remained negative. Family members reported that he kept psittacine birds, several of which were ill.

Complement-fixing antibodies to *Chlamydia* were found at a titer of 128, but IgM was not detected with use of indirect immunofluorescence (IF). Nevertheless, antimicrobial therapy was changed to doxycycline (200 mg iv once daily), and gentamicin (120 mg iv every 12 hours) was added because the patient began to appear septicemic. During the next 5 days a remittent fever persisted; the patient's respiratory function did not improve, and a repeated chest roentgenogram showed no improvement in his condition.

At that time *Chlamydia psittaci* was isolated from the cloaca of one of the patient's birds, and polymerase chain reaction (PCR) demonstrated the presence of *Chlamydia* in the BAL fluid. Eventually the patient's clinical condition improved, and he was discharged from the hospital in good health after 28 days.

Methods

The complement fixation (CF) test was performed according to the microtiter technique [8] with a commercial antigen containing *C. psittaci* (Behringwerke, Marburg, Germany). For detection of IgM, the serum samples were pretreated with Gullisorb (Biolab, Amersfoort, the Netherlands) to remove IgG and rheumatoid factors [9]. An IF test was performed by means of standard procedures with commercial *C.*

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psittaci antigen (Behringwerke) and FITC (fluorescein isothiocyanate)-labeled goat antibody to IgM (Tago; Sanbio, Uden, the Netherlands). PCR [10] was performed on the BAL fluid specimen. The PCR assay used is based on two primer sets: one that amplifies *Chlamydia* sequences, and one that detects only *Chlamydia trachomatis*. The specificity of this PCR was confirmed by Southern blot hybridization with an internal oligonucleotide as probe [10].

The cloaca of one of the patient's birds, which had died, was cultured on McCoy cells in flat bottom tubes at 37°C. After incubation for 48 hours, cultures were found to be positive for *Chlamydia* with a *Chlamydia* genus-specific monoclonal antibody labeled with FITC (De Beer Medicals, Hilvarenbeek, the Netherlands). The isolate was grown for study by transmission electron microscopy (TEM) and for use as antigen in the indirect IF test. The literature for the years 1963–1993 was reviewed with use of MEDLINE for case reports of severe psittacosis.

Results and Discussion

The diagnosis of psittacosis is difficult to make and can easily be missed. Exposure to birds is reported in 85% of the cases [1, 11, 12] and is the most valuable diagnostic clue to be obtained on admission. Since psittacosis can be transmitted by asymptomatic birds, a history of exposure to birds should be sufficient to raise the suspicion of psittacosis [1]. For our patient the diagnosis of psittacosis was made after information on exposure to birds was obtained. *C. psittaci*-specific IgM was not detected in the first serum sample when a commercial antigen was used. The failure to detect *C. psittaci*-specific IgM and the persistence of the patient's fever caused doubt about the correctness of the diagnosis. However, convincing evidence was obtained by culturing *Chlamydia* from the cloaca of the bird. On TEM, round elementary bodies were found that are characteristic of *C. psittaci* or *C. trachomatis* [13]. Whereas amplification of the patient's BAL fluid with use of PCR resulted in detection of *Chlamydia*, no specific amplification products were generated with primers directed against *C. trachomatis*. We concluded that *C. psittaci* was the etiologic pathogen, which led us to evaluate the indirect IF test. The indirect IF test was positive when it was repeated using the *C. psittaci* strain isolated from the patient's bird as antigen. This finding clearly shows that the indirect IF test can yield false-negative results, presumably because of strain variation [14]. Thus, serological data should be interpreted with caution.

Psittacosis presenting as severe respiratory insufficiency is uncommon; to our knowledge, only 12 cases have been reported to date [3–7]. Psittacosis is a disease of adults—mainly those 30–60 years of age [11]—and the ages of all patients were within this range. Ten (83%) of the 12 patients had a history of exposure to birds. Since psittacosis is a sys-

temic infection, extrapulmonary symptoms are often present. Seven of the patients presented with neurological manifestations [3, 4, 6, 7] and six presented with gastrointestinal features [3, 4, 6, 7]. Four patients presented with acute renal failure for which hemodialysis was required [3, 6, 7]. Risk factors for developing severe respiratory failure were not apparent in any of these cases.

Tetracycline and tetracycline analogues are considered to be the treatment of choice for infection with *C. psittaci* [2]. Erythromycin has been reported to be effective [2, 15]. However, in three cases in which erythromycin was administered alone, the patients died [3, 5], whereas in four cases (including the present report) in which tetracycline was administered, the patients survived [5, 7].

Death resulting from infection with *C. psittaci* is uncommon, and the overall mortality is estimated at 0.7% [12]. However, factors including increasing age, leukopenia, severe hypoxemia, renal impairment, confusion, and multilobar involvement have been associated with a poor prognosis [3]. Five of eight patients with documented hypoxemia [4, 5] and three of four patients who presented with renal impairment [3, 6] died. In these cases, leukocyte count, age, and confusion did not appear to be factors in the poor outcome. Chest roentgenograms from the time of admission were not available and therefore were not evaluated with respect to outcome. Eight patients (67%) who presented with severe respiratory failure died of psittacosis or related complications [3–6]. Three of these patients died within 48 hours of admission [3, 5]. For the remaining five patients, the mean interval between the onset of symptoms and diagnosis was 8.3 days, indicating that diagnostic delay could be an important factor with respect to outcome. Thus, rapid and sensitive diagnostic assays are of great importance. Several techniques, including the use of monoclonal antibodies [16] or DNA-based assays [17] of respiratory tract secretions or BAL fluid, have been used successfully, but further evaluation is needed.

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