

CASE REPORT

Chlamydia psittaci pneumonia with septic shock and hypoxic respiratory failure

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Abstract

Psittacosis is a zoonotic infectious disease causing community-acquired pneumonia. Septic shock and respiratory failure can develop. The symptoms, diagnosis, transmission and treatment of psittacosis are discussed. In the described cases, especially polymerase chain reaction has shown to be a promising tool in diagnosing the disease. Physicians awareness might be accelerated to ensure rapid treatment of the disease before it progresses to septic shock and respiratory failure.

Introduction

Community acquired pneumonia (CAP) is a serious illness and a frequent cause of intensive care unit (ICU) admission. A wide range of pathogens are responsible for these infections including the atypical pathogens, such as *Legionella pneumophila*, *Mycoplasma pneumoniae*, *Chlamydia pneumoniae* and *Chlamydia psittaci*. Of all patients admitted to the hospital with CAP, 15-28% are ascribed to these pathogens.¹⁻⁴ The mortality rate from severe CAP in patients admitted to the ICU was 27% after six months in a European study. *Streptococcus pneumoniae* remains the most commonly isolated organism, although no microbiological agent could be detected in one-third of the patients.⁵ The American Thoracic Society guidelines for treatment of severe CAP in patients on the ICU differ in part from the Dutch guidelines.⁶ The Dutch guidelines recommend to always include treatment against *Streptococcus pneumoniae* and *Legionella* spp. Cover for *Pseudomonas aeruginosa* is in general not necessary. This is only necessary in patients with chronic obstructive pulmonary disease and structural lung disease.^{7,8}

In the Netherlands 1-6% of CAP is caused by *Chlamydia* spp.⁵ The incidence of CAP in patients admitted to the ICU due to *Chlamydia psittaci* is unknown. Here, we present three

patients with psittacosis admitted to the ICU. The clinical signs and symptoms and the recent improvements in diagnostic options are described.

Case reports

Patient A

A 58-year-old male patient was hospitalised for right-sided pneumonia. He complained about fever (40.0 °C), a cough and severe headache. His girlfriend reported violent behaviour. His past medical history was unremarkable. He smoked about 20 cigarettes a day. On physical examination, he was in a state of delirium. Fine crackles were heard on auscultation of both lungs. His heart rhythm was in atrial fibrillation at a rate of 151 beats/minute; blood pressure was 149/81 mmHg. His temperature was 39.1 °C. The respiratory rate was 31/minute; with 100% oxygen the pO₂ was 97 mmHg (normal value 70-90), pCO₂ 33 mmHg (normal value 35-45), pH 7.38 (normal value 7.35-7.45), actual HCO₃ 18 mmol/l (normal value 22-29), and oxygen saturation 91%. The chest X ray was suggestive of pneumonia in the right lower lobe (*figure 1*). A lumbar puncture was performed because the emergency physician suspected meningitis. Culture and gram staining did not show any microorganisms in the cerebral spinal fluid. Treatment was started with amoxicillin/clavulanic acid and ciprofloxacin for severe CAP. Because respiratory failure developed the next day, he was intubated and mechanically ventilated. Norepinephrine was necessary for septic shock. Cultures were taken from bronchial secretions directly after endotracheal intubation and from blood, which were negative after several days. Serological tests were requested for atypical pathogens such as *Mycoplasma pneumoniae*, *Coxiella burnetii*, and *Chlamydia psittaci* which showed levels of antibodies below the detection limit. A *Legionella pneumophila* antigen test in the urine and also a pneumococcal

Figure 1. Patient A: Chest X-ray on admission to the hospital, before initiation of mechanical ventilation. A dense pneumonic infiltration is seen in the lower lobe of the right lung



antigen test were negative. Also a viral polymerase chain reaction (PCR) was performed for influenza. The results did not show viral RNA. On admission to the hospital, liver function tests were elevated (table 1). Atrial fibrillation was treated with amiodarone. Ventilation was necessary in the prone position with high levels of positive end-expiratory pressure and a high fraction of inspired oxygen. A thorough hetero-anamnesis was obtained from his girlfriend, because he did not improve on the therapy given. This revealed that he kept multiple tropical birds: toerakoos (*Musophagidae*). One of the birds had died recently. The deceased bird was still present in his aviary. Four days after admission to the ICU, PCR was positive for *Chlamydia psittaci* on a sample of bronchial secretion which was subtyped as genotype A. The patient was treated with doxycycline 100 mg twice a day. He improved gradually and could be discharged from the ICU three weeks after admission. As psittacosis is a notifiable disease in the Netherlands it was reported to the public health service. Unfortunately, no PCR for psittacosis was done on the dead bird.

Table 1. Laboratory results for the presented cases on admission to the hospital

	Patient A	Patient B	Patient C	Normal values
Leukocytes	8.6 x 10 ⁹ /l	7.3 x 10 ⁹ /l	8.5 x 10 ⁹ /l	4-10 x 10 ⁹ /l
CRP	440	338	246	0-6 mg/l
ASAT	356	306	131	0-30 U/l
ALAT	118	203	69	0-35 U/l
Gamma-GT	78	37	31	0-40 U/l
LDH	1591	609	282	< 248 U/l
CK	2257	2504	144	< 145 U/l
Bilirubin	79	13	22	0-17 μmol/l

Patient B

A 62-year-old male, non-smoker, was seen with fever (39.9 °C), chest pain, malaise and diarrhoea. His past medical history was unremarkable. The patient kept chickens in his backyard and had recently cared for his friend's pigeons. On physical examination he had a temperature of 37.6 °C, blood pressure of 102/53 mmHg, a regular pulse of 92 beats/minute. Pulmonary auscultation revealed crackles in the left lung. The results of laboratory findings on admission to the hospital are presented in table 1. The chest X-ray showed an infiltrate in the lower lobe of the left lung and also in the upper part of the right lung (figure 2). He was treated with moxifloxacin 400 mg once daily for bilateral severe pneumonia and was admitted to the pulmonary ward. One day after admission he was transferred to the ICU because of respiratory failure. A progressive dysarthria was observed. A CT scan of the brain was normal. Two days after ICU admission the patient's condition deteriorated and endotracheal intubation and mechanical ventilation was necessary. Simultaneously norepinephrine was started for severe and fluid-resistant hypotension. Blood cultures and a Legionella urinary antigen test were negative. A broncho-alveolar lavage did not show *Pneumocystis jiroveci*. His sister mentioned again the patient's recent contact with pigeons. Therefore, a multiplex PCR for *Chlamydia psittaci* and *Mycoplasma pneumoniae* was performed on the broncho-alveolar lavage fluid. The *Chlamydia psittaci* PCR was positive. The *Chlamydia psittaci* PCR on an acute-phase

Figure 2. Patient B: Chest X-ray on admission to the hospital. An infiltrate is visible in the lower lobe of the left lung and also in the upper part of the right lung



serum sample was also positive. Moxifloxacin was switched to doxycycline.

Seven days after ICU admission the patient was successfully extubated. Unfortunately the C-reactive protein rose and he developed fever again. The moxifloxacin was restarted in addition to the doxycycline. The next day, the patient could be transferred to the pulmonary ward. He was discharged 22 days after admission in a good clinical condition without any dysarthria. Serological testing on two consecutive sera drawn three weeks apart for respiratory viruses, *Mycoplasma pneumoniae*, *Coxiella burnetii* and *Chlamydia* species-specific antibodies was without a significant rise in antibody titres for any of the pathogens. Genotyping of the *Chlamydia psittaci* strain revealed a genotype B. PCR for *Chlamydia psittaci* on several faecal samples from the pigeons were positive. The chickens in his backyard tested negative for *Chlamydia psittaci*.

Patient C

A 84-year-old non-smoking male presented himself with a cough, and for one day dyspnoea and fever (39.2 °C). His medical history revealed Von Recklinghausen's disease and a prostate carcinoma two years ago.

On physical examination he was ill and dehydrated. Vital signs showed a temperature of 39.1 °C, a blood pressure of 136/86 mm Hg and a tachycardia of 115 beats/minute. On auscultation there were crackles at the right base of the lung. The results of the laboratory investigations on admission to the hospital are shown in *table 1*.

The chest X-ray showed an infiltrate in the lower lobe of the right lung (*figure 3*). Blood cultures were taken and treatment was initiated with amoxicillin/clavulanic acid for CAP. A Legionella urinary antigen test was negative. A sputum culture did not reveal a pathogen. Two days later he was transferred to the ICU because of respiratory failure and haemodynamic instability due to atrial fibrillation. On admission to the ICU, non-invasive ventilation was started and antibiotic treatment was switched to moxifloxacin. After two days he required endotracheal intubation and mechanical ventilation. Because of haemodynamic instability, norepinephrine was started. After eight days he was extubated and moxifloxacin was stopped. After 12 days he was discharged to the internal medical ward. Two days later he developed fever again with tachypnoea and an elevated CRP. Ceftriaxone was started empirically. Blood cultures were negative. The patient was not expectorating any sputum. A urine culture showed *Proteus mirabilis* > 10⁵ CFU/ml, sensitive to ceftriaxone. Because the urinary catheter was still in place, we judged this to be colonisation and not an infection. In a convalescent serum sample, obtained 13 days after admission, a tenfold increase in IgG *Chlamydia* spp. specific antibodies was detected suggestive of psittacosis. Antibiotic treatment was switched to doxycycline with a good

Figure 3. Patient C: Chest X-ray on admission to the hospital. An infiltrate in the lower lobe of the right lung is seen



response. On further questioning obvious bird contact could not be established. A PCR for *Chlamydia psittaci* on a stored sputum sample obtained upon admission appeared to be positive. Genotyping revealed a genotype A strain.

Discussion

We present three patients with *Chlamydia psittaci* pneumonia based on detection of *Chlamydia psittaci* DNA in respiratory secretions. They all required ICU admission for CAP with septic shock and respiratory failure. In two of them, contact with birds was recognised. Although in one case obvious bird contact was not established, he was definitely diagnosed as psittacosis as the *Chlamydia psittaci* PCR was positive and a significant rise in antibody titre was detected. Patient B did not show a significant rise in *Chlamydia* species-specific antibody levels after 21 days, but a *Chlamydia psittaci* PCR was positive on the broncho-alveolar lavage fluid as well as the acute-phase serum sample.⁹ No quantitative PCR of his blood was done. Signs and symptoms are often quite nonspecific for psittacosis. The disease can start gradually or develop as a rapid fulminant pneumonia with acute respiratory distress syndrome (ARDS) and multi-organ failure. No data are available on which patients develop these severe clinical presentations. Neurological features such as severe headache, photophobia, confusion or encephalitis have been described.¹⁰ Dysarthria, as was seen in patient B, has not been described previously.

Patients with *Chlamydia psittaci* pneumonia are of a younger age, are less frequent smokers, have less chronic disease and have a longer duration of symptoms before admission to the hospital compared with *Legionella pneumophila* pneumonia.¹¹ All the demonstrated patients were extremely hypoxic, but recovered with appropriate therapy. Intubation and mechanical

ventilation should be initiated in case of respiratory failure; however, a trial of non-invasive ventilation could be initiated under careful monitoring of oxygenation.^{12,13}

In this small series it is remarkable to see that leukocytes were within the normal range in all three cases.¹⁴ In addition, an elevated lactate dehydrogenase, aspartate aminotransferase and creatine kinase was seen in all three, although this increase was only marginal in patient C. In typical pneumonia, the total leucocyte count is usually elevated. Yung *et al.* described 135 serologically diagnosed psittacosis cases and reported abnormal hepatic serum enzyme levels in 49% and normal white cell count in 90% of cases.¹⁵

Diagnostic work-up

Culture of *Chlamydia psittaci* is impractical, slow, difficult to perform and requires a biosafety level 3 microbiological laboratory for safety reasons. For this reason culture has been abandoned in most diagnostic microbiology laboratories.

Serological tests are still widely used. Micro-immunofluorescence, complement fixation and ELISA tests are commonly used.¹⁶⁻¹⁸

The main disadvantage of serological testing is the delay while awaiting a second serum sample during convalescence. Serology provides only a retrospective diagnosis.

In the last decade several PCR protocols have been described.¹⁹⁻²¹ These tests provide an accurate, specific and timely diagnosis although the sample location is crucial as deep respiratory specimens seem to increase the sensitivity. *Chlamydia psittaci* PCR on throat swabs are insufficient for the diagnosis of psittacosis.^{16,22} Bronchoscopy with brush samples via a plugged double lumen catheter is the best diagnostic procedure in retrieving microorganisms in CAP. The collection of lower respiratory tract specimens should be done as soon as possible in the course of the disease and is better than tracheal aspiration and sputum culture. Addition of PCR to oropharyngeal and sputum samples increases the diagnostic yield.^{23,24} As these tests detect *Chlamydia psittaci* specific DNA, they do not require the presence of viable micro-organisms and are still positive when a first antibiotic dose has been administered.²⁵ A rapid diagnosis is important in order to adequately treat the infection and prevent or stop an outbreak.¹⁶ Molecular diagnostic tests provide a way to detect the causative agents in this bacterial genus more accurately and even subtyping is possible to clarify transmission to humans and establish the zoonotic reservoir.

All three strains in the demonstrated patients were subtyped to the genus level by sequencing a part of the *ompA* gene (Variable domain 4).

Zoonotic risk

Contact with birds is a risk factor in most of the cases described.^{26,27} *Chlamydia psittaci* can be transmitted by

asymptomatic birds. The micro-organism is resistant to drying and can remain viable for months at room temperature. Birds at home, environmental birds and occupational exposure to birds are the main sources.^{28,29} However in 25-50% of cases, such as patient C, no contact with birds is mentioned.¹⁴ Previously, it has been shown that other activities without obvious bird contact, such as lawn mowing, can be a risk factor for acquiring psittacosis.^{30,31}

Psittacine birds, mainly kept at home, were the first birds in which *Chlamydia psittaci* was discovered. Later on, other birds were also known to harbour *Chlamydia psittaci*, such as pigeons. In the last few decades several studies have shown that *Chlamydia psittaci* is endemic among poultry and thus an occupational hazard for poultry workers. *Chlamydia psittaci* is isolated in birds from faeces, cloacae, respiratory and conjunctiva secretions.¹⁹ Up to 465 bird species have been added to the list in which *Chlamydia psittaci* has been demonstrated.³² Although birds are assumed to account for the main part of the zoonotic transmission potential, *Chlamydia psittaci* could also be transmitted by mammals, as recent reviewed data show.²⁷

All genotypes of *Chlamydia psittaci* can be transmitted to humans and may cause psittacosis.^{33,34} Genotyping of *Chlamydia psittaci* can be used to aid in source tracing and to monitor the most prevalent genotypes in humans.¹⁶ Genotype A is often associated with psittacine birds and genotype B is associated with pigeons. The remainder of the genotypes suggest additional bird sources.³⁵

Treatment

According to the latest guidelines in the Netherlands, pulmonary infections with *Chlamydia psittaci* are preferably treated with a macrolide.⁸ As a second choice, doxycycline is advised. The Infectious Disease Society of America (IDSA) guidelines recommend a tetracycline as first choice for *Chlamydia psittaci* infection.⁶ The guideline by the National Association of State Public Health Veterinarians (NASPHV) also states that doxycycline is the first choice.³⁶ We recommend doxycycline as primary treatment of *Chlamydia psittaci*. Antibiotic therapy should be continued for at least 10-14 days after fever abates.³⁶ Many breeding facilities of birds treat their infected birds with tetracycline, doxycycline or enrofloxacin.³⁷ Drug-resistant strains can therefore develop. The use of quinolones, especially the newer compounds, in the therapy of psittacosis shows promising effects *in vitro* and in animal models. Their definite role in the treatment of human infection awaits further evaluation.³⁸

Conclusion

Psittacosis can present with respiratory failure and severe septic shock. PCR testing helps in a rapid diagnosis of *Chlamydia psittaci* infection. Source tracing is possible with

additional genotyping. In our opinion, in every CAP admitted to the ICU, *Chlamydia psittaci* should be considered. Typical symptoms of *Chlamydia psittaci* pneumonia are respiratory symptoms and also, as was the case in the three patients presented here, neurological symptoms such as headache and behavioural problems. Because these symptoms are not specific for psittacosis, we advise PCR testing in patients admitted to hospital with severe pneumonia. Psittacosis requiring mechanical ventilation for severe hypoxaemia is uncommon or at least under-diagnosed. Obvious contact with birds should make the clinician suspicious of psittacosis. Lack of bird contact cannot rule out the disease.

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Disclosure

All authors declare that no conflicts of interest are present.

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