REPORT

Clinical characteristics and treatment experience report of severe pulmonary infection after renal transplantation

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Abstract: This study was to discuss the clinical diagnosis and treatment features of severe pulmonary infections after renal transplantation, in order to improve the cure rate. Retrospective research was applied to analyze the 52 cases of patients with serve pulmonary infection after renal transplantation in the department of organ transplantation in People's Hospital of Zhengzhou from July, 2008 to December, 2013. The pathogens which caused the pulmonary infection after renal transplantation were bacteria, virus, fungi, mycobacterium tuberculosis, combined infection and unknown pathogens, and the rate were respectively 28.85%, 15.38%, 7.69%, 3.85%, 21.15% and 23.08%. In the 52 cases, there were 41 cases of patients successfully survived, which was 78.85% and 11 cases died, which was 21.15%. The mortality rate of combined infection and unknown pathogens infection was significantly higher than that of single pathogen infection. Pulmonary infection after renal transplantation was of rapid deteriorated progress and high mortality rate. It was significant for patients to receive the comprehensive and integrated treatment.

Keywords: Renal transplantation; severe lung infection; immunosuppression.

INTRODUCTION

Severe pulmonary infection is one of the most common complications after renal transplantation. It is the main factor causing the death of patients with renal transplantation, the incidence was 8% to 16% (San *et al*., 2007). As patients with renal transplantation had immunosuppression medicine for long term, the immune system had been suppressed. Once pulmonary infection occurred, the symptom would be elusive, rapidly deteriorated, and easily developed into acute respiratory distress syndrome (ARDS), threatening patient life. In this study, the retrospective research was applied to analysis the 52 cases of patients with severe pulmonary infection after renal transplantation in the department of organ transplantation in People's Hospital of Zhengzhou from July, 2008 to December, 2013. It mainly focused on clinical features, diagnosis process, infection transfer and disease development in order to receive better acknowledge and improve the cure rate.

MATERIALS AND METHODS

General information

This study had collected 52 cases of patients with severe pulmonary infection after renal transplantation in the department of organ transplantation in People's Hospital of Zhengzhou from July, 2008 to December, 2013. There were 39 cases of male, and 13 cases of female, with ranging 19-57 years of age, average age was 38.6 years old. The pulmonary infection had been divided into three periods: first period was the two months after surgery which was with 7 cases, second period was from the second month to sixth month which was with 33 cases, the third period was after the sixth month which was with 12 cases. The postoperative immunosuppressant drugs information was below: 30 cases of patients had applied combined therapy of tacrolimus (FK506), MMF and prednisone; 12 cases of patients had been treated with Ciclosporin capsules (CsA), Mycophenolate mofetil (MMF) capsules and prednisone; 6 cases of patient had received treatment of MMF, sirolimus and prednisone; 4 cases of patients had applied the duplex treatment of MMF and prednisone. During the severe pulmonary infection, there were 42 cases of patients with normal kidney function after the transplantation and 10 cases of patients with mild abnormal function.

Diagnostic criteria

The early clinical symptom was high fever, without obvious cough and expectoration. After the onsets of 3-5 days, it developed into diffuse pulmonary interstitial edema. And then patients could had bosom frowsty, asthma and different degree of cyanosis. The early pulmonary computer tomography (CT) scan illustrated interstitial leaking, then developed into cloud flake or mist shape. The detailed diagnostic criteria for severe pneumonia was based on *Guidelines for Diagnosis and Treatment of Community-acquired Pneumonia* revised by the Respiratory Disease Branch of Chinese Medical Association (Chinese Thoracic Society, 2006). Based on the clinical diagnosis of community-acquired or hospital-

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acquired pneumonia, patients with at least one of the following criteria were diagnosed with severe pneumonia: 1. Consciousness disorder; 2. Respiration rate was not less than 30 times per minute; 3. Arterial partial pressure of oxygen (PaO_2) was less than 60mmHg, PaO_2/FiO_2 was less than 300 mmHg and these patients required mechanical ventilation treatment; 4. Systolic blood pressure was less than 90 mmHg; 5. Complicated with septic shock; 6. Bilateral or multiple lobe involvement proved by the chest X-ray, or lesion expended not less than 50% within 48 hours after admission (fig. 1 and fig. 2); 7. Urine output was less than 20ml per hour or 80ml per 4 hours, acute renal failure patients required dialysis treatment.

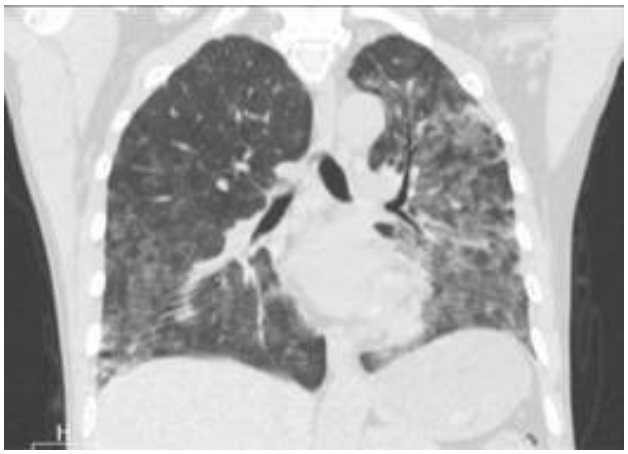

Fig. 1: Pulmonary features in chest CT

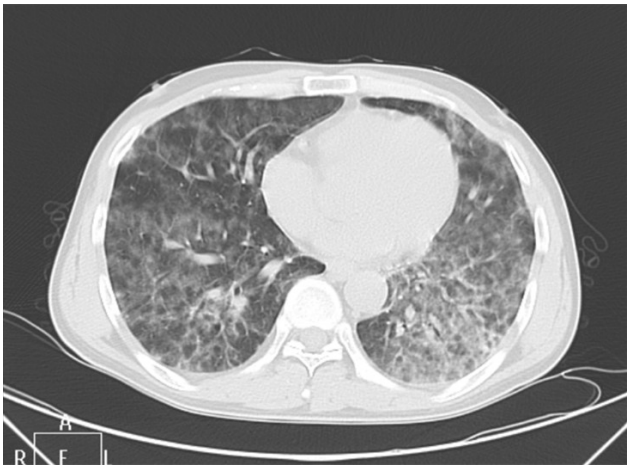

Fig. 2: Pulmonary features in transverse CT

Pathogen identification

The bacteria and fungi were cultivated in the sputum, throat swab, blood and midstream urine. Specimens were collected before the anti-infection treatment. It need to search for the pathogens. Drug sensitivity testing was performed when the culture results were positive. Some patients were performed fiber bronchoscopy testing and bronchoalveolar lavage. If possible, the histopathological biopsy shall be took. This study detected the 1,3-β-dextran (G) antigen (G test) and serum galactomannan antigen (GM) of the patients, along with the detection of blood cytomegalovirus (CMV) antibody (IgM) and deoxyribonucleic acid (DNA). This study also examined the anti-acid bacillus in the sputum and urine, along with the anti-neutrophil leukocyte cytoplasm antibody (ANCA) and the anti-tuberculosis antibody.

Treatment methods

Along with the pathogen detection, empirical anti-infection treatment was also applied, with therapy for bacteria, viruses, and fungi simultaneously and de-escalation therapy. Patients need to apply compound sulfamethoxazole oral treatment, if been suspected to be infected by cartesian pneumocystis. It also need to apply broad spectrum antibiotics, adequate resistance and full-term treatment. The sensitive drugs shall be applied after the etiology examination results. In antibacterials therapy, there were cefoperazone and sulbactam injection, imipenem and cilastatin sodium injection, linezolid injection and teicoplanin injection. In anti-viral therapy, there were ganciclovir for injection. The voriconazole injection was the favorite in anti-fungal therapy. Routine treatment was conversion treatment. It need to combine with caspofungin acetate injection for severe patients. According to the infection situation, it need to reduce or finalize the application of immunosuppressive agents. For dyspnea patients, it need to apply the nasal catheter or mask for inhaling oxygen. If disease situation approved, it need to apply noninvasive positive pressure ventilation to improve oxygenation.

STATISTICAL ANALYSIS

SPSS13.0 statistical software was utilized for data analysis. Measurement data among groups were compared using the t-test. Enumeration data were analyzed by chi-square test. A value of $P<0.05$ was considered to indicate statistical significance.

RESULTS

Pathogen test results

There were 15 cases of patients with bacterial infection, counting for 28.85%, of which it mainly were gram-negative bacteria, including spore acinetobacter, pseudomonas aeruginosa, klebsiella pneumoniae and drug-resistant escherichia coli; gram-positive bacteria mainly were methicillin resistant staphylococcus aureus and coagulase negative staphylococci. There were 8 cases of patients with virus infection, counting for 15.38%, of which it mainly were CMV virus, the rest were EB virus and influenza virus. There were 4 cases of patients with fungal infection, counting for 7.69%, of which mainly were aspergillus and candida albicans. There were 2 cases of patients with mycobacterium tuberculosis, counting for 3.85%. There were 12 cases of patients with unknown

Table 1: Efficacy comparison of severe pneumonia patients of different pathogen infection after renal transplantation

Item	Bacterial infection	Virus infection	Fungal infection	Tuberculosis infection	Mixed infection	Unknown pathogens infection
Infection cases	14	8	5	2	11	12
Cured cases	12	7	4	2	6	6
Death cases	2	1	1	0	3	4
Give-up-treatment cases	0	0	0	0	2	2
Cure rate	85.71%	87.50%	80%	100%	54.55%	50%
Mortality	14.29%	12.50%	20%	0%	27.27%	33.33%

pathogens infection, counting for 23.08%. There were 11 cases of patients with mixed bacterial infection, counting for 21.15%, including 5 cases of bacteria and viruses infection, 3 cases of bacteria and fungi infection and 3 cases of virus and fungi infection.

Treatment outcome

In the 52 cases of severe pulmonary infection, there were 41 cured cases, counting for 78.85%, 11 death cases, counting for 21.15% and 4 give-up-treatment cases. The mortality of mixed infection was significantly higher than single pathogen infection, as shown in table 1. In the cured 41 cases, there were 2 case of patients who developed transplant renal acute rejection. After the treatment of anti-human T-lymphocyte rabbit immunoglobulin (ATG) and solu-medrol, the renal function had recovered. The death cases of patients all had disease combining with acute respiratory distress syndrome (ARDS), including 5 cases of patients with concurrent multiple organ failure.

Compared with single pathogen infection, the mortality of mixed infection had increased and had statistical significance, $P<0.05$.

DISCUSSION

After renal transplantation, long-term application of immunosuppressant medicine caused the decrease of body immune function and high incidence of infection. Especially, the application of large doses of hormone and immune inhibitor two or three after surgery led to the inhibition of T lymphocytes and B lymphocytes, and seriously destroyed immune mechanism. Anti-rejection treatment decreased the immunity of patients against pathogen infection, such as virus infection, fungi infection, and etc. At the same time, it increased incidence rate and mortality of infection after renal transplantation. Lung was the organ to be easily infected. The severe pulmonary infection after renal transplantation was with onset conceals, fast progress and high mortality. Pulmonary infection was in diversity, including the conditional pathogenic bacteria, fungi and virus. Pathogen was difficult to detected, with low detection rate and delay. After anti-infection treatment, some patients had cured, but still did not know the pathogen. It significant for the lung CT examination and empirical medicine, especially the high resolution CT examination for the interstitial pneumonia, pulmonary aspergillus infection and blood-disseminated tuberculosis. It was with good early diagnosis sensitivity (Teng *et al*., 2010 and Jiang *et al*., 2010) and provided medical proofs before the outcome of exact pathogen.

The treatment of severe pneumonia after renal transplantation should follow the principle of early combination of medicine and demotion comprehensive anti-infection treatment, of which the effect was significantly higher than other treatment method (Wang *et al*., 2007 and Chen *et al*., 2008). Based on the outcome of pathogen detection and drug susceptibility, it shall adjust the treatment method and immunosuppressive therapy, in order to decrease or stop the application of immunosuppressive medicine, in order to restore body immune system and control the infection. Nutrition supported treatment was equally significant, and correct hypoalbuminemia and hypoproteinemia in time, and seriously detect each biochemical indexes. Patients shall receive timely mask oxygen inhale through oxygen mask, high frequency ventilation, tracheal intubation and auxiliary artificial mechanical ventilation, in the event of respiratory failure and acute respiratory distress syndrome (Zhang *et al*., 2003).

In conclusion, the severe pneumonia after renal transplantation was with rapid progress and high mortality (Wang *et al*., 2010 and Mysorekar *et al*., 2008). The key to prevent developing severe pneumonia was on paying much attention to the appeared upper respiratory infection and early postoperative lung infection (Chen, 2008).

In the early stage, based on the clinical manifestation and etiology features, the patients shall be given experimental anti-infection treatment. The treatment cure rate could dropped rapidly, if the treatment got delayed due to waiting the outcomes of etiology reexamination (Wang *et al*., 2010). In the early etiology diagnosis, the effective antibiotics was applied to combine with the treatment.

According to the disease condition, it shall adjust the immunosuppression treatment method, in order to enhance the body nutrition-supported treatment. The timely application of comprehensive treatment of ventilator supported treatment and improve ventilation could effectively control the infection, decrease the mortality, in order to increase the success rate of the treatment.

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