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Case Report

Multi-organ failure with necrotic skin lesions due to infection with *Chlamydia psittaci*

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ABSTRACT

Presented is a patient with dyspnea and painful ulcers finally resulting in multi-organ failure. A detailed history resulted in positive PCR testing for *Chlamydia psittaci*. We emphasize the importance of a definitive history in establishing the correct diagnosis. When clinicians observe dyspnea with multi-organ failure, they should be aware of psittacosis.

Introduction

Chlamydia psittaci (C. psittaci), an obligate intracellular gram-negative bacterium causing psittacosis, is transmitted to humans predominantly from birds (Hogerwerf et al., 2017). Most patients with psittacosis present with influenza-like symptoms, often resulting in a diagnostic delay (Beeckman and Vanrompay, 2009; Stewardson and Grayson, 2010). It is imperative to diagnose and detect the source of a *C. psittaci* infection from a public health view. We describe a patient with psittacosis who presented with rare, atypical extrapulmonary manifestations, including multi-organ failure.

Case description

A 63-year-old woman was admitted to the emergency department because of a 4-day history of painful cutaneous abnormalities of both lower legs accompanied by progressive dyspnea. She had a history of right-sided ulcerative breast cancer for which she underwent both surgery and adjuvant chemo-radiotherapy thirteen years ago. She had an active lifestyle, including gardening and cycling. Because of dyspnea, bumetanide 2 mg, doxycycline 100 mg, and prednisone 30 mg, all once daily, were prescribed by her general practitioner. The skin abnormalities appeared two days after initiating the medication mentioned above. Two days later, both doxycycline and prednisone were discontinued. There was no history of drug-allergic reactions. On physical examination, she appeared somnolent. Her blood pressure was 104/84 mmHg; irregular heart rate, 179/min; respiratory rate, 22/min; temperature, 36.0 °C (98.8 °F) and oxygen saturation, 96% with 1 L oxygen supplementation. Pulmonary and cardiac auscultation revealed diffuse rhonchi and a prominent holosystolic murmur, respectively. The skin examination revealed acrocyanosis of the nose (Figure 1, right panel) and remarkable palpable purpura with bullae on both lower extremities (Figure 1, right panel).

Laboratory test results showed normocytic anemia (11.44 g/L), thrombocytopenia (57×10^9/L), and a marked leukocytosis (27.3×10^9/L) with neutrophil left shift and toxic granulation with C-reactive protein 120 mg/L. Hemolysis was absent. The remaining laboratory tests showed severe liver and kidney failure with disseminated intravascular coagulation (DIC) and lactic acidosis of 8.4 mmol/L. Computed tomography (CT) of the chest revealed diffuse, bilateral, interstitial infiltrates with ground-glass opacities (Figure 1, right panel). Furthermore, pleural effusion and subsegmental pulmonary embolisms were present. One day after admission, she developed respiratory failure and was transferred to the intensive-care unit for mechanical ventilation and supportive care. No cardiac vegetation was found. Due to suspicion of vasculitis, methylprednisolone 1000 mg was administered intravenously. The patient was empirically started on a 7-day plan of ceftriaxone 2000 mg intravenously twice daily and ciprofloxacin

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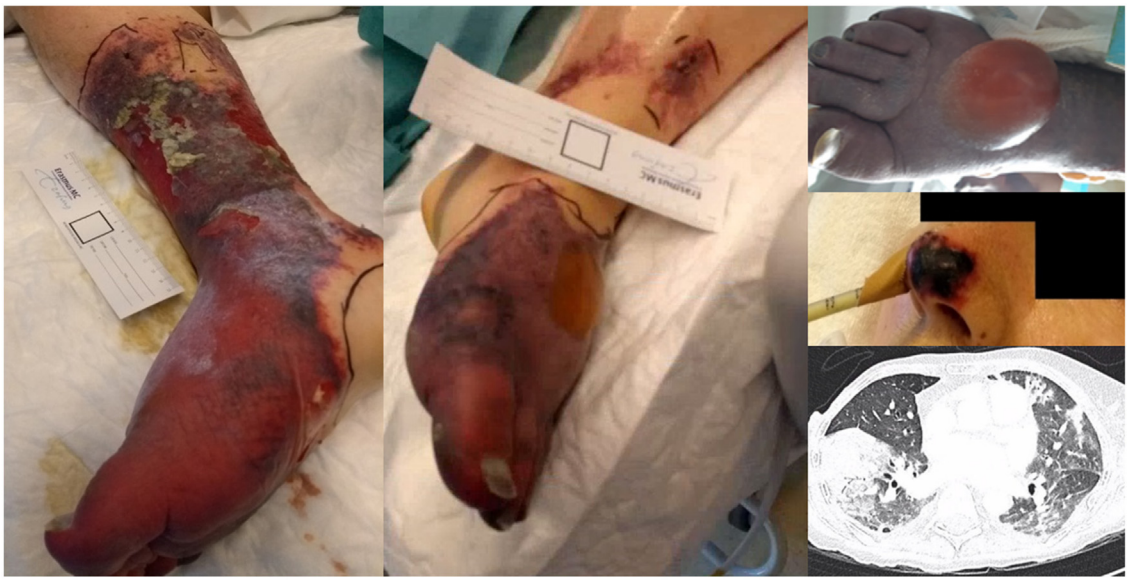

Figure 1. Acrocyanosis of the nose and remarkable palpable purpura with bullae on both lower extremities with interstitial infiltrates with ground-glass opacities at CT-scan.

400 mg intravenously twice daily due to concern for septic shock. Several blood-, urine- and bronchoalveolar-lavage (BAL) fluid samples were sent for cultures but were all negative. Clinical tests excluded a viral infection. Neither fungi nor mycobacteria were present. Also, the galactomannan antigen was negative. A skin biopsy of the left leg showed thrombotic vasculopathy with a polyclonal pattern of immunoglobulin A (IgA), IgG, and IgM. Cryoglobulins (measured twice), antiphospholipid antibodies, anti-neutrophil cytoplasmic antibodies, and anti-double-stranded DNA (anti-dsDNA) antibodies were absent.

Her skin lesions progressively worsened with necrosis of the distal nose (Figure 1) and large areas of both lower extremities. No macrovascular pathology was found on angiography. These findings inevitably led to the amputation of both legs.

Polymerase chain reaction (PCR) of BAL fluid for tuberculosis, mycobacteria, *Coxiella burnetii*, *Legionella* species, and *Mycoplasma pneumonia* were all negative. Many diagnoses were rejected because of negative test results. During the evaluation of the remaining entities in the differential diagnosis of dyspnea with skin lesions, together with many negative diagnostic test results, psittacosis was considered. A detailed history revealed contact with birds, including domestic pigeons. Additional real-time PCR testing of BAL fluid for *C. psittaci* was positive with a cycle threshold (Ct)-value of 35. Moreover, serologic testing for *Chlamydia* immunoglobulin(Ig) M and IgA was positive (IgG negative), compatible with an active infection.

Although there was a treatment delay, we suppose that the patient was treated appropriately. Despite significant morbidity, which resulted in the amputation of both legs, our patient survived the multi-organ failure and was repatriated for further rehabilitation. At a 6-month follow-up, she is doing well and has no further symptoms.

Discussion

Psittacosis has an estimated incidence of 1 percent among cases with CAP (Hogerwerf et al., 2017). However, its precise epidemiology is unknown due to the lack of routine testing and the variability in sensitivity and specificity of commonly used diagnostic tests (Stewardson and Grayson, 2010). Patients are infected by inhalation of *C. psittaci* that is shed by excreta or dust from feathers of many different birds, mostly psittacines. In the Netherlands, a total of 61 patients with psittacosis were reported in 2018. Pigeons were considered the contaminated bird in 23 patients (38%) (Dutch Centre for Infectious Disease Control, www.rivm.nl) (rivm, 2021).

Patients with psittacosis most commonly present with non-specific symptoms of fever, dyspnea, dry cough, and headache (flu-like symptoms), but clinical manifestations may vary (Yung and Grayson, 1988; Verweij et al., 1995). Our patient presented with fulminant psittacosis, manifested by respiratory failure, DIC with pulmonary embolisms, acute tubular necrosis, liver disease, and skin manifestations including acrocyanosis of the nose and palpable purpura with bullae on both lower legs. Multi-organ failure and skin manifestations, though rare, have been reported (Semel, 1984). To our knowledge, multi-organ failure together with acrocyanosis leading to amputation have not been previously reported in cases of psittacosis uncomplicated by endocarditis. To date, notably absent are skin manifestations in two series of respectively 135 and 397 cases with psittacosis (Yung and Grayson, 1988; Schmahmann, 1982). As our case shows, *C. psittaci* may be efficient in disseminating in a patient, causing fulminant systemic disease. The exact mechanisms of chlamydial cell entry are not well understood but are controlled by specific surface proteins and result in chlamydial inclusions (Knittler and Sachse, 2015). Processes at both the cellular and molecular level facilitate this efficient mechanism. For example, *C. psittaci* uses intracellular pathways to the mitochondria and Golgi apparatus (Knittler and Sachse, 2015). Chlamydial inclusions mature, causing Golgi fragmentation using effector proteins, thereby ensuring bacterial growth and finally cell lysis (Knittler et al., 2014).

Patients with psittacosis typically have a recent history of bird exposure. Our patient gave a history of direct bird contact, including feeding garden birds such as pigeons and cleaning up bird feces. Moreover, her neighbors have a bird aviary. We hypothesize that any of the exposures mentioned above could have infected our patient by inhalation of aerosolized *C. psittaci.* This is particularly true since there is a prolonged survival of this bacterium in the environment (Branley et al., 2014).

Other etiologies of atypical pneumonia with systemic manifestations were considered, including *Mycoplasma pneumoniae* and *Legionella.* However, additional tests showed neither atypical

bacteria nor viruses. A catastrophic antiphospholipid syndrome could explain the pulmonary embolisms and skin manifestations. However, specific tests for antiphospholipid antibodies were negative, making this syndrome unlikely. A (doxycycline-induced) vasculitis could explain the impressive and progressive dermatologic manifestations. However, testing for antibodies was negative. Also, vasculitis is unlikely since the patient received prednisone simultaneously with doxycycline, thereby suppressing the potential adverse effect of doxycycline. On top of that, no effect was observed of high-dose prednisone. Moreover, vasculitis fails to account for many of the other findings in this case. A psittaci infection that started locally in the lungs, spread systemically and caused multi-organ failure, could explain all the features of this case.

In diagnosing psittacosis, PCR is preferred over serology because the latter uses an antigen of lipopolysaccharide anchored to the outer membrane of both *C. psittaci* and *C. pneumoniae* (Stewardson and Grayson, 2010). Due to cross-reactivity, discrimination with serology is impossible. In the current case, real-time PCR using primers targeting the inclusion membrane protein A (incA) genes showed a Ct-value of 35. The patient had been treated with doxycycline for a few days, which could explain this relatively high value. Doxycycline, a tetracycline derivative, is the antibiotic of choice for psittacosis. Ciprofloxacin, a fluoroquinolone, has in vitro activity against *C. psittaci* with an MIC_{90} value of 2 mg/L (Miyashita et al., 2002). However, it is important to realize that the use of antibiotics in the poultry and pet bird industry has increased; therefore, antibiotic resistance should be taken into consideration (Beeckman and Vanrompay, 2009).

Conclusion

We have proven that this multi-organ failure is due to *C. psittaci* by PCR and serology with a history of direct bird contact. We recommend a thorough evaluation of the medical history of any patient with respiratory symptoms, including professional and leisure occupations, in order to link respiratory symptoms to a *C. psittaci* infection. When a patient has multi-organ failure, a compatible clinical syndrome, and a history of contact with birds, psittacosis should be considered. As described in this case, PCR identifies *C. psittaci* specifically and eliminates cross-reactivity of other *Chlamydia* species. Also, PCR quantifies the rate of infection. BAL fluid is a suitable source and could have a cornerstone place in diagnosing psittacosis.

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Conflict of interest

None of the other authors report a conflict of interest. All authors attest they meet the ICMJE criteria for authorship.

Ethical considerations

Not applicable.

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References

Beeckman DSA, Vanrompay DCG. Zoonotic Chlamydophila psittaci infections from a clinical perspective. Clin Microbiol Infect 2009;15(1):11–7.
Branley JM, Weston KM, England J, Dwyer DE, Sorrell TC. Clinical features of endemic community-acquired psittacosis. New Microbe New Infect 2014;2:7–12.
Hogerwerf L, de Gier B, Baan B, van der Hoek W. Chlamydia psittaci (psittacosis) as a cause of community-acquired pneumonia: a systematic review and meta-analysis. Epidemiol Infect 2017;145:3096–105.
Knittler MR, Sachse K. Chlamydia psittaci: update on an underestimated zoonotic agent. Pathog Dis 2015;73:1–15.
Knittler MR, Berndt A, Bocker S, Dutow P, Hanel F, Heuer D, et al. Chlamydia psittaci: new insights into genomic diversity, clinical pathology, host-pathogen interaction and anti-bacterial immunity. Int J Med Microbiol 2014;304:877–93.
Miyashita N, Fukano H, Yoshida K, Niki Y, Matsushima T. In-vitro activity of moxifloxacin and other fluoroquinolones against *Chlamydia* species. J Infect Chemother 2002;8:115–7.
Rijksinstituut voor Volksgezondheid en Milieu (RIVM), Staat van Zoönosen 2019, https://www.rivm.nl/bibliotheek/rapporten/2020-0130.pdf, 2020 (last accessed 22 March 2021).
Stewardson AJ, Grayson ML. Psittacosis. Infect Dis Clin N Am 2010;24:7–25.
Semel JD. Cutaneous findings in a case of psittacosis. Arch Dermatol 1984;120:1227–9.
Schmahmann JD. Psittacosis centenary — 'pneumotyphus' reviewed. S Afr Med J 1982;62(24):898–901.
Verweij PE, Meis JF, Eijk R, Melchers WJ, Galama JM. Severe human psittacosis requiring artificial ventilation: case report and review. Clin Infect Dis 1995;20(2):440–2.
Yung AP, Grayson M. Psittacosis: a review of 135 cases. Med J Aust 1988;148(5):228–33.