

# *Research progress of mNGS in the diagnosis and treatment of chlamydia psittaci pneumonia*

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**Keywords:** Research progress; mNGS diagnosis; chlamydia psittaci pneumonia

**Abstract:** Chlamydia psittaci pneumonia is an atypical pathogen pneumonia that ranges in severity from mild to severe with multiple organ failure. Due to the lack of specific clinical features and rapid and simple means of diagnosis, there is a high rate of misdiagnosis and missed diagnosis in clinical work. Therefore, this article reviews the clinical characteristics of chlamydia psittaci pneumonia patients, the application of mNGS technology in diagnosis and treatment, in order to improve the diagnosis rate of the disease by clinicians for accurate treatment.

## 1. Introduction

Psittacosis, also known as bird disease, is a zoonotic [1]. Disease caused by infection of the obligate intracellular gram-negative bacterium Chlamydia psittaci, which is intermediate in size between bacteria and viruses and infects humans primarily by inhaling aerosols formed from the urine, feces, or respiratory secretions of birds infected with Chlamydia psittaci [2]. Chlamydia psittaci often causes small outbreaks worldwide. Therefore, close contact with infected bird feathers and tissues and cleaning cages is also a risk of infection. Chlamydia psittaci can cause lung infection in humans if accidentally inhaled. Chlamydia psittaci pneumonia usually causes respiratory infection through inhalation of the pathogen, and when the body's immunity is reduced, the host immune response is induced [3]. Chlamydia psittaci pneumonia occurs when the body's immune system is compromised, triggering an immune response from the host. Through the proliferation of blood mononuclear macrophage system and spread to other organs, severe pneumonia may develop, and even respiratory and multiple organ failure, Chlamydia psittaci pneumonia is one of the causes of community-acquired pneumonia [4].

For a long time, the diagnosis of Chlamydia psittaci pneumonia often relies on etiological examination and epidemiological investigation. However, due to the difficulty of Chlamydia psittaci culture, poor specificity, and the pathogen is highly infectious, most hospitals cannot routinely carry out etiological diagnosis, so it is very difficult. So that doctors in the clinical work for this atypical pneumonia diagnosis of the number of cases is not large. In recent years, with the wide application of macrogenome second generation sequencing technology (mNGS) in fever of unknown cause and infectious diseases,

the confirmed cases of chlamydia psittaci pneumonia are increasing, but they are reported in single digits or dozens of cases. Due to the lack of a large number of case studies and individual differences, the clinical manifestations of chlamydia psittaci pneumonia are not typical. Easy misdiagnosis, missed diagnosis, severe cases can develop acute respiratory failure and serious extrapulmonary complications and complications, some need to be admitted to the intensive care unit, and even life-threatening, therefore, clinicians should strictly control the epidemiological history, have the ability to quickly identify the disease, and constantly summarize the clinical characteristics of existing confirmed cases. We should improve the reasonable etiology examination as soon as possible, provide targeted antibiotics for precise treatment in the early stage, thus avoid misdiagnosis and missed diagnosis. In view of the above, this article reviews the clinical characteristics of chlamydia psittaci pneumonia patients, the application of mNGS technology in diagnosis and treatment, in order to improve the diagnosis rate of the disease by clinicians for accurate treatment.

## 2. Genotype classification and epidemiology

### 2.1. Genotyping

Chlamydia psittaci belongs to the family Chlamydia, is a gram-negative pathogen, obligate intracellular parasite, is a microbe between Rickettsiae and viruses [5]. The developmental cycle of Chlamydia psittaci flourishes in two stages, a metabolically inactive form of infection, i. e., the protoplasm; Protoplasts are in the infection stage and often exist outside the cell. They are small in size and do not have biological activity, but have strong resistance to the external environment and can survive outside the host. As well as another metabolically active, non-infective form, the reticular body, psittacosis is a zoonotic disease known as psittacosis in humans, however, the name can be somewhat misleading as psittacosis can infect hundreds of birds based on isolation, antigen testing and serological results.

A total of 10 genotypes (A-G, E/B, M56 and WC) [6] can be classified according to the differential typing of Chlamydia psittaci in vitro membrane protein A gene sequence. Currently, the known genotypes are host-specific. Genotype A and B strains are usually associated with parrot birds and pigeons, respectively, genotype C is mostly isolated from ducks and geese, while genotype D is mostly found in turkeys. Genotype F was isolated from parrot birds and turkeys. Host range genotype E is the most diverse; 20% of genotype E strains were isolated from pigeons. In addition, genotype E has been isolated from humans during many fatal cases of chlamydia flatula, during respiratory outbreaks in ducks and turkeys, and occasionally. At present, genotype E/B has been isolated mainly from ducks. WC and M56 have been isolated from epizootic populations of Wolof cattle and muskrats, respectively. All genotypes are thought to be easily transmissible to humans and can cause serious illness and even death [2].

### 2.2. Epidemiology

Chlamydia psittaci pneumonia is common in adults but rare [5] in children. The main way of transmission is through inhalation of nasal secretions of infected birds or birds aerosols, can also be inhaled dust when handling feces, feathers, and human and animal transmission. Although contact with birds or birds is the main risk factor for the occurrence of the disease, some patients have no direct contact with infected birds or poultry history, easy to develop the disease. Results of a meta-analysis showed that Chlamydia psittaci accounted for only 1% [7] of community-acquired pneumonia pathogens. The disease is essentially atypical pneumonia, ranging in severity from mild to severe, with a low mortality rate if timely and reasonable treatment is provided.

It has also been reported that globally, the highest incidence of chlamydia pTI infection is mainly

concentrated in veterinary hospital staff, poultry slaughterhouses or poultry farmers used for food production. Therefore, in our clinical work, if patients with a history of contact with birds and poultry, as well as poultry slaughter ing and processing experience high fever, respiratory symptoms or progressive dyspnea. The possibility of psittacosis infection needs to be considered, and the key point to assist in clinical diagnosis is to inquire about the relevant epidemiological history of the patient. In addition, human-to-human transmission of chlamydia psittaci pneumonia is possible, especially in severely ill patients who may be more infectious, which may be related to its high viral load in severely ill patients, and similar to the novel coronavirus, there may be family-associated infections. The process of Chlamydia psittaci infecting humans can be seen as a chain with three main links, the first link being the host of pathogenic microorganisms, the source of infection. Infection in people with chlamydia psittaci can be traced primarily to birds and poultry and, to a lesser extent, to pigeons, so any infected bird could be considered a source of infection. The second link is the process by which the pathogen escapes from the source of infection via the exit and infects the host via the entrance. Chlamydia psittaci can remain infectious in organic matter for months. Human infections usually occur when people inhale an infectious agent atomized from dry infected feces or eye, nasal, or pharyngeal secretions of infected birds, and there are zoonotic risks associated with handling infected birds, birds' feathers, tissues, or carcasses, and cleaning contaminated bird cages. Even brief contact with birds or bird droppings can lead to systemic infection, the third link is the potential host, people at higher risk are pet bird owners, especially parrot bird lovers and people with occupational contact with birds, such as poultry workers, breeders.

Chlamydia psittaci can cause a variety of infectious diseases, such as pneumonia, and lacks specific manifestations, so it is often overlooked. In addition, due to the lack of specific tests, the diagnosis of psittacosis is difficult, and the current lack of large- scale epidemiological data, the incidence of psittacosis may be underestimated in the past

### 3. Clinical features

#### 3.1. Clinical manifestations

The incubation period of chlamydia psittaci pneumonia is usually 5~14 days, or even longer, and its clinical symptoms vary in severity, from asymptomatic to severe, and even life-threatening multi-organ diseases. In general, the clinical manifestations of chlamydia psittaci pneumonia are non-specific, mainly manifested as chills, high fever, fatigue, shortness of breath, cough, myalgia, white sputum cough, mainly dry cough. Among them, fever is the main form of onset. According to multiple cases reported [8] from home and abroad, all patients have fever, most of them are manifested as high fever, most of the body temperature is greater than 39°C, the heat type is flaccid fever, and some may appear relative buffering pulse. In addition to respiratory symptoms such as cough, phlegm, chest tightness, shortness of breath and dyspnea, there are also pulmonary manifestations, such as headache, myalgia and general fatigue, etc. A few patients have neurological and digestive symptoms, such as irritability, diarrhea, nausea and vomiting. In addition, severe patients may have disturbance of consciousness, respiratory failure, septic shock, and multiple organ failure. There are cases reported that parrot fever chlamydia pneumonia combined with rhabdomyolysis, meningitis, myocarditis, endocarditis, hepatitis, arthritis, conjunctivitis and other clinical manifestations [9,10].

In addition, there are literature reports [6] that liver failure may occur when the liver is involved; Interstitial nephritis and acute renal failure may occur when the kidney is involved, myocarditis, pericarditis and endocarditis may occur when the heart is involved; Pancreatitis may occur when gastrointestinal tract is involved. Cranial nerve palsy, cryptogenic epilepsy and lateral neuritis may occur when the central nervous system is involved. For patients in the middle and late stages of pregnancy, once infected with psittaci chlamydia, other pathogens can be infected at any time due to rapid

progression of the disease. And it can lead to life-threatening complications, such as respiratory failure, liver insufficiency, acute respiratory distress syndrome, etc. Therefore, *Chlamydia psittaci* can also pass through the placental barrier. At this time, due to the proliferation of a large number of bacteria in the placenta, it will lead to uterine placental perfusion injury, and then cause intrauterine fetal distress. Therefore, once pregnant women are infected, they need to be treated as soon as possible, choose appropriate antibiotics according to different pregnancy cycles, and even terminate the pregnancy in advance.

Therefore, *chlamydia psittaci* infection should be considered in addition to common atypical pathogens such as *legionella pneumonia* and *mycoplasma pneumonia* for patients with community-acquired pneumonia accompanied by extrapulmonary symptoms. Studies have found that *Chlamydia psittaci* virulence is stronger than other *chlamydia*, so the disease progresses quickly, and the proportion of development to severe disease is high.

### **3.2. Laboratory examination and imaging features**

#### **3.2.1. Laboratory examination**

Blood routine examination showed that most of the white blood cells (WBC) were in the normal range, a few could be elevated or decreased, and the lymphocyte count (LYM) was decreased [7,11]. Neutrophil count (NEUT), procalcitonin (PCT), hypersensitive C-reactive protein (hs-CRP), erythrocyte sedimentation rate (ESR) and other indicators of infection were elevated. Lactate dehydrogenase, aspartate aminotransferase and alanine aminotransferase were increased in varying degrees. In addition, most patients had electrolyte disturbance and hypoalbuminemia, mainly hyponatremia and hypokalemia, in which hyponatremia was more significant. In conclusion, decreased lymphocyte count, low sodium, elevated aminotransferase and CRP levels may have suggestive significance for this disease.

In addition, in a literature review of 40 cases, it was found that during the acute phase of pneumonia infection with *Nautilus pneumonia*, white blood cell counts were usually normal or slightly decreased [12]. In addition, a decrease in white blood cells was observed in an average of 25% of patients. In addition, secondary anemia of varying degrees can be found. In addition, rare diffuse intravascular coagulation may occur in patients with severe infection. In the same study, PT and APTT were significantly prolonged in 41.7% of patients and D -dimer levels were significantly elevated in 91.7% of patients, indicating that *psittacosis* may have an effect on coagulation. At the same time, they also observed several abnormalities in the liver function test, 35% of patients showed liver function abnormalities in the upper limit of twice the normal value, the main abnormal marker was aminotransferase, accounting for 44%. However, elevated levels of these markers did not appear to be significantly associated with disease severity. Blood gas analysis mostly suggested hypoxemia, with some presenting with respiratory failure, which also suggested that *chlamydia psittaci* pneumonia was prone to hypoxemia.

#### **3.2.2. Imaging features**

Chest HRCT or chest radiography mainly showed exudation and consolidation of one or both pulmonary lobes, and the extent of consolidation was closely related to the severity of the disease. Unilateral lesions were dominant, and most cases were complicated with a small amount of unilateral pleural effusion [5]. Air bronchogram and cystic changes can be seen in some patients.

Although the radiographic features of *chlamydia psittaci* pneumonia are not sufficiently distinguishable from other types of CAP, they are nonetheless characteristic. Abnormal chest radiographs were found in 90% of hospitalized cases, often showing various degrees of exudation

and consolidation. Patellar shadow and reticular infiltration were the most common manifestations. Chest CT showed patellar or large fused patches of solid shadow distributed along the lung segment, mainly involving the lower lobe and occasionally pleural effusion. In some severe cases, there may also be a large lobe shadow and extensive bilateral pneumonia. Therefore, it is difficult for doctors to diagnose *Chlamydia psittaci* pneumonia in clinical work, so understanding the chest CT imaging features of *chlamydia psittaci* pneumonia is helpful for its early clinical diagnosis and guide treatment.

## 4. Diagnostic methods

### 4.1. Serology

At present, the traditional detection methods of *chlamydia psittaci* mainly include the following: pathogen isolation and identification, immunofluorescence, indirect hemagglutination inhibition test, complement binding test, ELISA, conventional (polymerase chain reaction) PCR and fluorescent PCR (polymerase chain reaction) [13]. Specific diagnostic criteria are as follows: (1) *Chlamydia psittaci* was isolated and cultured from respiratory secretions [14]; (2) The titer of *Chlamydia psittaci* specific IgG antibody was increased by 4 times or more in the double serum at the acute stage and the recovery stage; (3) *Chlamydia psittaci* DNA was detected positive by PCR. Polymerase chain Reaction (PCR) gene amplification analysis - It is a faster, more specific diagnostic test that can be performed in a specialized diagnostic laboratory. But in clinical *chlamydia psis* nucleic acid PCR detection and antibody detection have not been carried out in most hospitals, the above detection means of laboratory biological requirements on schedule, long culture time, low positive rate, complex operation steps, high probability of deviation of results, and relatively high cost, most hospitals in China cannot routinely carry out. Therefore, the diagnosis of *chlamydia pti* pneumonia has been ignored in our country, and the diagnosis and treatment guidelines for domestic community-acquired pneumonia do not mention the diagnosis of *chlamydia pti* pneumonia, and the misdiagnosis rate is high.

### 4.2. Macro Gene second generation sequencing (mNGS)

High throughput sequencing, also known as metagenomic next generation sequencing (mNGS), is a new type of microbial detection technology, using genomic methods to study the types and contents of all microorganisms in specimens, to achieve the relative quantification of human and pathogen nucleic acids, with high accuracy and fast detection speed. Generally, the results can be obtained within 24~48 h, with the characteristics of high throughput and low cost. Metagenomic second generation sequencing (mNGS) can detect more pathogen gene sequences at the same time. Its theory is that it can uniquely detect almost all pathogens based on specific nucleic acid sequences, and it has obvious advantages for the detection of rare, emerging and complex pathogens. In addition, mNGS is less affected by the use of antibiotics prior to detection.

Through sequence alignment, MNGS can quickly and accurately identify the characteristics of microbial species, providing a reliable and important basis for the rapid diagnosis of infectious diseases of unknown cause [13]. It is widely used in clinical practice, and is also the main diagnostic method reported in cases of *chlamydia psitsiti* pneumonia from abroad. With the routine development of bronchoscopy, alveolar lavage fluid is easy and convenient to obtain. Usually, alveolar lavage fluid is retained in infectious diseases of unknown cause as a specimen to be sent for mNGS, and the detection rate is high. In addition, mNGS does not need to be cultured, and can be directly extracted from clinical specimens for sequencing of the whole gene sequence of all microorganisms, which can be more accurately identified to the species level of various pathogens such as bacteria, fungi and viruses. Severe *pti chlamydia* pneumonia can lead to respiratory failure and ARDS, which is life-

threatening. If the infection is combined with *Klebsiella pneumoniae*, MRSA, *Pseudomonas aeruginosa* or *Candida albicans*, the treatment of *Chlamydia pneumoniae* is more difficult, and other antibiotics should be added more sensitively on the basis of tetracyclines. In summary, it is more fully demonstrated that macro gene second generation sequencing (mNGS) has become the most promising method for the diagnosis of *Chlamydia pneumoniae*, that is to say, this detection method has become a very promising method for the detection of complex infectious disease pathogens. Bronchoalveolar lavage fluid can be used as a sample for mNGS detection, which can clarify the etiology and point out the direction for clinical treatment.

## 5. Treatment

*Chlamydia pneumoniae* is resistant to drugs that act on the cell wall and sensitive to drugs that inhibit membrane and cytoplasmic protein synthesis. The current recommended first-line drugs are macrolides and tetracyclines [14]. Tetracycline antibiotics are the first choice for treatment, mainly oral doxycycline, the course of treatment is at least 10 to 14 days, if there are contraindications (such as children, pregnant women or allergies), the second choice of macrolides, fluoroquinolones also have a certain effect on psittacosis, for pregnancy psittacosis pneumonia, early delivery fetus can obtain good maternal and infant outcomes [15]. However, clinically, considering that doxycycline and tigacycline often appear obvious gastrointestinal symptoms, liver function impairment and other adverse reactions, and *Chlamydia pneumoniae* is easy to cause liver function impairment, accompanied by gastrointestinal symptoms, in order to facilitate the identification of the disease itself or the above results caused by adverse drug reactions. With the advent of a new semi-synthetic tetracycline (omacycline), due to its small adverse reactions, good lung permeability, and significant activity on *Chlamydia psittaci*, it is almost independent of gender, age, liver and kidney function, omacycline has shown good efficacy, liver and kidney safety, and related gastrointestinal adverse reactions are few [14]. Therefore, it plays an important role in the treatment of *Chlamydia psittaci* pneumonia. Luo Yu and Wang Jiou et al. reported 5 and 4 cases of *Chlamydia pneumoniae* patients respectively. Fluoroquinolones were used in the initial treatment, but the fever was repeated and the lesions in the lung progressed. After the pathogen was detected, the condition of the patients was significantly improved after they were replaced with tetracycline (doxycycline) -based antibiotics [14]. Based on these studies, it can be seen that fluoroquinolones do not show a significant advantage over tetracycline and macrolides in the treatment of *Chlamydia psittaci*. Due to the clinical distribution of *Chlamydia pneumoniae*, there have been no clinical trials on different drug treatment regimens for *Chlamydia pneumoniae*. The current literature reports on the treatment of *Chlamydia pneumoniae* in foreign countries also recommend tetracycline and macrolides as the first and alternative drugs, while fluoroquinolones as the second choice. Severe *Chlamydia pneumoniae* can lead to respiratory failure, ARDS, life-threatening, if combined with *Klebsiella pneumoniae*, MRSA, *Pseudomonas aeruginosa* or *Candida albicans* infection, increase the difficulty of the treatment of *Chlamydia pneumoniae*, on the basis of tetracycline drug treatment need to be more drug sensitive to add other antibiotics. Such patients are usually admitted to the intensive care department and need endotracheal intubation, ventilator to assist breathing and even extracorporeal membrane oxygenation (ECMO) support. ECMO is of high efficacy in the rescue and treatment of critically ill *Chlamydia pneumoniae* patients.

It has been reported [14] that *Chlamydia parrot* belongs to the *Chlamydia* family. Tetracyclines and quinolones can interfere with DNA and protein synthesis. They are the first choice for the treatment of *Chlamydia psittaci*. Tetracyclines (doxycyclines) and quinolones (moxifloxacin) can interfere with DNA and protein synthesis. In summary, doxycyclines are currently the first choice for treatment, and their efficacy is certain. The use of hormones as adjunctive therapy for severe

pneumonia is still controversial.

## 6. Summary

There are 4 common types of chlamydia: *Chlamydia bovis*, *Chlamydia trachomatis*, *Chlamydia pneumoniae* and *Chlamydia psittaci*. *Chlamydia bovis* exists only in cattle and sheep, and *Chlamydia trachomatis* can lead to trachoma and urogenital tract infection. *Chlamydia pneumoniae* is the most common, but it has insipid onset and mild symptoms, while *Chlamydia pti pneumonia* has severe clinical symptoms and its prognosis is related to the timidity of diagnosis. Previous clinical reports of *chlamydia psittaci pneumonia* were rare, which was mainly due to the low incidence of the disease on the one hand, and the limited routine clinical detection methods and low sensitivity rate on the other hand, so the diagnosis rate was not high. With the application of mNGS in clinical practice, the detection rate of *chlamydia psittaci* increased.

The manifestations of *chlamydia psittaci pneumonia* are varied, including fever, cough, sputum, headache, muscle aches, dyspnea, etc. Some patients may be accompanied by relatively slow pulse. Severe cases may also involve other organs, including the heart, liver, muscles and central nervous system, lack specificity, the overall prognosis is good, but if the severe patients are not treated in time, the fatality rate can rise to 15%-20% [14]. Studies have shown [16] that *psittacosis* can also involve the nervous system, including epilepsy, headache, meningencephalitis, cerebellar ataxia, Guillain-Barre syndrome and other symptoms. However, the cases with headache as the first symptom are rare, so the central nervous system symptoms are diverse. Therefore, in the first clinical treatment of patients with simple headache, we must ask the patient's epidemiological history. In addition, for patients with headache accompanied by fever, and suspected birds, poultry contact history, active cerebrospinal fluid puncture in addition to routine etiological detection, it is recommended to send mNGS, because *chlamydia pti* can directly invade the central nervous system.

Most of the laboratory tests showed normal white blood cells, high neutrophils, inflammatory indicators such as hypersensitive C-reactive protein, erythrocyte sedimentation rate, and procalcitonin infection indicators were high, and CK, ALT, AST were elevated to varying degrees. It is often accompanied by hyponatremia, hypokalemia and hypoalbuminemia. In addition, with the exception of leukocytes, neutrophils, C-reactive protein, erythrocyte sedimentation rate, calcitonin and other pro-inflammatory factors, the study found [17] that interleukin-6 (IL-6) was significantly increased in patients with *Chlamydia psiti pneumonia*, suggesting that the IL-6/IL6R axis may be involved in the pathophysiological process, indicating that the inflammatory response after *chlamydia psiti* infection is obvious.

In almost all patients with *chlamydia nautii* infection, chest radiological abnormalities are seen, with chest radiographs showing the presence of infiltrating plaques showing uneven density that can severely affect all lung lobes. In past case reports, the most common imaging abnormality on chest CT has been unilateral dense solid changes in the lower lobe, followed by bilateral, nodular, keratosis, or interstitial infiltration. The main manifestations are exudation, consolidation, and ground glass shadow, radiating outward from the hilum of the lung in a fan-shaped shape, or subpleural wedges with uneven density. In severe cases, the entire lung lobe may be involved. The pleura on the affected side may be involved, and a small amount of pleural effusion may occur, with both single and multiple lesions. In addition, CT images of the lungs showed solid or ground glass-like changes in the lower lungs, especially pleural involvement and pleural effusion.

Imaging findings of *Chlamydia pti pneumonia* can also be seen in multiple reported cases. Chest CT showed unilateral lower pneumonia, mostly single nodules, patellar ground glass shadows or large fused solid shadows distributed along the subpleura, often distributed along the lung segment, with the lower lobe mainly involved, and bilateral, nodular, miliary or interstitial infiltration changes can

also be seen. The imaging findings of *Chlamydia psittaci* pneumonia share many similarities with other cases of atypical pneumonia, showing a variety of non-specific manifestations. In addition, in the context of the epidemic of novel coronavirus disease 2019 (COVID-19) since 2020, more attention should be paid to the differential diagnosis of *Seri psittaci* pneumonia and COVID-19. Under bronchoscopy, the trachea of the patients was smooth and the mucosa was red, and sputum was visible in the bronchial lumen of 18.0% of the patients [17], indicating that most *Chlamydia psittaci* pneumonia had little secretions in the tracheal lumen, and also confirmed the clinical manifestations mainly characterized by dry cough. The inflammatory reaction of the body after infection with *Chlamydia psittaci* pneumonia is obvious, but it does not have specific clinical manifestations. Its symptoms vary with the severity of the disease, so it is difficult to distinguish from other types of CAP.

In the course of clinical treatment, if the pneumonia patient has repeated high fever (body temperature  $>39^{\circ}\text{C}$ ) in the early stage of the disease, the routine use of quinolones and  $\beta$ -lactam antibiotics is ineffective. At this time, we should be on high alert and carefully inquire about the epidemic history of patients, whether they have direct or indirect contact with parrots, chickens, ducks and other birds and their secretions, and highly suspect *Chlamydia psittaci* infection. At this time, we should timely improve tracheoscopy and other examinations to obtain relevant alveolar lavage fluid or blood, sputum and other specimens for mNGS detection, and identify the pathogenic pathogen as soon as possible. According to the condition, tetracycline drugs can be used empirically before the results are reported. mNGS has a rapid, efficient detection rate. Therefore, mNGS is a promising detection method in infectious diseases of unknown cause, and it is also the main means of diagnosis of *Chlamydia psittaci* pneumonia. At the same time, in the detection of mNGS in the lung infection, it is generally believed that the detection rate of alveolar lavage fluid is better than that of sputum, because the content of human nucleic acid in alveolar lavage fluid is the lowest, and the detection results are more reliable, while the content of human nucleic acid in sputum is high, and there may be colonizing bacteria and pollution, and the measured sequence number is low. Therefore, alveolar lavage is the most preferred specimen for the detection of mNGS.

Therefore, epidemiological history and clinical features play an important role in the diagnosis of the disease, and the detection of *Chlamydia psittaci* sequence by mNGS can be confirmed as early as possible. Clinicians should constantly familiarize themselves with and summarize the clinical characteristics of *Chlamydia psittaci* pneumonia, combine the epidemiological history and imaging and other relevant examinations to achieve accurate diagnosis and targeted treatment, avoid widespread antibiotic use, reduce drug resistance, shorten hospital stay, reduce the occurrence of severe pneumonia, and improve the skill level of medical staff. In addition, due to the lack of specificity in clinical features and imaging manifestations of *Chlamydia psittaci*, timely diagnosis is difficult, and it is easy to develop into severe pneumonia. This also indicates that epidemiological history and timely pathogen detection are of great significance for diagnosis. mNGS can shorten the time required for diagnosis, and it can be used for early diagnosis of *Chlamydia psittaci* infection. Therefore, we can also summarize the following four important characteristics, which can indicate *Chlamydia psittaci* pneumonia, including: (1) having a clear poultry contact history; (2) the main clinical manifestations are fever, or accompanied by dry cough, headache and myalgia; (3) white blood cell count in peripheral blood was normal; High transaminase, low sodium, low albumin. (4) The chest CT showed a wide subpleural base solid shadow outside the lung and a small amount of unilateral pleural effusion.

*Chlamydia psittaci* pneumonia should be immediately diagnosed and anti-infective treatment, *Chlamydia psittaci* belongs to the *Chlamydia* family, it is a strict intracellular parasitic gram-negative anaerobic bacteria, therefore, antibiotics should be selected to have strong antibacterial activity on the cell wall, such as tetracycline, macrolides, fluoroquinolones. Among them, tetracycline drugs are the first-line drugs for the treatment of *Chlamydia psittaci* infection at this stage, and its representative drug doxycycline is the first choice for the treatment of *psittaci* fever. Generally, the



body temperature can return to normal within 48 hours after treatment, in order to avoid recurrence, the course of treatment lasts at least 10 to 14 days, there are no reports of drug resistance of doxycycline for the treatment of chlamydia psittaci infection. In addition, omacycline has been continuously used in clinical practice because of its characteristics of small liver and kidney damage and few adverse reactions of digestive tract. For patients with contraindications of tetracycline, such as pregnant women and children under 8 years old, azithromycin or erythromycin can be selected as alternative drugs. It is necessary to pay attention to the changes in liver function of patients during the treatment of azithromycin, but the effect is poor for severe patients. Therefore, we can summarize the experience to conclude that in clinical work, if the patient has a high suspicion of atypical pathogen infection, especially when there is a history of poultry contact, and there are varying degrees of liver damage, low white blood cells, and persistent high fever, it is recommended to use doxycycline as soon as possible rather than moxifloxacin or levofloxacin.

In short, for patients with community-acquired pneumonia, if there are multiple system involvement such as high fever, dry cough, myalgia, headache, poor appetite and diarrhea, laboratory tests show low or decreased white blood cells, the proportion of lymphocytes decreases, biochemical indications indicate abnormal liver function and myocardial enzymes, and electrocardiogram finds relatively slow pulse. At this time, as a clinician, it is necessary to carefully inquire about the contact history of poultry, pet birds, and birds within 2 weeks before the onset of pneumonia. If blood gas analysis indicates hypoxemia, rapid progression of lung lesions, common anti-infection high fever does not return, it is necessary to be highly vigilant about the risk of developing severe pneumonia, improve BALF etiology (macro gene second generation sequencing) mNGS detection as soon as possible, identify the etiology early, and strive to start targeted antibiotic treatment early, so as to avoid worsening the disease and reduce the risk of death. And when the patient through the mNGS technology diagnosis process has not detected other pathogens that cause disease, it will significantly reduce the unnecessary use of antibacterial drugs, but also to a certain extent reduce the patient's hospitalization time and economic pressure, effectively prevent the production of drug-resistant bacteria in the patient's body, so as to avoid aggravating the disease and reduce the risk of death. Shorten the treatment time and improve the prognosis of patients.

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