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CASE REPORT

Respiratory Syncytial Virus Infection in an Adult with Immunodeficiency

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SUMMARY

Background: **Respiratory syncytial virus (RSV) is a single-stranded RNA virus that commonly causes symptoms of upper respiratory tract infections in humans, with a clear seasonal trend. However, in immunocompromised and elderly patients, RSV infections still result in high rates of hospitalization and even risk of death.**
Methods: **We report a case of RSV infection in an adult with immunodeficiency, which initially showed only mild symptoms of upper respiratory tract infection, which did not improve after receiving empirical anti-infective treatment, and the foci of infection in the lungs continued to expand, which led to the aggravation of the disease. The diagnosis of RSV infection was finally confirmed by electron bronchoscopy and pathogenetic examination of the bronchoalveolar lavage fluid. The patient was given intravenous ribavirin treatment for one week. After one week of intravenous ribavirin treatment, the patient's symptoms improved significantly. A repeat chest CT suggested that the lung lesions were smaller than before. In order to improve clinicians' awareness of this disease, we jointly conducted a literature analysis.**
Results: **The final diagnosis of RSV was made by analyzing the patient's history, symptoms, and signs and performing relevant examinations.**
Conclusions: **For patients with poor results of empirical application of antibiotics, electronic bronchoscopy and pathogenetic examination should be carried out at an early stage to clarify the nature of the lesions and to avoid rapid deterioration of the condition leading to life-threatening conditions in the patients. More consideration should be given to the possibility of disease diagnosis to avoid misdiagnosis and underdiagnosis, and appropriate treatment should be given at an early stage.**
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KEYWORDS

respiratory syncytial virus, diagnosis, treatment, infection

INTRODUCTION

Respiratory syncytial virus (RSV) infection is an infectious disease of the respiratory tract that is common in infants, young children, and immunocompromised persons and can present with mild symptoms of upper respiratory tract infection and potentially life-threatening lower respiratory tract involvement [1]. Previous epidemiological studies have shown that RSV is a relatively common pathogen in elderly and high-risk adults hospitalized for acute respiratory symptoms in winter [2].

When patients are infected with RSV, symptoms are often associated with a variety of clinical syndromes, including upper respiratory tract disease, acute bronchitis, exacerbation of chronic obstructive pulmonary disease (COPD), and pneumonia. RSV infection in infants and young children usually presents with fine bronchiolitis; however, the clinical manifestations of RSV infection in adults are non-specific, including fever, nasal congestion, coughing up sputum, and wheezing, and are difficult to differentiate from other common respiratory infectious diseases [3]. Therefore, pathogenetic testing is an important basis for identifying RSV infection. However, previous studies have shown that RSV viral titers in respiratory secretions are lower in adults, and the duration of shedding is shorter than in infants and children [4]. With the popularization of electronic bronchoscopy, the definitive diagnosis of RSV infection is no longer a problem for clinicians when alveolar lavage fluid is obtained by bronchoscopy and examined pathogenetically. In this paper, we report a case of acute myeloid leukemia with RSV infection, after empirical antibiotic treatment, the symptoms did not improve significantly, while the lung inflammation continued to progress, and finally using electronic bronchoscopy to obtain the alveolar lavage fluid, Metagenomic Next-Generation Sequencing (mNGS) to confirm the diagnosis of RSV infection. The symptoms improved after administering ribavirin treatment, and the review of the chest CT can be seen in the lungs of infected foci of the disease have been absorbed compared with the previous CT. The review of chest CT showed the absorption of the infected lesions in the lungs. This should remind the clinicians that RSV infection is a disease that should not be ignored, and to understand the progress of the research on the diagnosis and treatment of this disease by reviewing the relevant literature.

CASE REPORT

The patient is a 60-year-old female who was admitted to our hematology department on December 19, 2023, mainly because of the diagnosis of acute myeloid leukemia for 2 years and 4 months. One week before admission, the patient suffered from a cold and flu, intermittent cough, and cough sputum which is a small amount of white mucus-like phlegm and not easy to cough up. There is no fever, dyspnea, and other symptoms. The patient was given oral cough and phlegm medication treatment for 5 days. When the cough and sputum symptoms did not significantly improve, physical examination after admission found that the patient's bilateral lungs respiratory sounds were thick, no rales on lung auscultation, and no abnormalities on percussion.

After admission to the hospital, relevant laboratory tests were carried out: routine blood tests showed that: leukocytes 2.3 x 10^9/L, erythrocytes 1.63 x 10^{12}/L, hemoglobin 63 g/L, lymphocytes 0.59 x 10^9/L, neutrophils 1.29 x 10^9/L, C-reactive protein (CRP) 26.6 mg/L, interleukin 6 (IL-6) 4.504 pg/mL, procalcitonin (PCT) 0.066 ng/mL, respiratory pathogens, antibodies to Mycobacterium tuberculosis, nucleic acid test of novel coronavirus, influenza A antigen, and other tests were all negative. Chest CT examination showed two pneumonic lesions, hypertrophic adhesions of the pleura on both sides. After admission, empirical anti-infective treatment with moxifloxacin was given, along with medication to relieve cough and resolve phlegm.

December 20, 2023. At night, the patient suddenly developed wheezing, chest tightness and dyspnea, with ECG monitoring suggesting a cardiac rhythm of 126 beats/minute, a respiratory rate of 22 breaths/minute, a blood pressure of 110/56 mmHg, an oxygen saturation of 91%, thick breath sounds in both lungs on auscultation, and the rest of the body had no obvious abnormality. He was given transnasal catheters for low-flow oxygen intake, glucocorticosteroids intravenously, and dihydroxypropyl theophylline intravenously. The patient's wheezing symptoms improved and oxygen saturation increased to 97%. After 1 week of moxifloxacin anti-infective treatment, chest CT showed that the two pneumonic lesions were absorbed and the pleural hypertrophy and adhesion on both sides were relieved.

The patient had a history of acute myeloid leukemia. After admission, the lung infection improved, and the CHG regimen was started on December 27, 2023. The patient had malignant hematological diseases, combined with lung infection, being immunocompromised, with a history of long-term antibiotic application, and prone to fungal infections; therefore, he was given oral prophylactic antifungal treatment with voriconazole. During the chemotherapy period, the patient still had cough and coughed up a small amount of sputum. January 1, 2024, on the 6th day of chemotherapy with the CHG regimen, the patient's cough worsened compared with the previous day, and the sputum became yellow mucus-like phlegm, accompanied by chest tightness, wheezing, and no fever. The electrocardiographic monitoring showed that the cardiac rhythm was 62 beats/minute, respiratory rate was 23 beats/minute, and the blood pressure was 89/60 mmHg. The review of the CT chest suggested that the two pneumonitis lesions had progressed compared with the previous day, and there was fluid accumulation in the pleural cavity on both sides. Chemotherapy was stopped and glucocorticoids and dihydroxypropyl theophylline were given intravenously. The routine blood test showed: leukocytes 14.8 x 10^9/L, erythrocytes 1.93 x 10^{12}/L, hemoglobin 72 g/L, lymphocytes 0.77 x 10^9/L, neutrophils 10.75 x 10^9/L, CRP 43.3 mg/L, serum amyloid A (SAA) 36.63 mg/L, PCT 0.043 ng/mL, respiratory pathogens, fungal test, Mycobacterium tuberculosis antibody, Aspergillus test, sputum bacterial culture, and other tests were all negative. Considering that the patient belonged to the immunocompromised population and had a high incidence of hospital-acquired infections, anti-infective treatment with meropenem was added. The patient is currently experiencing increased wheezing, and the previous application of di-

hydroxypropyl theophylline was ineffective, so the patient was adjusted to doxophylline intravenous pumping and asthma treatment.

January 4, 2024. The patient had electronic bronchoscopy under general anesthesia. The microscopy shows the sound gate closure shows good airway patency, ronchi sharp, the main bronchial tube of both lungs and each lobe segment bronchial opening is smooth, mucosal congestion, edema, scattered yellowish-white secretion can be seen, no neoplastic organisms, stenosis, and ulceration are seen. Alveolar lavage was performed in the lower lobe of the left lung in the anterior basilar section of the bronchial tube. The bronchoalveolar lavage fluid was sent for pathogenetic testing. Bronchoalveolar lavage fluid mNGS results suggest human respiratory syncytial virus type A. After 1 week of ribavirin antiviral treatment, the patient's cough and sputum improved, with no symptoms of chest tightness and wheezing. A repeat chest CT showed that the two pneumonic lesions were significantly absorbed compared with the previous one, and the pleural effusions on both sides had been absorbed. The patient was discharged after treatment.

DISCUSSION

Human respiratory syncytial virus (hRSV) was first isolated in 1956 from nasal secretions of chimpanzees with upper respiratory tract infections [5], and subsequently in infants suffering from severe lower respiratory infectious disease [6]. Based on antigenic and molecular studies, it is currently believed that only a single RSV serotype exists, which can be divided into two major antigenic subgroups, where A and B strains of both subtypes can cause transmission and pathogenesis of RSV [7]. RSV is mainly transmitted by close contact through respiratory secretions and droplets. After transient replication of the virus in the epithelial cells of the nasopharynx and upper respiratory tract, released viral particles can be translocated to the fine bronchioles of the lower respiratory tract or to the alveoli. The immune response in patients infected with RSV leads to neutrophil infiltration and narrowing of the respiratory tract, resulting in respiratory diseases such as capillary bronchitis [8]. Early infection is usually confined to the upper respiratory tract, with clinical manifestations such as fever, dry cough, nasal congestion, and runny nose. When the lesion progresses to the point that it involves the lower respiratory tract, it can lead to bronchiolitis and pneumonia, and patients often present with high fever, severe cough, coughing up sputum, and shortness of breath. In severe cases, it may involve other systemic diseases and even cause death of the patient. Hospital-acquired and community-acquired RSV infections are common in adult patients with hematological and autoimmune primary diseases [9]. Immunocompetent adult patients often present with mild to moderate upper respiratory tract inflammation. However, immunocompromised patients, patients with chronic cardiopulmonary disease, the frail, and the elderly are at risk of severe lower respiratory tract involvement and even death. Although all immunocompromised individuals are at risk of RSV infection, the incidence is highest in severely immunosuppressed patients (e.g., allogeneic hematopoietic stem cell transplant (HSCT) recipients) [10].

In the diagnosis and management of RSV infection, even in critically ill hospitalized patients, the imaging presentation fails to show a high degree of sensitivity and specificity. A clinical study of 118 RSV-infected patients found that 42% of chest images were described by imaging physicians as normal or did not show acute disease [3]. Another meta-analysis study found that the most common imaging findings on chest CT in patients with RSV infection were bilateral lung involvement, mainly with a predominant pattern of organizing pneumonia, followed by interlobular septal thickening, ground-glass nodules, nodular lesions, and granulomatous lesions. Of the total cases included in this study, 16.2% of patients with RSV infection had normal chest CT [11]. Therefore, in the clinical diagnosis of RSV infection, CT images can be an important method of confirming lung infection, but do not provide a reliable diagnostic basis. In such cases, pathogenetic examination is essential for the correct diagnosis of RSV infection. Therefore, early electronic bronchoscopy to obtain alveolar lavage specimens for pathogenicity determination is very beneficial for the diagnosis and treatment of patients.

The current treatment of mild RSV infection in adults continues to be supportive and symptomatic. The US Food and Drug Administration (FDA) has approved the use of inhaled ribavirin for the treatment of infants and children with respiratory syncytial virus (RSV) pneumonia. It has also been used to treat severe respiratory syncytial virus infections in adults. Studies have shown that ribavirin treatment reduces progression from RSV upper to lower respiratory tract infections in immunodeficient patients who have undergone hematopoietic stem cell transplantation and may be effective in reducing mortality [12]. Although several previous studies have affirmed the role of ribavirin in the treatment of RSV infection in immunodeficient populations, the sample sizes of these studies are small, and the effects of ribavirin via different routes of administration, such as inhalation, oral, and intravenous, need to be further explored. So, the use of ribavirin in the treatment of RSV infection remains controversial. Other less commonly used treatments in immunocompromised adults include intravenous immunoglobulin, RSV immunoglobulin, and the monoclonal antibody pembrolizumab. Four studies in which immunoglobulin therapy was used found that although it may be effective in reducing viral titers, it does not appear to be associated with improved clinical outcomes [13]. Pembrolizumab, a monoclonal antibody against the RSV F protein, has been approved by the U.S. Food and Drug Administration (FDA) for the prevention of severe lower respiratory tract infections caused by RSV in infants and young children at high risk,

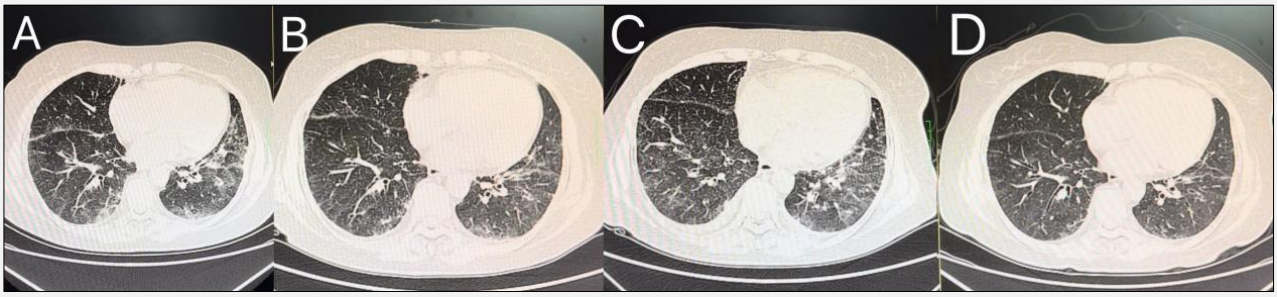

Figure 1. Chest CT Changes.

December 18, 2023. Chest CT (A) shows two pneumonic lesions. December 25, 2023 Chest CT (B) shows two pneumonic lesions absorbed compared to A. January 2, 2024. Chest CT (C) shows two pneumonic lesions progressed compared to B, with pleural effusions on both sides. January 10, 2024. Chest CT (D) shows two pneumonic lesions significantly more resorbed than C, and pleural effusions have been absorbed on both sides.

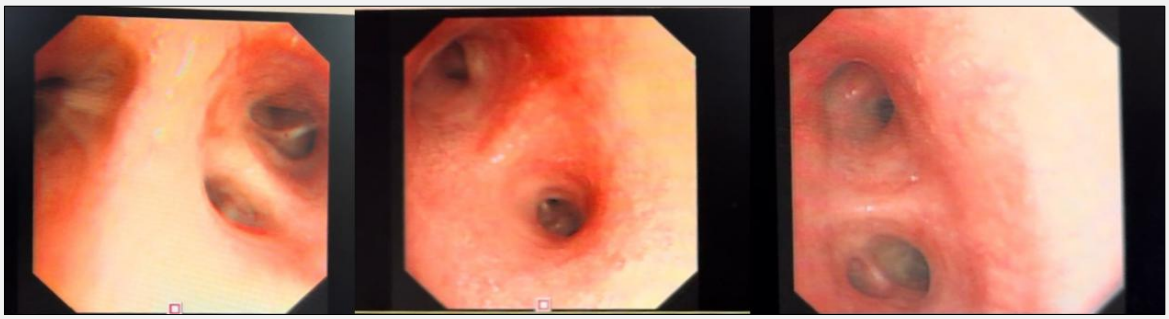

Figure 2. The picture shows an electron bronchoscopy.

The bronchial opening has congestion and edema of the mucosa, and scattered yellowish-white secretions were seen without neoplasm, stenosis or ulceration.

and may reduce mortality in children at high risk for RSV infection. It is currently in clinical trials as a therapeutic agent for RSV; however, studies have demonstrated that it does not affect the survival of RSV-infected hematopoietic cell transplant recipients [14].

None of the three drugs now included in extensive research and clinical use, namely ribavirin, intravenous immunoglobulin, and pembrolizumab, have been shown to be definitively beneficial and effective treatments. Therefore, the optimal regimen for the treatment of RSV infections still needs to be further explored. At least 14 anti-RSV therapeutic products are currently undergoing clinical trials (Phase I and Phase II only), five of which have been enrolled in pediatric patients to date. The novel types of therapeutic molecules that have been developed include fusion inhibitors, non-fusion inhibitors, polymerase inhibitors, antibodies, nucleoside analogues, small-interface RNAs, and benzodiazepines. They have a variety of target RSVs such as F proteins, RNA polymerases, nucleoproteins, and nucleocapsid mRNAs [15].

CONCLUSION

As a common respiratory pathogen, RSV is a life-threatening disease in immunocompromised people, although it causes only mild symptoms of upper respira-

tory tract infection in most cases. Meanwhile, the development of effective preventive and therapeutic drugs still needs to be actively promoted, and the research on RSV still needs to be continued and strengthened to save more patients in the future.

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Ethical Approval:
This study was approved by the ethics committee of North China University of Science and Technology Affiliated Hospital. All procedures performed in studies were in accordance with the ethical standards. Informed consent was obtained.

Declaration of Interest:
No conflicts of interest.

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