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A Case of Chlamydia Psittacosis with Severe Pneumonia Combined with Acute Hepatitis B and Literature Review

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Abstract

Chlamydia psittaci infection can lead to severe clinical manifestations in humans, including rapidly progressive severe pneumonia, adult respiratory distress syndrome (ARDS), sepsis, multiple organ dysfunction, and even death. Here, we reported a 47-year-old man who presented with shortness of breath, fever and diarrhea. His chest CT showed right pneumonia with consolidation, and severe psittacosis pneumonia was confirmed by metagenomic sequencing of bronchoalveolar lavage fluid. The condition continued to worsen under ventilator treatment, and ARDS occurred. VV-ECMO was used to support for five days to improve hypoxia. In the middle and late stage of the disease course, the ALT of the patient showed an upward trend, and the HBV DNA and hepatitis B surface antigen were positive. Considering the medical history, it might be acute hepatitis B, and antiviral therapy was given. After three weeks of combined therapy, the patient recovered and was discharged from the hospital. Chlamydia psittacosis pneumonia is prone to misdiagnosis and misdiagnosis when the symptoms are not typical, and high-throughput sequencing is needed for definite diagnosis. Short-term use of ECMO in severe pneumonia of Chlamydia psittaci can help shorten the course of the disease and reverse the disease. The route of viral hepatitis B infection is unknown. If acute hepatitis B co-infection with other pathogens initiates antiviral therapy, it may prevent its transformation to chronic.

Keywords: Chlamydia psittacosis, severe pneumonia, Metagenomic next-generation sequencing (mNGS), ECMO, acute hepatitis B virus

1. Introduction

Psittacosis is a zoonotic natural foci disease caused by Chlamydia psittaci (C. psittaci). Diverse routes of transmission and strong virulence (Read TD, Joseph SJ, Didelot X, Liang B, Patel L & Dean D., 2013). 1% of community-acquired pneumonia (CAP) is caused by Chlamydia psittaci (Hogerwerf L, DE Gier B, Baan B & VAN DER Hoek W., 2017). The clinical manifestations are diverse and can involve multiple organs in the body. The symptoms are non-specific and can range from mild to severe. Metagenomic next-generation sequencing (mNGS) of bronchoalveolar lavage fluid has great potential for community-acquired pneumonia pathogen identification (Wu X, Li Y & Zhang M, et al., 2020). Greatly improve the accuracy of psittacosis diagnosis and reduce the delay of diagnosis and treatment (Chen X, Cao K & Wei Y, et al., 2020). There is no report of psittacosis combined with acute hepatitis B at home and abroad. There are two main outcomes after acute hepatitis B virus infection: acute self-limiting and chronic persistent, but most adults can recover spontaneously, and only a few become chronic. Here we report a case of a patient with severe psittacosis pneumonia and acute hepatitis B diagnosed by bronchoalveolar lavage fluid mNGS and the diagnosis and treatment of ECMO, anti-pathogen, and anti-virus. Parrot fever has been reported more and more in recent years. With the popularization of NGS, the diagnosis rate has greatly increased. Parrot fever is a contagious disease that can

easily turn into severe disease, and the proportion of patients on ventilators is high. However, there are not many case reports of successful treatment after ECMO, which is worth learning. And this case report with acute hepatitis, the discussion value is higher.

2. Case Presentation

2.1 History of Present Illness

A 47-year-old male patient was admitted to the hospital on March 2, 2021, due to "fever with diarrhea for 3 days, aggravation with shortness of breath for 1 day". The patient started to have fever 3 days ago, and the monitored temperature was up to 38.5°C, accompanied by yellow watery stools, 4-5 times/day, no unclean diet, no nausea, vomiting, no yellow skin, no abdominal pain, no tenesmus, no dizziness, headache, no cough, expectoration, shortness of breath, no palpitations, no chest pain, no joint and muscle pain, no obvious weight loss, after taking antipyretic and antidiarrheal drugs (specifically unknown) body temperature can return to normal temporarily, no attention. One day ago, the above symptoms aggravated, and shortness of breath, general weakness, unsteady gait, feeling of stepping on cotton, no visual field defect, no slurred speech and disturbance of consciousness, no limb movement disorder and limb twitching, went to our outpatient clinic for treatment, the results of chest CT examination showed right upper lobe inflammation with local consolidation; brain CT and CTA examination showed no abnormality. The initial diagnosis considered "pulmonary infection" and was admitted to the surgical ward for hospitalization. He was healthy and had no family history.

2.2 Physical Examination

Body temperature 36.8°C, heart rate 98 beats/min, respiration 24 beats/min, blood pressure 135/78mmHg. Acute sickness, lethargy, conscious, answer to the point, and cooperate in physical examination. There was no yellowing, petechiae, ecchymosis and rash on the skin and mucous membranes of the whole body, and there was no palpable enlargement of the superficial lymph nodes. There was dullness on percussion of the right lung, enhanced breath sounds in the right lung, and moist rales were audible. Physical examination of other parts and nervous system showed no abnormality.

2.3 Abnormal Results of Auxiliary Examination After Admission

Blood routine: white blood cell 7.28´10^9/L (reference value 3.5-9.5´10^9/L, the same below), neutrophil ratio 86.2% (40%-75%); procalcitonin 2.230ng/ ml (0-0.05 ng/ml); erythrocyte sedimentation rate 32mm/h (0-20 mm/h); liver function: alanine aminotransferase 70.6U/L (<40 U/L), aspartate Aminotransferase 160.8 U/L (<40 U/L), lactate dehydrogenase 740 U/L (100-300 U/L); renal function: creatinine 105.7 umol/L (59-104 umol/L), urea 7.3 mmol/L (3.1-8.0mmol/L); Electrolyte: potassium 3.08mmol/L (3.5-5.3 mmol/L), sodium 124mmol/L (136-145 mmol/L); HBsAg quantification 4.82U/ml (<0.05 U/ml), hepatitis B DNA quantification 5.29E+2 U/ml (<1.00E+2 U/ml).

2.4 Condition Changes and Diagnosis and Treatment After Admission

According to the patient's fever symptoms and signs of pulmonary crackles and lung CT examination showing pulmonary lobe inflammation and consolidation (Figure 1A), "community-acquired pneumonia" was diagnosed, and the third-generation cephalosporin "cefotaxime sodium" was empirically administered intravenously. "Sulbactam 2.25g qd" anti-infective treatment, supplemented by phlegm reduction, correction of electrolyte imbalance and other treatments. However, 24 hours after admission, the patient still had fever, shortness of breath, increased respiratory rate, 30 breaths/min, fingertip oxygen saturation was 91% under the condition of mask oxygen inhalation, arterial blood gas analysis (FiO2 61%): pH 7.569 (7.35-7.45), carbon dioxide partial pressure 3.03kPa (4.65-5.98 kPa), bicarbonate concentration 20.3 mmol/L (21-28mmol/L), anion gap 18.4 mmol/L (10-16 mmol/L), osmotic pressure 252 Osm (275.0-305.0 mmol/L), oxygen partial pressure 60.6 mmHg (95-100 mmHg); suggesting type I respiratory failure and respiratory alkalosis, the patient's condition was considered to have progressed to severe pneumonia, and non-invasive ventilator-assisted ventilation was given after transfer to ICU (FiO2 70%), plus "moxifloxacin 0.4g qd" combined with "cefotaxime sodium sulbactam 3g q8h" anti-infective therapy, fingertip blood oxygen saturation gradually increased to 97%, respiratory rate decreased to 25 beats/min. 12 hours later, the patient reappeared with high fever and shortness of breath, and the respiratory rate increased to 44 beats/min. The re-examination of arterial blood gas analysis showed that the partial pressure of oxygen was 50 mmHg, indicating that the respiratory failure had not been corrected. The patient received ventilator-assisted ventilation therapy, and was given hormone anti-inflammatory treatment; in addition, the patient's current antibacterial therapy has covered common pathogens, but the disease progresses rapidly, and the possibility of viral pneumonia cannot be ruled out. "Ganciclovir 0.4g q12h" antiviral treatment treat. 15 hours later, the partial pressure of oxygen was detected at 60 mmHg, and Pa02/FiO2 100 mmHg, indicating severe hypoxemia. The chest CT lesions progressed (Figure 1B, F). The patient's condition further progressed and deteriorated. ECMO treatment was started. Picked up (Figure 3). Chlamydia psittacosis was detected by high-throughput sequencing of pathogenic microorganisms in bronchoalveolar lavage fluid (BALF)

(Table 1). The patient was asked if he had been to the flower and bird market to buy parrots half a month ago. Ciclovir was added with the macrolide antibiotic “azithromycin 0.5g qd” which is sensitive to Chlamydia psittacosis. The patient’s oxygen partial pressure increased and body temperature decreased, indicating that the condition was improved. However, one day after discontinuation of ECMO according to the indication, the patient developed fever again, and the inflammatory indexes increased again (Figure 4), and the chest CT showed that the inflammatory lesions had shrunk (Figure 1C). Considering that the patient continued to use ventilator-assisted ventilation after admission, no Excluding the possibility of combined fungal infection, “voriconazole 0.2q q12h oral” antifungal treatment was added, and “moxifloxacin” was replaced with “piperacillin sodium tazobactam 2.5g q8h”, however, the BALF pathogenic microorganisms were sent again for inspection. The number and relative abundance of Chlamydia psittacosis sequences were significantly decreased, and no other pathogens were found (Table 1). After 8 days of discontinuation of ECMO, the chest CT scan showed obvious absorption of the lesions (Figure 1D), the intravenous azithromycin was discontinued, and the tetracycline antibiotic doxycycline was used orally (Figure 2); he was transferred from the ICU to the general ward for continued treatment.

In addition, the test results of the patient on admission showed that the hepatitis B surface antigen was positive, the DNA copy number of hepatitis B virus was increased, the e antigen/antibody and core antibody were all negative, and the aminotransferase was slightly increased. The antigen quickly turned negative and surface antibodies were produced, but the hepatitis B virus DNA could still be detected (Table 2). The patient still had fever under broad-spectrum antibacterial and antifungal therapy (Figure 2). The liver function ALT showed an upward trend (Figure 5), and the bilirubin was normal. Although there were no acute infection symptoms such as anorexia, fatigue, nausea, and vomiting, it was judged that acute hepatitis B infection was possible. The patient is currently suffering from Chlamydia psittacosis with severe pneumonia. The level of autoimmunity is low, and the nucleoside analog “entecavir” antiviral treatment should be considered comprehensively. The patient was observed in the general ward for 5 days without re-fever, and his condition improved and was discharged from the hospital. The patient did not continue taking “entecavir” after discharge. After returning to the hospital for re-examination 2 weeks later, chest CT showed that the lesions were completely absorbed (Figure 1E); while the hepatitis B virus surface antigen was re-positive again, and the surface antibody was negative, but HBV DNA was not detected (Table 2).

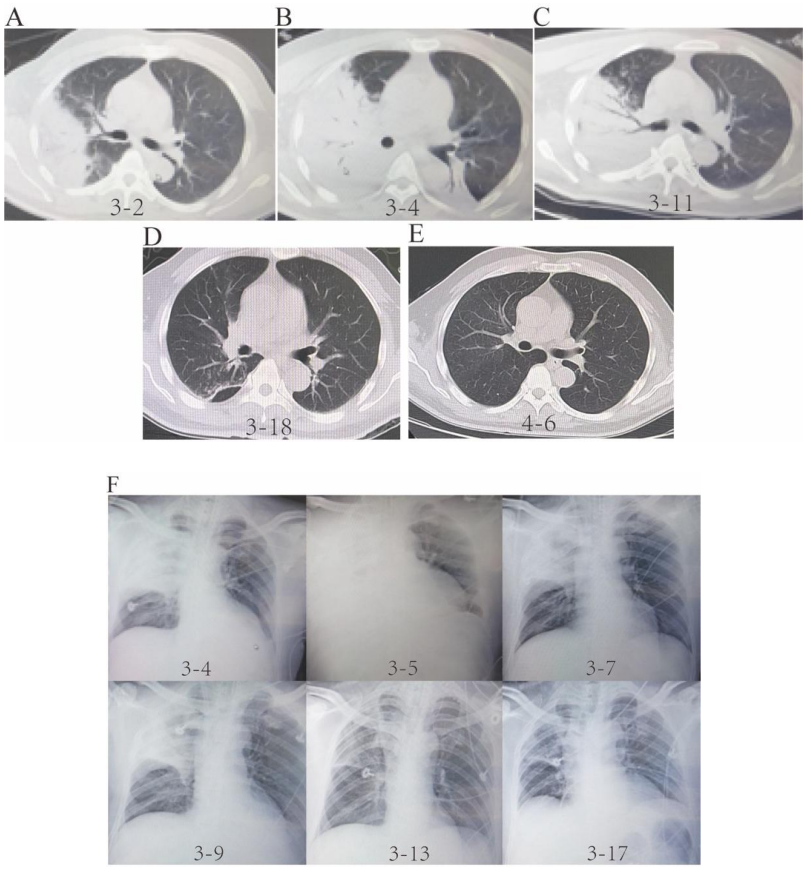

Figure 1. The lung CT and X-ray examinations of the patient during hospitalization showed the lesions in the

upper right lung, and the numbers on the lower right indicate the date of examination

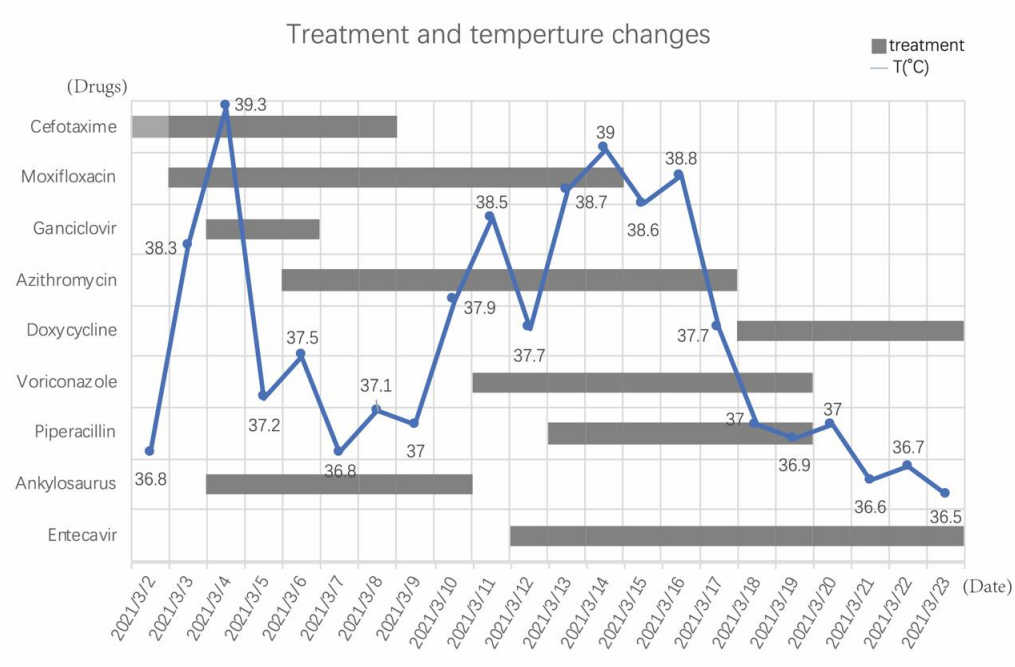

Figure 2. Schematic diagram of the patient's body temperature changes and medication during hospitalization

The abscissa represents the hospitalization time of the patient, the ordinate represents the specific medication, the bar graph represents the start and end time of the drug use, and the numbers on the blue line represent the highest body temperature of the patient on that day.

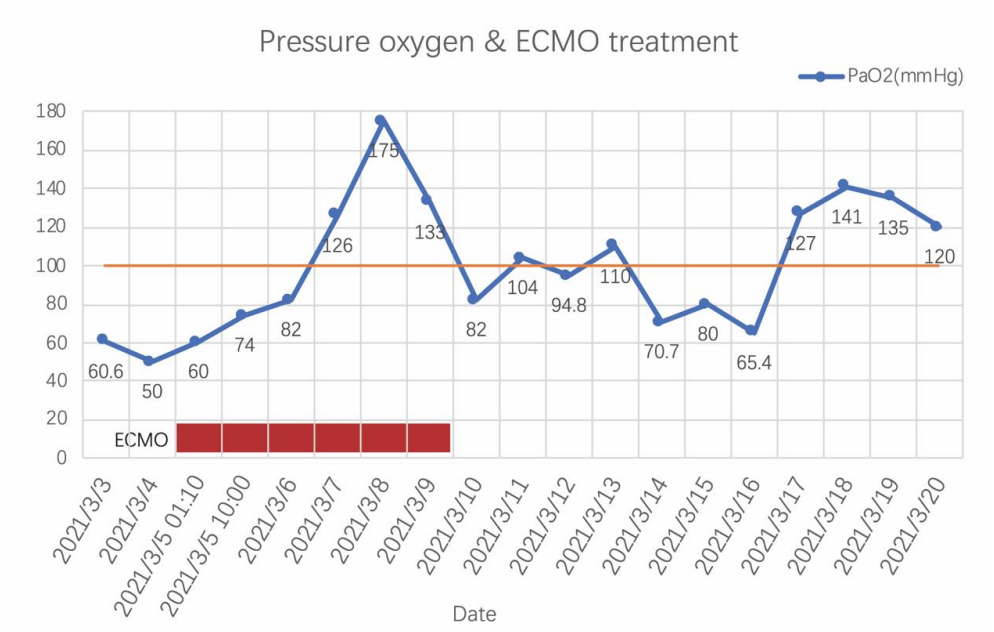

Figure 3. Schematic diagram of changes in partial pressure of oxygen and use of ECMO during hospitalization in this patient

The abscissa represents the length of hospital stay, the ordinate represents the partial pressure of oxygen, and the yellow line represents the normal value of partial pressure of oxygen; the red bar represents the start and end

dates of ECMO use.

Table 1.

Report date	Sample	detected Pathogens	Reads number	relative abundance
2021-3-6	BALF	chlamydia psittacosis	17806	99.4841%
2021-3-13	BALF	chlamydia psittacosis	220	2.319%

Table 2.

Detected date	HBV DNA copy number (<1.00E+2 U/ml)	Surface antigen quantification (<0.05 U/ml)	surface antibody quantification (<10 U/L)
2021-3-3	5.29E+2 U/ml	4.82U/ml	/
2021-3-5	/	Negative	177.90 U/L
2021-3-9	2.42 E+2 U/ml	negative	354.00 U/L
2021-4-6	<1.00E+2 U/ml	77.78 COI	< 2.00 U/L

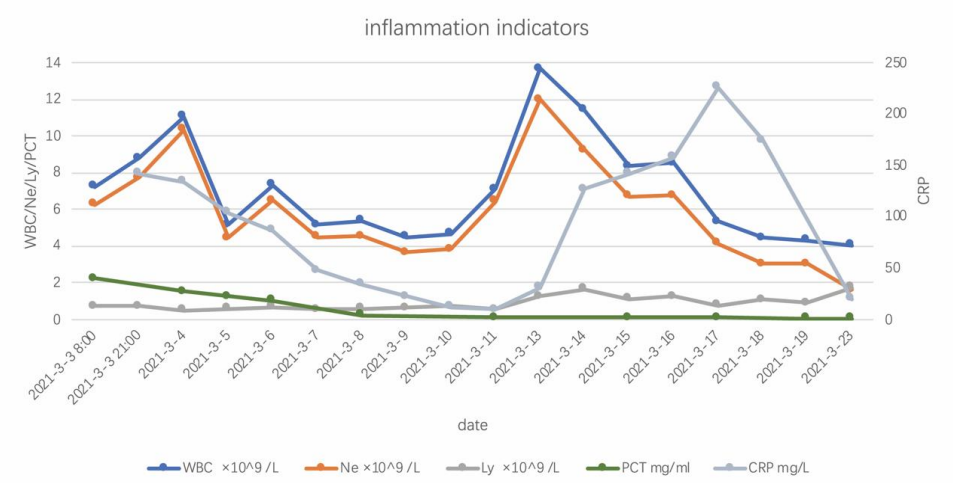

Figure 4. Changes in inflammatory markers (leukocytes and neutrophils and lymphocytes, procalcitonin, C-reactive protein) were measured during hospitalization in this patient

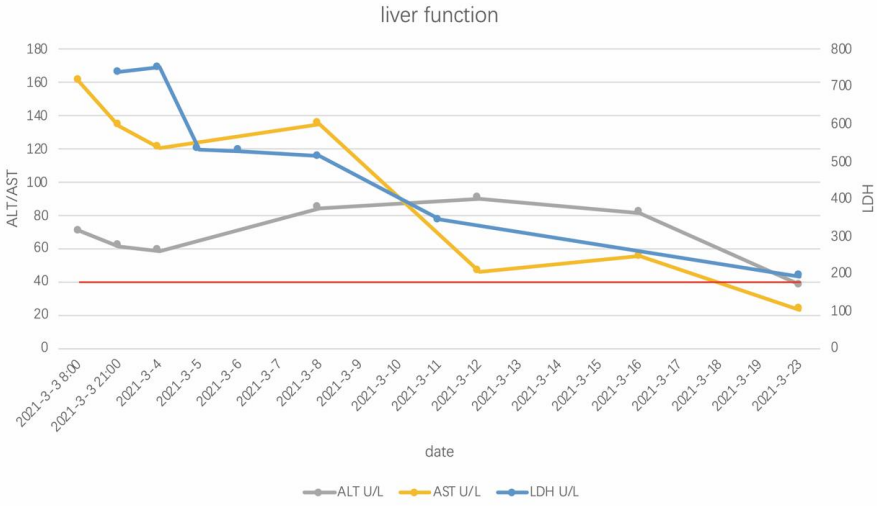

Figure 5. Changes in liver function in this patient during hospitalization

3. Discussion

Chlamydia psittaci is a strictly eukaryotic intracellular parasitic pathogen, Gram-negative, with a unique developmental cycle. Based on the sequencing of the antigenic structure's major outer membrane protein gene(ompA), there are ten genotypes existed, each of which has different host preferences (Knittler MR & Sachse K., 2015). Although all genotypes may infect humans, genotype A is believed to be the most common cause of human disease (Wolff BJ, Morrison SS & Pesti D, et al., 2015). In addition, Chlamydia psittaci also appears to modulate virulence by altering host immunity (Miyairi I, Laxton JD & Wang X, et al. 2011). The source of infection is the birds infected with Chlamydia psittaci. Humans are infected by contact with secretions, excreta, tissues and feathers of infected birds, or by inhalation of aerosolized microorganisms in feces, urine, respiratory and ocular secretions, even brief exposured to contaminated environments. But human-to-human transmission is rare (Wallensten A, Fredlund H & Runehagen A., 2014; Ito I, Ishida T, Mishima M & et al., 2002; Hughes C, Maharg P, Rosario P & et al., 1997). Pepole are generally susceptible, and it can occur at any age and gender, but with a peak age of onset at 35-55 years of age (Harkinezhad T, Verminnen K, De Buyzere M, Rietzschel E, Bekaert S & Vanrompay D., 2009). In 2018, there were 13 confirmed cases in Georgia and Virginia in the United States (DE Boeck C, Dehollogne C, Dumont A & et al., 2016), and outbreaks have also been reported in China (Song J, He QF., 2012). There is a possibility of re-infection after onset (Vassallo M & Shepherd RJ., 1997). When pathogens enter the lungs from the respiratory tract, they cause the body's inflammatory cascade and activation of reactive oxygen species, leading to tissue damage and rupture of alveolar capillary membranes. and other organs.

The incidence of Chlamydia psittaci has no obvious seasonality. The incubation period is 5-14 days (Harkinezhad T, Verminnen K, De Buyzere M, Rietzschel E, Bekaert S & Vanrompay D., 2009), and human infection varies from person to person, ranging from insignificant symptoms to severe systemic disease, with respiratory manifestations of varying degrees of pneumonia, pleurisy, acute respiratory distress syndrome and respiratory failure, and cardiovascular system manifestations of Pericarditis, myocarditis, endocarditis, pericardial effusion, arrhythmia, and vasculitis, arterial embolism; renal involvement can manifest as proteinuria, acute kidney injury, and acute interstitial nephritis; liver involvement manifests as hepatitis; hematologic involvement it manifests as hemolytic anemia, thrombocytopenic purpura, and hemophagocytic syndrome; involvement of the nervous system manifests as myelitis, meningoencephalitis, and psychiatric symptoms; in addition, there are skin manifestations such as erythema and arthritis (Chu J, Yarrarapu SNS & Durrani MI., 2022; Ojeda Rodriguez JA, Modi P & Brady MF., 2022). The patient in this case only had fever and non-specific manifestations of the digestive system in the early stage.

Due to the lack of routine testing, the incidence of psittacosis is difficult to determine and may even be underestimated (Rybarczyk J, Versteele C, Lernout T, Vanrompay D., 2020). The traditional isolation and culture efficiency of Chlamydia psittaci is low. Serological examination Micro-immunofluorescence test to detect double serum antibody titers increased by more than 4 times or IgM antibody titer ≥ 1:16 has diagnostic value, but they have poor specificity and limited sensitivity. qPCR can rapidly identify human psittacosis patients, but there is only high sensitivity in the acute phase and a limited detection time window (Nieuwenhuizen AA, Dijkstra F, Notermans DW & van der Hoek W., 2018; McGovern OL, Kobayashi M, Shaw KA & et al. 2021). mNGS can detect pathogens from very few clinical samples, and it is relatively easy to perform. So mNGS has reliable results, and has potential advantages in both sensitivity and specificity. Lung CT findings include patchy shadows, lung parenchyma changes, and some patients have air bronchus sign and pleural effusion, but they cannot be used as a basis for differential diagnosis. The patient in this study was diagnosed by bronchoalveolar lavage fluid sequencing.

Chlamydia psittaci belongs to the Chlamydia family, and the tetracycline antibiotic doxycycline is the first choice for treatment; macrolides such as azithromycin, roxithromycin and erythromycin are the preferred drugs for pregnant women and children, but azithromycin may be not sensitive to sulfonamides due to the presence of 23S rRNA gene (Stewardson AJ & Grayson ML., 2010). The patient in this case was given intravenous azithromycin and later changed to oral doxycycline to avoid the emergence of drug-resistant bacteria. Secondly, respiratory distress syndrome (ARDS) with psittacosis pneumonia can be treated with systemic hormone shock therapy (Hirata M, Noto M, Oda K, Tofuku Y, Takeda R & Kitagawa S., 1988). A domestic study reviewed 27 patients with severe psittacosis pneumonia in Southwest China. Glucocorticoids were used when ARDS occurred (Yang F, Li J, Qi B & et al., 2021). There are also reports in China that the application of low-dose glucocorticoid therapy to patients with hepatitis B-related acute-on-chronic liver failure or severe infection prone to infection can significantly improve the liver function of the patients. The patients in this study were also treated with methylprednisolone for a short period of time when they were seriously ill.

ECMO is used to treat patients with severe, life-threatening cardiopulmonary disease. A study in UK found that 95% of patients with severe respiratory failure received VV-ECMO respiratory support alone to achieve good

short-term outcomes (Warren A, Chiu YD, Villar SS & et al., 2020). There are also reports in China that clinicians successfully used ECMO to treat patients with ARDS caused by Chlamydia psittaci for the first time (Wang L, Shi Z, Chen W, Du X & Zhan L., 2021). The patients in this study continued to deteriorate under the condition of ventilator treatment, and the adjustment of ventilator parameters could not meet the needs of the patients. They were also treated with ECMO, and the outcome was good.

In this case, the hepatitis B virus surface antigen was detected positive in the early stage of the disease, and the surface antigen quickly turned to negative, while the surface antigen antibody gradually increased. During the period, the HBcAg and HBeAg could not be detected. Our patient was not vaccinated in childhood. He has received hepatitis B vaccine, has no history of blood product infusion, and has no other bad habits. Although the route of hepatitis B virus infection is not clear, it is not known whether it is related to Chlamydia psittacosis infection. Combining with the medical history, this patient should have acute hepatitis B virus infection with no obvious associated symptoms, and not a chronic hepatitis B carrier. However, we have added antiviral therapy in the middle and late stages of the disease course, and it is still worth discussing whether the drug is necessary. Once antiviral drugs are used, the timing of discontinuation should also be considered. The traditional opinion is that acute hepatitis B does not require antiviral treatment, mainly because 90-95% of patients can recover on their own. However, 5-10% of acute hepatitis B may become chronic. How to identify these patients and whether early intervention is needed is still inconclusive. The pathological examination of liver biopsy has an important reference value for the identification of acute hepatitis and chronic hepatitis, but the patient did not perform relevant differential examinations. For severe acute hepatitis B patients, early antiviral treatment is recommended. It has been observed from domestic and foreign reports that the liver kinetic energy damage caused by psittacosis is more obvious than the increase of AST and LDH than ALT (Xiao Q, Shen W, Zou Y & et al., 2021; Kawamura S, Ikematsu H & Ogimoto H., 1990; Shi Y, Chen J, Shi X & et al., 2021). The upward trend may be abnormal liver function caused by hepatitis B. It has been reported that patients with chronic hepatitis B have decreased immunity, which may be a predisposing factor for psittacosis (Shi Y, Chen J, Shi X & et al., 2021). Therefore, is there a certain link between Chlamydia psittacosis pneumonia and acute hepatitis B virus infection? Or does acute hepatitis B infection combined with psittacosis affect its outcome? The patient's re-examination of hepatitis B surface antigen turns positive again 2 weeks later, does it indicate that the patient has become a chronic hepatitis B carrier?

The prognosis for psittacosis depends largely on the patient's health status, disease severity, and early diagnosis and treatment. Full recovery may take 6 to 8 weeks. The mortality rate of Chlamydia psittaci infection in foreign countries is less than 1% (Macfarlane JT & Macrae AD., 1983). However, two recent retrospective studies in our country showed that 4 out of 27 patients died due to secondary infection (Yang F, Li J, Qi B & et al., 2021), and 2 out of 13 patients died (Wu HH, Feng LF & Fang SY., 2021). In some other countries, psittacosis is a notifiable disease and must be reported within 48 hours (DE Boeck C, Dehollogne C, Dumont A & et al., 2016). There have been reports of an epidemiological investigation based on an interdisciplinary, multi-team approach in Brazil following the confirmation of psittacosis cases, which resulted in the reorganization of shops selling bird pets and the referral of all infected parrots to veterinarians for treatment (Ferreira VL, Silva MV, Bassetti BR, Pellini ACG & Raso TF., 2017). Due to the potential public health risk of Chlamydia psittaci, the 2017 National Public Health Veterinary Association updated its Compendium of Tests and Strategies for the Management of Disease in Birds and Humans (Balsamo G, Maxted AM, Midla JW & et al., 2017). Therefore, when Chlamydia psittaci infection is found, it can be reported to the local health department or the Center for Disease Control so that appropriate public health response measures can be taken.

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