ORIGINAL ARTICLE

Treatment practices for multidrug-resistant *Acinetobacter baumannii* infection in the lungs — with a case report

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ABSTRACT

Objective: Using a multidisciplinary cooperation model with clinical pharmacists, we carried out drug treatment for elderly patients with pulmonary infections caused by pan-resistant *Acinetobacter baumannii* to improve clinical outcomes for resistant bacterial infections.

Methods: One elderly patient with interstitial pneumonia accompanied by pan-drug-resistant *Acinetobacter baumannii* infection in the lungs, type II respiratory failure, and multiple underlying diseases was selected. We adopted a multidisciplinary cooperation model, with full participation of clinical pharmacists in clinical analysis and drug treatment. Based on relevant guidelines and literature, the patient's clinical symptoms and sputum culture and drug sensitivity results were evaluated, and the antibacterial treatment plan was optimized. The team provided pharmaceutical services, including medication monitoring and education.

Results: After 36 days of comprehensive treatment, the patient's condition improved significantly. There is no fever, no cough or expectoration, and no symptoms of chest tightness or shortness of breath. All anti-infection drugs have been discontinued, and the patient has been discharged from the hospital after recovery.

Conclusions: Clinical pharmacists, leveraging their professional expertise and clinical judgment, can participate in clinical treatment to ensure patients receive safe, effective, and economical medication.

Key Words: Pulmonary infection, Pan-drug-resistant *Acinetobacter baumannii*, Drug treatment, Clinical pharmacist

1. INTRODUCTION

Acinetobacter baumannii is a conditionally pathogenic bacterium that is widely present in both natural and hospital environments. It has strong capabilities for survival, reproduction, transmission, and bacterial resistance. It can colonize multiple sites in hospitalized patients.[1] In recent years, with the widespread clinical use of drugs such as immunosuppressants, glucocorticoids, and broad-spectrum antibiotics, *Acinetobacter baumannii* has emerged as a major concern, and researchers have identified complex resistance mechanisms. The incidence of multidrug-resistant, pan-resistant, and even total-resistant *Acinetobacter baumannii* infections has been increasing year by year. Resistant *Acinetobacter baumannii* infections involving multiple systems, such as the respiratory, blood, and urinary systems, have become a major clinical challenge.[2,3] This study will describe the practical process of the anti-infection treatment for a patient with multidrug-resistant *Acinetobacter baumannii* (MDRAB) in-

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fection, where a clinical pharmacist was involved throughout the entire process. The purpose is to explore how clinical pharmacists can participate in the drug treatment team and provide professional pharmaceutical services, thereby ensuring the safety, effectiveness, and economy of the patient's medication.

2. DATA AND METHODS

2.1 General data

A 71-year-old female patient was admitted with "cough, shortness of breath, and fever for over 20 days." About 20 days earlier, she developed a dry cough and fever without any obvious precipitating factors, with a peak temperature of 39°C. The chest CT scan revealed interstitial changes in both lungs, suggesting "interstitial pneumonia." At the external hospital, the patient was treated with methylprednisolone sodium succinate for anti-inflammatory purposes, and with piperacillin-tazobactam sodium combined with levofloxacin and voriconazole for anti-infection, as well as gamma globulin to enhance immunity (the specific dosage and treatment course are unknown). However, the condition did not improve significantly, and the patient was transferred to the Department of Respiratory and Critical Care Medicine at our hospital.

The patient has a history of hypertension for over one year and has not taken medication regularly; she has type 2 diabetes for half a year and is taking acarbose tablets; she has hypothyroidism for two years and is treated with levothyroxine tablets.

Admission physical examination

T 36.8°C, P 118 beats/min, R 35 breaths/min, BP 135/85 mmHg, height 160 cm, weight 60 kg, BMI index 23.44 kg/m^2. SpO_2 98% (oxygen supply 15 L/min). Auscultation revealed coarse breath sounds. Tapping sounds can be heard in both lower lungs. No edema in either lower extremity. The blood gas analysis showed: pH: 7.29, carbon dioxide partial pressure: 94 mmHg, oxygen partial pressure: 288 mmHg, oxygen saturation: 100% (after oxygen inhalation).

Admitting diagnosis

(1) Interstitial pneumonia with infection; (2) Type II respiratory failure; (3) Rheumatoid arthritis; (4) Hypertension; (5) Type 2 diabetes; (6) Hypothyroidism.

2.2 Treatment process

After admission, the patient underwent comprehensive examinations and was given electrocardiogram monitoring, non-invasive ventilator-assisted ventilation, intravenous infusion of piperacillin sodium and tazobactam sodium (4.5 g, every 8 hours), ganciclovir (0.25 g, twice a day), fluconazole (400 mg, once a day, with the first dose doubled), oral compound sulfamethoxazole (2 tablets, three times a day) for anti-infection treatment. At the same time, intravenous methylprednisolone (40 mg twice daily) was given for anti-inflammatory treatment, along with doxofylline for bronchodilation, ambroxol for expectoration, and injection of hydrochloric chuanqunzhen for anti-fibrosis, etc., for symptomatic treatment.

3. RESULTS

On the third day of hospitalization, the patient's breathing became more severe, and the body temperature fluctuated. Two sputum cultures showed multi-drug-resistant *Acinetobacter baumannii* and sensitive *Candida parapsilosis*. Based on the drug sensitivity test results, the antibacterial regimen was adjusted to intravenous cefoperazone-sulbactam sodium (3.0 g, Q8h) combined with oral minocycline (100 mg, Bid) for infection treatment, and intravenous fluconazole for antifungal therapy. On the 19th day of hospitalization, the patient complained of recurrent chest tightness. Chest CT showed diffuse ground-glass opacities in both lungs, with no significant change from before. Sputum culture grew pan-resistant *Acinetobacter baumannii*. Discontinue minocycline and switch to intravenous tigecycline (200 mg QD, with the first dose doubled) to improve infection control. After starting the medication, the patient's temperature returned to normal and chest discomfort improved significantly. The sputum culture was *Acinetobacter baumannii*, which was sensitive only to minocycline. The treatment plan remained unchanged. On the 36th day of hospitalization, the patient's condition improved significantly, with no fever, cough, expectoration, or symptoms of chest tightness or shortness of breath. All anti-infection drugs were discontinued.

4. DISCUSSION

4.1 Risk factors for *Acinetobacter baumannii* infection

This patient is an elderly female. She has suffered from various diseases such as hypertension, type 2 diabetes, hypothyroidism, and rheumatoid arthritis in the past. Because lung structure and function often decline with age and disease, alveolar elasticity decreases, and ciliary movement in the bronchi also declines. Before admission, this patient had been using glucocorticoids for a long time. After admission, she also received multiple antibacterial drugs, which both caused a significant decline in the patient's own immune function and significantly increased the possibility of severe lung infections.[4] In addition, the patient received mechanical ventilation and had a long hospital stay. A study found that bacteria continued to grow in the 3-day ventilator tubing

and its condensate water. The possibility of detecting Gram-negative bacilli or anaerobic bacteria increased significantly. As the duration of mechanical ventilation increased, the incidence of hospital-acquired pulmonary infections also rose significantly.[5] Reports abroad indicate that as patients begin mechanical ventilation, the incidence of hospital-acquired lung infections increases by 1% for each additional day of use.[6] At the same time, because this patient has been hospitalized for a long time, fibronectin in the salivary glands and secretory immunoglobulin A in the respiratory tract may decrease, increasing pathogenic bacterial adhesion and the risk of cross-infection. Eventually, the normal distribution of oral flora changes, and bacterial strains also become more drug-resistant. In conclusion, given the patient's current condition, the clinical pharmacist believes multiple factors can significantly increase the patient's risk of infection due to bacterial colonization.[7]

4.2 Analysis of the patient's drug treatment plan selection

The patient suddenly experienced breathing difficulties, with intermittent rises in body temperature. Multiple sputum cultures indicated an infection caused by *Acinetobacter baumannii*, and multiple drug sensitivity tests suggested multidrug resistance, with one test indicating pan-drug resistance. Re-examination of the CT for infection showed no significant improvement. This patient meets multiple risk factors for *Acinetobacter baumannii* infection.[8] Therefore, the diagnosis of pulmonary infection caused by *Acinetobacter baumannii* is clear. According to the authoritative "Expert Consensus on Diagnosis, Treatment and Prevention of *Acinetobacter baumannii* Infections in China" released in 2012,[9] the main principles for treating *Acinetobacter baumannii* infections include: (1) Select antibiotics based on the results of drug sensitivity tests; (2) Use combination therapy, especially when treating infections caused by extensively drug-resistant *Acinetobacter baumannii* (XDRAB) or pan-drug-resistant *Acinetobacter baumannii* (PDRAB), as it is often necessary to combine drugs; (3) Usually a larger dose is required; (4) The treatment course is often longer; (5) Choose drugs with high tissue concentrations based on the affected infection site, and formulate an appropriate administration plan according to the PK/PD theory; (6) For patients with abnormal liver and kidney functions and the elderly, the dosage of antibiotics should be adjusted appropriately based on serum creatinine clearance rate and liver function; (7) The proportion of mixed infections is high, so it is often necessary to combine clinical coverage of other infecting bacteria; (8) It is often necessary to combine clinical treatment with supportive therapy and good nursing. Therefore, for the patient with *Acinetobacter baumannii* infection, initially, based on the drug sensitivity results and the patient's liver and kidney functions, it can be considered to administer intravenous infusion of cefoperazone sodium sulbactam sodium (3 g, every 8 hours) combined with oral administration of minocycline (100 mg, twice a day). According to the "Monitoring Report on the Resistance of Common Clinical Isolated Bacteria in Elderly Patients from the National Bacterial Resistance Monitoring Network from 2014 to 2019,"[10] data for *Acinetobacter baumannii* from 2014 to 2019 showed that resistance rates to most antibacterial drugs were generally above 50%. The resistance rate to cefoperazone/sulbactam fluctuated between 29.7% and 38.0%, and the resistance rate to minocycline fluctuated between 18.7% and 22.2%. The combination of cefoperazone sodium/sulbactam sodium and minocycline aligns with the main treatment principles of relevant guidelines for multidrug-resistant *Acinetobacter baumannii* infections. At the same time, the clinical pharmacist noted that when minocycline remains in the esophagus and disintegrates, it can cause esophageal ulcers. This patient is currently bedridden, and it is recommended that the patient drink plenty of water after taking the medication and avoid taking it before bedtime. After 7 days of medication, the sputum culture results indicated that the *Acinetobacter baumannii* isolated from this patient might be a pan-drug-resistant strain, and the drug sensitivity test results showed that it had developed resistance to minocycline. The clinical pharmacist has monitored the patient's medication for 7 days, but the condition has not improved significantly. This elderly patient currently has gastrointestinal dysfunction, which may reduce oral absorption of minocycline, affecting its antibacterial efficacy and potentially contributing to further bacterial resistance. One possible reason is that pathogenic bacteria are exposed to sub-lethal doses of minocycline, increasing the likelihood of drug-resistance gene mutations and enhancing their ability to resist external pressure and avoid being killed by minocycline.[11] It has been reported in the literature[12] that the combination of cefoperazone sodium sulbactam sodium and tigecycline has a better therapeutic effect than the combination of cefoperazone sodium sulbactam sodium and minocycline in the treatment of infections caused by multidrug-resistant *Acinetobacter baumannii*. Therefore, it is recommended to switch to tigecycline combined with cefoperazone sodium sulbactam sodium for anti-infection therapy. Multiple studies have shown[13] that when these two drugs are used in combination to treat patients with multidrug-resistant *Acinetobacter baumannii* pneumonia, the study group's effective rate is significantly higher than that of the control group, without significantly increasing adverse reactions. Tigecycline is the first member of the glycylcycline class of antibacterial drugs and has certain antibacterial

activity against MDRAB and XDRAB. It is now one of the preferred options for treating pneumonia. For the patient's current condition, it is relatively applicable. Studies have shown that a loading dose is protective against tigecycline failure in treating MDRAB pneumonia patients.[14] However, the current recommended dosage for infections caused by multidrug-resistant *Acinetobacter baumannii* is often insufficient to achieve satisfactory clinical efficacy.[15] Randomized controlled studies have shown that increasing the initial dose of tigecycline to 200 mg and then maintaining 100 mg Q12h intravenous administration can improve clinical efficacy in severe infections.[16] Considering the current poor treatment feedback results of this elderly patient, referring to the "Expert Consensus on the Clinical Application of Pharmacokinetics/Efficacy Theory of Antimicrobial Drugs,"[17] after the clinical pharmacist's comprehensive evaluation, it is recommended that the clinical tigecycline administration plan be to give a 200 mg loading dose in the first administration, followed by a 100 mg Qd intravenous infusion. At the same time, it is suggested to monitor changes in the patient's liver and kidney function indicators. The clinical treatment was adopted accordingly.

4.3 The full participation of clinical pharmacists in the formulation of drug treatment plans

The patient was an elderly female with multiple underlying diseases. She had been using glucocorticoids for a long time outside the hospital and had intermittently used antibacterial drugs. After admission, her condition was critical, and she stayed in the hospital for a long time. She received mechanical ventilation. Multiple sputum cultures showed multidrug-resistant Acinetobacter. Various anti-infective drugs were used successively, but the therapeutic effects were all unsatisfactory. During treatment, clinical pharmacists closely monitor patients' condition changes in real time, provide individualized medication monitoring, consult professional literature, and strive to propose suggestions to adjust the drug treatment plan precisely. The clinical team adopts and recognizes the clinical pharmacists' suggestions. They utilize their professional advantages to participate in the clinical drug treatment team and play an active role in improving the effectiveness of drug treatment, ensuring the safety, economy, and effectiveness of patients' medication.

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AUTHORS CONTRIBUTIONS

Jia Ning: Concepts, design and manuscript writing; Zilong Zhao: Data collection and organization.

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The authors declare no conflicts of interest.

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