Severe Pneumonia With Thrombocytopenia Caused By *Chlamydia Psittaci*: A Case And Literature Review

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Case Report

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Abstract

Background: Severe pneumonia caused by *Chlamydia psittaci* is a rare infectious disease associated with living environment. The causes of thrombocytopenia were infection, leukemia, idiopathic thrombocytopenia and many other factors. The determination of platelet parameters could reflect the compensatory situation of bone marrow and provide a basis reason of thrombocytopenia identification.

Case presentation: Based on the patient's symptoms, exposure history, computerized tomography (CT) and next-generation sequencing, a preliminary diagnosis of the patient were made, at the same time other infections are excluded. We reported a case of severe pneumonia with severe thrombocytopenia caused by *Chlamydia psittaci*. During the treatment, he was diagnosed as parrot fever and secondary immune thrombocytopenia. Anti-infection and rising platelet with Doptelet treatment were in effect. The presence of high fever, feeling faint, gastrointestinal symptoms, images of chest CT and platelet reduction, *Chlamydia psittaci* might be considered as a priority reason of this case, other infections and hematology disorders excluded.

Conclusion: This is the first reported case of *Chlamydia psittaci*-induced thrombocytopenia associated with bone marrow changes and treatment. The efficacy of mokexin in the treatment of thrombocytopenia may be further generalized.

Introduction

Parrot fever is a zoonotic disease caused by *Chlamydia psittaci*, which is mainly found in birds and can be transmitted to human through the respiratory tract. Its typical clinical manifestations are fever, headache, cough and so on. These patients might be developed severe pneumonia, heart dysfunction, and others organ abnormal^[1]. The pathogen could be identified by high throughput sequencing, and clearly diagnosed by clinical symptoms and lung CT, etc. The causes of thrombocytopenia were infection, leukemia, idiopathic thrombocytopenia and many other factors. Some patients with idiopathic thrombocytopenia had an increased rate of destruction is caused by antiplatelet autoantibodies, which inhibited the platelets production of megakaryocyte. Due to the presence of antiplatelet antibodies in the body, platelets were destroyed by phagocytes^[2]. The determination of platelet parameters could reflect the compensatory situation of bone marrow and provide a basis reason of thrombocytopenia identification^[3–5]. Parrot fever itself could lead to thrombocytopenia, but its relationship to hematopoietic system was not clear. We reported a case of parrot fever with thrombocytopenia and review the literature.

Case Presentation

A 48-year-old man patient was admitted with dizziness 3 days, chest pain and fever 1 day and a history of possible hemorrhoids for 2 months, gastric ulcer, cervical spondylosis, penicillin allergy. On day 0, Outpatient Chest CT displayed an infective lesion in the left upper lobe of lung, and no obvious abnormality was found on craniocerebral CT. The patient was admitted to the department of cardiology

as "The cause of chest pain be investigated". Physical examination on day 0 showed body temperature 39.6°C, pulse 126 times/min, respiration 20 times/min, blood pressure 148/77 mmHg. Lung auscultation was clear, other physical examination were negative. Blood tests on the first day, a white blood cell count was 2910 per microliter of blood ($3.5\text{--}9.5\times 10^9/\text{L}$), 2630 neutrophils per mm^3 . Lymphocyte count was $100/\text{mm}^3$, hemoglobin 82g/L (130-175 g/L), a platelet count $7300/\text{mm}^3$ ($125\text{--}350\times 10^9/\text{L}$), C-reactive protein 193.9mg/L (normal value <10), serum amyloid A protein (SAA) >300mg/L (normal value <10). After admission, the patient was treated with anti-infection and lipid-regulating. The next day, the patient had dyspnea, oxygenation decreased, and low blood pressure, then transferred to the intensive care unit. Mechanical ventilation was treated to him assisting breathe, and at the same time he was given to fluid resuscitation. Chest X-ray on 3th showed large patches of high-density shadows in the upper field of the left lung, with visible air bronchial sign and unclear boundary. Lung infection was significantly worse on day 7th. Patchy shadows were seen in the middle field of the right lung, more than before (Figure 2). Nucleic acid tests for respiratory pathogens showed *chlamydia* DNA positive. High throughput sequencing of respiratory infection pathogen detection showed *acinetobacter baumannii* and *Chlamydia psittaci* infection, coverage of up to 99%. And humoral immunity showed immunoglobulin 7.57g/L (8.6-17.4g/L), immunoglobulin M 0.556 g/L (0.3-2.2g/L), complement C3 0.305g/L (0.7-1.4g/L), complement C4 0.060 g/L (0.1-0.4 g/L), cellular immunity showed CD3 30 /uL (723-2737/uL), CD4 21 /uL (404-1612/uL), CD8 5 /uL (220-1129/uL), CD19 18/uL (80-616/uL), CD16+56 22 /uL (4-724/uL), ferritin 89.8ng/mL, Natural Killer (NK) cell count showed CD16+56 29.06% (5-26%), CD16+56 count 24/uL (84-724/uL). Anti-platelet IgG was positive. Though platelet supplementation, the number of platelets were less than $20\times 10^9/\text{L}$ for many times (Figure 3D). Bone marrow biopsy displayed active bone marrow hyperplasia (50%), grain to red ratio was low. The granule system was mainly in the middle and young stages. The red system was slightly hyperplasia, mainly middle to late juvenile erythrocytes. Megakaryocytes were common, dominated by lobulated nuclei. The immunohistochemical result of marrow biopsy showed CD117(-), CD15(granule +), CD34 (-), CD38 (scattered +), CD56 (-), CD61 (meganucleus +), myeloperoxidase (MPO) (myeloid +), Mun-1 (scattered +) (Figure 3E). The type of leukemic cells displayed that the proportion of granulocytes were increased, and a small part of erythrocytes expressed CD56 (14%). The erythrocytes in the nucleated area were accounted for about 14.5% of all the nucleated cells. An increased proportion of neutrophils and reticular cells were found in the cytological examination of bone marrow. The proportion of lymphocytes were reduced and we could detect myelocytes in the peripheral blood (Figure 3F/3G). Bone marrow karyotype of the patient were 46, XY (Figure 3H). The bone marrow fusion gene FISH was negative. He was treated with anti-infection (including doxycycline), organ protection, component blood transfusion, elevated platelet (recombinant human thrombopoietin and Doptelet), extracorporeal membrane oxygenation (ECMO) short term adjuvant, nutrition and symptomatic supportive therapy (Figure 1). His diagnoses were septic, septic shock, severe pneumonia (*Chlamydia psittaci* and other infections), multiple organ dysfunction, thrombocytopenia, moderate anemia, intestinal obstruction and small intestine perforation.

Discussion

The rate of pneumonia with *Chlamydia psittaci* infection were fluctuated between 0 and 6.7%, and usually associated with other bacterial infections^[6]. NK cells were affected by *Chlamydia psittaci*, which promoted secretory functions maturation and released in a non-infectious with highly immunogenic that induced the T helper type 1 immune response and enhanced antimicrobial effects powerfully^[7]. However, the mortality rate of patients with low immunity and severe illness were extremely high. Studies showed that pregnant women with *Chlamydia psittaci* infection were prone to miscarriage, malformation and stillbirth, and even increasing the risk of maternal death^[8, 9]. A case questionnaire in Sweden found that exposed to wild bird or domestic feces or aerosols would predispose to *Chlamydia* infections^[10]. The patient might be at risk of being exposed to *Chlamydia psittaci* in the environment where he lived. He had dizziness, fever, chest pain, poor appetite and other clinical manifestations, then clearly diagnosed by multiple next-generation sequencing and DNA tests of respiratory pathogens. *Coronavirus* disease 2019 (COVID-19) and other special bacterial infections were excluded. This disease usually last between 10 to 14 days, and in more severe cases might last between 3 to 7 weeks^[11].

Hemoglobin abnormalities might occur in some patients, and the number of leukocytes was initially reduced in this case. And the primary symptoms were included dizziness and chest pain indicating that other organ systems might be abnormal. Studies also had found that patients with severe pneumonia might have multiple organ damage, such as disorder of heart, liver, kidney, coagulation, etc. The blood tests of the patient showed abnormal kidney function, and chest CT showed partial localized plaque from hilum with left lung. The number of platelets were persistently low with positive antiplatelet antibodies, and coagulation abnormalities were found with multiple critical values. Bone marrow biopsy revealed hematopoietic system abnormal were closely related to infections. Mainly disorder of megakaryocyte maturation had not been found, so he was diagnosed with secondary immune thrombocytopenia.

The patient was found to be infected with *Chlamydia psittaci* after repeated tests and screening. Multiple organ dysfunction was deteriorated, and he was treated with doxycycline, quinolones, azithromycin and other antibiotics in conjunction active therapy. His physical condition had improved for a time and wean off the ventilator. However, the patient was assessed to be able to eat and recognized to be able to receive some form of enteral nutrition. After a period of time, he suddenly developed intestinal obstruction and then intestinal perforation. The outbreak of bacterial infections was a double whammy to the patient. In addition, *Chlamydia psittaci* could inhibit the immune system^[12], and might affect the hematopoietic system. The physical condition was worse with immunodeficiency. Under platelet transfusions and drug therapies, the number of platelets rose for short duration and then declined. At the same time, we found increased levels of antiplatelet antibodies. The bone marrow aspiration and bone marrow biopsy were procedure to collect and examine bone marrow, and the bone marrow biopsy showed no obvious abnormalities. Studies had shown that thrombocytopenia in self-expendable could also be occur during ECMO with systemic heparinization and dialysis^[13, 14]. ECMO and dialysis treatment were carried out on day5 to day12 both, and thrombocytopenia were observed under the condition of platelet infusion and recombinant human thrombopoietin injection. Therefore, it could conclude that the influence of ECMO and dialysis on thrombocytopenia of this patient could not be excluded. From day20 to day33, the patient

received Doptelet, 3 portions of platelets treatment, and intermittent dialysis. To our surprise, platelets were increased from the lowest 20×10^9 /L to the highest 96×10^9 /L, which indicated that Doptelet might have a significant effect on increasing platelets and better than recombinant human thrombopoietin. Doptelet, also known as avatropapa, was experienced two phase 3 clinical trials to show the superiority and safety to reducing platelet transfusion of patients with thrombocytopenia and chronic liver disease^[15]. It was a thrombopoietin receptor agonist that bound to the thrombopoietin (TPO) receptor in the transmembrane domain and could be taken orally. Not only was it very effective, but it could be taken orally daily and there were no dietary restrictions^[16].

Reducing contact with birds and poultry, we would cut off the source of infections. And pneumonia with *Chlamydia psittaci* infections should be found as early as possible and given early intervention treatment as far as possible. It was also need to distinguish legionella infection from other types of pneumonia. The result of this patient suggested that severe pneumonia caused by *Chlamydia psittaci* led to hematologic diseases with positive antiplatelet antibodies and secondary platelets decreased and indicated that the prognosis of the patient was bad. Organ dysfunction were difficult to recover. Therefore, it was necessary to providing the reference for the diagnosis, treatment and prognosis of *Chlamydia psittaci* related diseases in the future.

Conclusion

In summary, this is the first case of severe pneumonia with thrombocytopenia caused by *Chlamydia psittaci* occurring in a patient in China, suggesting that thrombocytopenia was related to platelet antibody, infection, dialysis and ECMO anticoagulation, and moksitin has a satisfactory therapeutic effect. With the patient's consent (supply figure), this case reminds the clinician that early identification of the pathogen and effective anti-infective therapy are important for the patient's prognosis.

Abbreviations

CT: computerized tomography

SAA: serum amyloid A protein

MPO: myeloperoxidase

NK: Natural Killer

ECMO: extracorporeal membrane oxygenation

COVID-19: *coronavirus* disease 2019

TPO: thrombopoietin

Declarations

Funding

Not applicable

Availability of data and figures

The datasets and figures used during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent

This study was conducted with the approval of the Clinical Research Ethics Committee of Renmin Hospital of Wuhan University (approval number: WDRY2020-K219).

Consent for publication

All data from this article are available with patient consent.

Conflict of interest

The authors declare that they have no conflict of interest.

References

1. Shaw KA, Szablewski CM, Kellner S, Kornegay L, Bair P, Brennan S, et al., Psittacosis Outbreak among Workers at Chicken Slaughter Plants, Virginia and Georgia, USA, 2018. *Emerg Infect Dis*, 2019. 25(11): p. 2143-2145.
2. Cooper N, Ghanima W, Immune Thrombocytopenia. *N Engl J Med*, 2019. 381(10): p. 945-955.
3. Chiasakul T, Akkawat B, Rojnuckarin P, The Procoagulant Profile in Patients with Immune Thrombocytopenia and Its Association with Bleeding Symptoms. *Thromb Haemost*, 2019. 119(7): p. 1194-1197.
4. Yazdanbakhsh K, Imbalanced immune homeostasis in immune thrombocytopenia. *Semin Hematol*, 2016. 53 Suppl 1: p. S16-9.
5. Qi J, You T, Pan T, Wang Q, Zhu L, Han Y, Downregulation of hypoxia-inducible factor-1alpha contributes to impaired megakaryopoiesis in immune thrombocytopenia. *Thromb Haemost*, 2017. 117(10): p. 1875-1886.
6. Hogerwerf L, B DEG, Baan B, W VDH, Chlamydia psittaci (psittacosis) as a cause of community-acquired pneumonia: a systematic review and meta-analysis. *Epidemiol Infect*, 2017. 145(15): p. 3096-

7. Radomski N, Franzke K, Matthiesen S, Karger A, Knittler MR, NK Cell-Mediated Processing Of *Chlamydia psittaci* Drives Potent Anti-Bacterial Th1 Immunity. *Sci Rep*, 2019. 9(1): p. 4799.
8. Katsura D, Tsuji S, Kimura F, Tanaka T, Eguchi Y, Murakami T, Gestational psittacosis: A case report and literature review. *J Obstet Gynaecol Res*, 2020. 46(5): p. 673-677.
9. Paul L, Comstock J, Edes K, Schlager R, Gestational Psittacosis Resulting in Neonatal Death Identified by Next-Generation RNA Sequencing of Postmortem, Formalin-Fixed Lung Tissue. *Open Forum Infect Dis*, 2018. 5(8): p. ofy172.
10. Chereau F, Rehn M, Pini A, Kuhlmann-Berenzon S, Ydring E, Ringberg H, et al., Wild and domestic bird faeces likely source of psittacosis transmission-A case-control study in Sweden, 2014-2016. *Zoonoses Public Health*, 2018. 65(7): p. 790-797.
11. Gaede W, Reckling KF, Dresenkamp B, Kenkies S, Schubert E, Noack U, et al., *Chlamydia psittaci* infections in humans during an outbreak of psittacosis from poultry in Germany. *Zoonoses Public Health*, 2008. 55(4): p. 184-8.
12. Chu J, Zhang Q, Zhang T, Han E, Zhao P, Khan A, et al., *Chlamydia psittaci* infection increases mortality of avian influenza virus H9N2 by suppressing host immune response. *Sci Rep*, 2016. 6: p. 29421.
13. Renou A, Neuschwander A, Kimmoun A, Brodie D, Pirracchio R, Group H-ES, Modified 4T score for heparin-induced thrombocytopenia diagnosis in VA-ECMO patients. *Intensive Care Med*, 2020. 46(7): p. 1481-1483.
14. Ferreira JA, Johnson DW, The incidence of thrombocytopenia associated with continuous renal replacement therapy in critically ill patients. *Ren Fail*, 2015. 37(7): p. 1232-6.
15. Poordad F, Terrault NA, Alkhouri N, Tian W, Allen LF, Rabinovitz M, Avatrombopag, an Alternate Treatment Option to Reduce Platelet Transfusions in Patients with Thrombocytopenia and Chronic Liver Disease-Integrated Analyses of 2 Phase 3 Studies. *Int J Hepatol*, 2020. 2020: p. 5421632.
16. Bussel JB, Avatrombopag. *Br J Haematol*, 2018. 183(3): p. 342-343.

Figures

Figure 1

A timeline of the patient's condition

Figure 2

Patient's CT scan and chest X-ray. (Figure 2 A show CT scans on the 0th after admission, Figure 2B, C show chest radiographs at the time of 3th and 7th days after admission, suggesting that the lung infection worse.)

Figure 3

Platelets changes and bone marrow test results. (Figure 3D show Platelets changes after admission, Figure 3E show 40x Bone marrow imaging, Figure 3F show 100x Bone marrow imaging, Figure 3G show 100x Bone marrow cytology imaging, Figure 3H Bone marrow karyotype.)