CASE REPORT

Psittacosis pneumonia with the reversed halo sign: a case report and literature review



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Abstract

Background *Chlamydia psittaci* is a rare pathogen that causes community-acquired pneumonia. The reversed halo sign (RHS) is a computed tomography (CT) finding that is commonly observed in diseases such as cryptogenic organizing pneumonia, invasive fungal infections, tuberculosis, sarcoidosis, and pulmonary thromboembolism, but has seldom been described in association with psittacosis pneumonia.

Case presentation We report a case in which a 26-year-old man with a history of close contact with pigeons and chicken manure presented with fever and cough for 6 days. A CT examination revealed the RHS in the right lower lobe of the lung. Psittacosis pneumonia was diagnosed by metagenomic next-generation sequencing of the patient's bronchoalveolar lavage fluid. Treatment with omadacycline abolished his symptoms. We also discuss six other cases of psittacosis pneumonia with the RHS identified by literature search.

Conclusions When clinicians encounter patients with atypical pneumonia with the RHS and a history of contact with poultry, psittacosis should be considered.

Keywords *Chlamydia psittaci*, Reversed halo sign, Computed tomography, Metagenomic next-generation sequencing, Case report

Background

Psittacosis is a zoonotic disease caused by *Chlamydia psittaci* that is transmitted to humans primarily from birds. Non-avian animals also harbor the bacterium [1]. Interpersonal transmission is rare but still possible [2]. Annually, psittacosis accounts for 1–2% of community-acquired pneumonia cases [3, 4]. As an obligate intracellular bacterium, the diagnosis of *Chlamydia psittaci*

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¹Department of Respiratory Diseases, The First Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, China ²State Key Laboratory for Diagnosis and Treatment of Infectious Diseases, Collaborative Innovation Center for Diagnosis and Treatment of Infectious Diseases, National Clinical Research Center for Infectious Diseases, The First Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, China infection is challenging because traditional culture is technically difficult and time-consuming (up to several weeks), and serological antibody testing requires acute and convalescent samples and delays confirmation [5]. With the widespread application of metagenomic nextgeneration sequencing (mNGS), the number of reported psittacosis cases has increased [6, 7]. Thus, the incidence of this disease may be underestimated [8].

When not treated in time, psittacosis can lead to death [9, 10]. Accordingly, early identification of this disease is critical. However, the clinical manifestations of *Chlamydia psittaci* infection lack specificity [3, 11] and the mNGS technique is costly. Therefore, the patient's history of contact with birds and imaging manifestations must be considered if the disease is suspected. Common imaging manifestations of psittacosis pneumonia include



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consolidation, single nodules, and ground-glass opacities [12, 13]; the reversed halo sign (RHS) is rare.

The RHS is a computed tomography (CT) finding that appears as a focal ring-shaped area of ground-glass attenuation surrounded by a partial or complete rim of consolidation [14, 15]. When originally described, it was thought to be fairly specific to cryptogenic organizing pneumonia (COP), but it has subsequently been found to manifest with numerous noninfectious and infectious diseases, including pulmonary paracoccidioidomycosis, mucormycosis, tuberculosis, pulmonary lymphomatoid granulomatosis, Wegener's granulomatosis, and pulmonary infarction [14, 16, 17]. The RHS has also been observed in patients with 2019 coronavirus disease (COVID-19) [18, 19].

Here, we present a case of psittacosis pneumonia characterized by the RHS that was diagnosed by mNGS of bronchoalveolar lavage fluid (BALF) and treated successfully with antimicrobial agents. We also discuss other cases of psittacosis presenting with the RHS identified by literature review.

Case presentation

A 26-year-old man was referred to our hospital on 26 January 2023. He presented with fever and cough with sputum for 6 days and a maximum temperature of $39.3 \,^{\circ}$ C. On the third day of onset, he visited a local hospital and underwent testing. His white blood cell (WBC) count was normal, and his C-reactive protein (CRP) level was 54 mg/L (ref., 0–8 mg/L). A chest CT examination revealed inflammatory infiltration in the lower lobe of the patient's right lung (Fig. 1A). After treatment for 3 days with cefuroxime, levofloxacin, dexamethasone, and azvudine, the patient's fever persisted. A repeat CT examination performed on day 6 revealed the RHS in the right lower lobe (Fig. 1B). The patient was subsequently admitted to our hospital for further treatment.

The patient kept more than 10 pigeons and had mistakenly inhaled chicken manure before symptom onset. He resided in Zhejiang Province, southern China, and had not traveled recently. He did not smoke or use drugs. He had no relevant past medical or family history.

On admission to our hospital, the patient's vital signs were as follows: body temperature, 39.3 °C; pulse rate, 136 beats/min; respiratory rate, 21 breaths/min; and blood pressure, 114/61 mmHg. His oxygen saturation was 98% on room air. No rales were heard in either lung on auscultation. Laboratory tests revealed the following: WBC count, 9.16×10^9 /L; neutrophil count, 6.89×10^9 /L (75.2%); lymphocyte count, 1.22×10^9 /L (13.3%); CRP level, 46 mg/L; erythrocyte sedimentation rate, 49 mm/h; and procalcitonin level, 0.16 ng/mL. Bronchoscopy showed mild hyperemia and swelling of the bronchial mucosa in the right basal branches (Fig. 2). mNGS of the patient's BALF yielded sequence reads corresponding to Chlamydia psittaci (reads 12). No other potential pathogens were found. Additionally, BALF samples were tested on bacterial and fungal smear and culture, as well as geneXpert MTB/RIF. All results were negative. Omadacycline was empirically given (first dose 0.2 g, then 0.1 g/ day) at the admission and continued after confirmation of psittacosis. The temperature was normal since the following day. He was discharged after five days and switched to oral azithromycin (0.5 g/day for 9 days). His cough completely resolved 2 weeks later. A CT examination performed 26 days later showed radiological improvement, leaving mild linear opacities (Fig. 1C).

Literature review

To identify other cases of psittacosis pneumonia with the RHS reported between 2003 and 2023, and to clarify the clinical features of this disease, we searched the PubMed, Embase, and Web of Science databases using the keywords ("psittacosis" OR "*Chlamydia psittaci*" OR "psittacosis pneumonia") AND ("reversed halo sign" OR "atoll sign" OR "CT"). We identified five full-text articles with images describing six cases [20–24].



Fig. 1 Chest CT images from the patient's third (23 January 2023; **A**) and sixth (26 January 2023; **B**) days of illness at the local hospital, and 26 days later (15 February 2023; **C**). Note the exudation in the right lower lobe in (**A**) and the RHS in the right lower lobe in (**B**). In (**C**), the exudation is mostly absorbed, leaving mild linear opacities



Fig. 2 Bronchoscopic characteristics of the patient's psittacosis pneumonia: mild hyperemia and swelling of the bronchial mucosa in the right basal branches. (A) main carina, (B) left main bronchus, (C) right intermediate bronchus, and (D) right basal branches

(We apologize for the error in citation. Case 5 and 6 should be cited as reference 40 "Clinical and imaging features of Chlamydia psittaci pneumonia: an analysis of 48 cases in China", not reference 24 "Clinical features of psittacosis in 46 Chinese patients". Please kindly assist in removing reference 24 and replacing it with reference 40, and ensure that the citation in the Table 1 is updated accordingly. Thank you for your assistance.) The clinical characteristics of these cases are summarized in Table 1.

The ages of the patients in this sample ranged from 26 to 61 years. Five of the six patients were women. No underlying disease was identified. Psittacosis pneumonia had an acute onset in all cases, and symptoms included fever, cough, headache, and dizziness. Previous studies reported that *Chlamydia psittaci* infection typically presents with an abrupt onset of fever accompanied by rigors,

sweats, myalgia, headache, dry cough, dyspnea, chest pain, hemoptysis, and diarrhea. Less frequently observed manifestations include altered mental status, hepatitis, endocarditis, arthritis, myositis, encephalitis, disseminated intravascular coagulation, erythema nodosum, and keratoconjunctivitis [21]. Among the patients in this sample, nobody presented with such uncommon manifestations or multiple organ failure. One patient developed acute respiratory distress syndrome due to the lack of timely effective antibiotic administration. Effective treatment rapidly alleviated this condition, as confirmed by imaging. All patients had good prognoses.

Among the six patients, three affected the right lobe, one affected the left lobe, and two affected bilateral lungs. In four out of six patients, the RHS was situated in the lower lobe of the right lung. In our case, the lesion of the

Table	1 Char.	acteristics c	of repor	ted cases of (Chlamydia	<i>psittaci</i> infe	ction								
Case	Sex, age (years)	Country	Year	Symptoms	Under- lying disease	History of avian exposure	The time of RHS detection	Location of lung lesion (Location of RHS)	Con- tours of RHS	Pleural effusion	Diag- nostic methods	Medication	Treatment duration	Radio- graphic de- tection of absorption	Clinical outcome
1 [20]	F, 26	Japan	2021	Cough and fever	None	Pigeon feces	2 weeks	Left upper lobe	Thick- ened walls	Absence	serology	Azithromycin (oral, 500 mg/day)	Ч	26 days	Symptoms im- proved within 3 days, mild cough persisted for 2 months
2 [21]	F, 35	Nepal	2022	High-grade fever with chills, rigors, and headache	None	Dead parrot	2 weeks	Right upper and right lower lobes (both)	Thick- ened walls	Absence	clinical assessment	Doxycycline (oral, 100 mg twice daily)	2 weeks	2 weeks	Condition im- proved within 48 h, asymp- tomatic after 2 weeks
3 [22]	F, 52	Japan	2007	High fever, non- productive cough, and general fatigue	None	Dead parakeet	3 days	Right lower lobe	Thick- ened walls	Absence	serology	Minocycline (NA)	AA	Mostly, 28 days	Temperature returned to nor- mal in 1 day
4 [23]	F, 61	China	2020	Fever, rigor, weakness, productive cough, and dizziness	None	Pet parrot	3 days	Both lungs (Right lower and left lower lobes)	Thick- ened walls	Absence	mNGS	Moxifloxacin (NA)	¥Z	Partial, 8 days	Temperature returned to nor- mal in 1 day
5 [24]	M, 52	China	2021	Fever	AN	NA	3 days	Right lower Iobe	Thick- ened walls	Absence	mNGS	NA	NA	AN	AA
6 [24]	F, 49	China	2021	Fever and cough	AN	NA	10 days	Both lungs (Right upper lobe)	Thick- ened walls	Absence	mNGS	NA	NA	AN	AN
7 This study	M, 26	China	2023	Fever and cough with sputum	None	Pigeons	6 days	Right lower Iobe	Thick- ened walls	Absence	mNGS	Omadacycline(first dose 0.2 g, then 0.1 g/day for5 days) + oral azithromycin (0.5 g/day for 9 days)	2weeks	Mostly, 26 days	Temperature returned to normal on the following day, cough com- pletely resolved 2 weeks later
F, female	s; M, male	e; mNGS, met	agenomi	c next-generati	on sequenci	ng; NA, not av	ailable; RHS, r	eversed halo sig	5						

RHS was also located in the lower lobe of the right lung. The results are consistent with the findings of previous studies. In psittacosis pneumonia, the lower lobes were involved most frequently, followed by the upper and middle or lingular lobes [12, 25].

Radiological features of psittacosis pneumonia are characterized by varying degrees of exudation and consolidation, as well as the presence of bronchial inflation signs, pleural effusion, pleural thickening, and enlargement of mediastinal lymph node. The occurrence of the RHS is relatively rare [26]. Most patients with severe pneumonia caused by Chlamydia psittaci have been observed to exhibit multiple lobar distribution, consolidation, and ground-glass opacities on CT images; some present pleural effusion [3, 27]. The extent of consolidation was related closely to the severity of the disease [12]. In our case and the other six cases we reviewed, exudation and consolidation were observed, while pleural effusion was absent. Pleural effusion tends to be more prevalent in severe cases of psittacosis pneumonia. Additionally, the RHS in these cases was characterized by a thickened wall, with small nodules absent both on the walls and within the area, distinguishing it from the nodular RHS typically associated with active granulomatous diseases [28].

In case 3, the initial CT scan revealed the RHS in the right lower lobe. Despite cefpirome treatment, symptoms persisted, and the infiltrates migrated to the left upper lobe. Acute respiratory failure developed despite glucocorticoid treatment, but recovery followed minocycline administration. Another study reported a case of psittacosis pneumonia with migratory infiltrates due to ineffective pharmacological interventions. Doxycycline treatment improved the patient's cough, sputum, and pulmonary lesions. Migratory infiltrates are observed in conditions like COP, chronic eosinophilic pneumonia, and ANCA-associated vasculitis, and may indicate disease progression in psittacosis [29].

As in our case, four patients in the sample had confirmed histories of exposure to poultry and/or other birds; exposure information was incomplete in the remaining two cases. *Chlamydia psittaci* can be transmitted to humans following close contact with birds and/ or their discharge, fecal material, or feather dust [1]. In a study conducted in Japan, the main sources of *Chlamydia psittaci* infection were parrots in females and pigeons in males [30]. Consistently, the male patients in our case and the other cases reviewed had contact with pigeons, and three of the four female patients had exposure to parrots.

The four patients for whom valid medication information was available were treated with azithromycin, doxycycline, minocycline, and moxifloxacin, respectively. We treated our patient sequentially with omadacycline and azithromycin. Tetracyclines are the primary choice for the treatment of psittacosis. Macrolides and quinolones can be used as alternatives [31]. After treatment with these drugs, the patients in our case and the reviewed cases recovered and had good prognoses.

Based on our case and those reported in the literature, the clinical manifestations of psittacosis pneumonia with the RHS are mostly mild. Affected patients tend to be young and in good health, with mild symptoms and favorable prognoses. The RHS in psittacosis pneumonia exhibits thickened walls and is frequently situated in the lower lobes.

Discussion

Different pathological processes can lead to similar CT appearances of the RHS. In COP, the central ground-glass opacity corresponds to alveolar septal inflammation with intact alveolar air spaces, and the denser rim reflects intraluminal organizing fibrosis in distal air spaces [32]. In tuberculosis, the ring corresponds to granulomata [11]. In sarcoidosis, the central granulomatous lesion has a restored normal tissue structure and the periphery is a newly developed inflammatory granuloma. In invasive fungal infections and pulmonary thromboembolism, the RHS reflects infarction, with more hemorrhaging occurring in the periphery than in the center [14, 16]. In COVID-19, ground glass opacities in the alveolar RHS correspond to exudative and interstitial inflammation, fibrin exudation, and alveolar hemorrhage [33, 34].

Here we show cases of psittacosis pneumonia with the RHS. The underlying mechanism of RHS formation in psittacosis pneumonia may differ from that observed in the aforementioned diseases. Upon entry of Chlamydia psittaci into the human body, a cascade of inflammatory cytokines is secreted, and various immune cells are engaged in mounting an immune response against the pathogen [35, 36]. The radiological manifestations of psittacosis pneumonia demonstrate variability throughout the different stages of the disease. Initially, it elicits an inflammatory response in the perivascular regions, which is characterized by the appearance of ground-glass opacities surrounding the small central vessels. As the inflammatory response intensifies, lesions progress from the core of the lobules to the secondary lobules. In the progressive phase, the image reveals prominent consolidation and interstitial alterations. In the repair-absorption phase, exudative shadows start to resolve, typically originating from the older central area, resulting in the emergence of a RHS. Following treatment, the disease advances to the dissipation stage [27, 37]. Haba Y et al. [20] offered a similar perspective, proposing that the RHS in psittacosis pneumonia may reflect the patient's strong immune response. The response facilitates the

spread of pneumonic lesions through Kohn's pores in a non-segmented manner, with rapid healing of their older central portions. This clinical presentation may cause the pneumonia to have transient imaging features. Further studies, particularly those involving histopathological examination, are needed to elucidate the mechanism of RHS formation in psittacosis pneumonia.

In our case, the RHS was observed on the sixth, not the third day of onset. Despite the administration of levofloxacin and corticosteroids, the patient continued to experience high fever. Additionally, case 3 presented with migratory lesions and acute respiratory distress syndrome. The phenomenon may be attributed to a robust immune response. Furthermore, we observed that in the case we presented and the other cases we reviewed, the RHS was characterized by a thickened wall. Notably, cavity formation was absent in cases of psittacosis pneumonia. The presence of a thickened rim indicates a rapid healing process or a vigorous immune response, rather than structural necrosis.

In our case, the potential influence of antibiotics and steroids on the formation of RHS should be considered. Notably, in cases 3 to 5, patients did not receive antibiotic or steroid treatment, yet the RHS was observed on the third day of illness. This suggests that RHS primarily arises from the natural progression of the disease rather than pharmacological intervention. The host inflammatory response is the major factor in the progression of psittacosis pneumonia [38].

All cases reviewed in our study involved East Asian patients, prompting questions about whether this is representative of the global distribution of psittacosis or indicative of a racial predisposition. The issue deserves further exploration. *Chlamydia psittaci* is distributed worldwide, with cases reported in several Asian countries, as well as in South and North America, and some European and Oceania countries [39]. In countries such as the USA, the UK, and the Netherlands, microbiological investigation is not recommended in the treatment of uncomplicated pneumonia [4], which might partly explain this issue. Further investigation is warranted to fully address this issue.

Our study is subject to some limitations: firstly, the sample size is comparatively small, precluding the possibility of conducting robust statistical analyses. Secondly, histopathological examination is essential for gaining deeper insight into the mechanism of RHS formation in psittacosis pneumonia.

In conclusion, psittacosis pneumonia should be considered in patients with the RHS and histories of contact with poultry or other birds. The early diagnosis of the disease and proper adjustment of medication to reduce its severity are critical.

Abbreviations

RHS	Reversed halo sign
CT	Computed tomography
mNGS	Metagenomic next-generation sequencing
COP	Cryptogenic organizing pneumonia
COVID-19	2019 coronavirus disease
BALF	Bronchoalveolar lavage fluid
CRP	C-reactive protein

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Not applicable.

Author contributions

Shumeng Zhang and Yiqi Fu carried out the data collection, literature review, and drafting of the manuscript. Liangjie Fang and Qiaomai Xu participated in the data collection and figure generation. Silan Gu and Jianying Zhou acquired the funding and revised the manuscript. Hua Zhou reviewed and edited the manuscript. All authors read and approved the final manuscript.

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Data availability

All data generated or analysed during this study are included in this published article.

Declarations

Ethics approval and consent to participate

The study was performed in accordance with the Declaration of Helsinki. The Clinical Research Ethics Committee of the First Affiliated Hospital, Zhejiang University School of Medicine approved this study (No. HT20231084A).

Consent for publication

Written informed consent for publication of this case report and accompanying images were obtained from the patient.

Competing interests

The authors declare no competing interests.

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