Late Onset Pulmonary *Lophomonas blattarum* Infection in Renal Transplantation: A Report of Two Cases

Qiang He¹, Xiuju Chen¹, Bo Lin¹, Lihui Qu¹, Jianyong Wu¹ and Jianghua Chen¹,²

**Abstract**

*Lophomonas blattarum*, a rare protozoa, was involved in pulmonary infections of transplant recipients. We report 2 cases of late onset pulmonary *L. blattarum* infection in renal transplant recipients with normal graft function and relative normal immune function. The diagnosis in both cases was confirmed by bronchoscopy and bronchoalveolar lavage (BAL) fluid examination. Both cases were sensitive to metronidazole treatment, but one case did not completely recover during the follow-up. The diagnosis and treatment were discussed to facilitate improvement in the recognition of this rare infection, especially in transplant recipients.

**Key words:** kidney transplantation, *Lophomonas blattarum*, pulmonary infection


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**Case Reports**

**Case 1**

A 41-year-old Chinese male presented with symptoms of chills, dry cough, recurrent high fever and exertional dyspnea for 6 days before admission to this hospital. Nonspecific infiltration in the right lower lung lobe was found on chest X-ray examination. He was given 3-days’ empirical antibiotic therapy with Cefuroxime (1.5 g i.v. every 12 hours) and traditional Chinese medicine, but showed no clinical improvement. He had end-stage renal failure (ESRD) secondary to Immunoglobulin A nephropathy and received a deceased donor renal transplantation 3 years prior to this presentation. He did not experience any episode of acute rejection or infection after transplantation. His maintenance immunosuppressive medication consisted of tacrolimus (2 mg twice a day, with the trough concentration 5-8 mg/L), mycophenolate mofetil (MMF, 500 mg twice a day, with the MPA area under curve 46-58 mg.h/L) and prednisone (5 mg/d). During the early stage after transplantation, he was given 14 days intravenous ganciclovir and 3 months oral Trimethoprim-sulfamethoxazole for prophylaxis against cytomegalovirus (CMV) and *Pneumocystis carinii* infection.

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respectively. His other medications included Diltiazem and amlodipine. The patient denied any history of smoking or exposure to tuberculosis, and he had been working as a farmer in a village of Zhejiang.

On physical examination, his body temperature was 39°C, with the typical temperature spiking each morning. His peripheral SpO2 was 95% by oxygen face mask but dropped to around 85% by nasal catheter oxygen inhalation. Chest auscultation did not reveal any abnormal breath sound initially. On the 3rd day of hospitalization, exaggerated breath sound was heard over the upper lung, while diminished breath sound heard over the lower lung. Both chest X-ray and computed tomography (CT) scan revealed lower lung field nonspecific infiltration with small to moderate hydrothorax (Fig. 1A).

The laboratory data showed moderate leukocytosis with a left shift, and an increment of the neutrophilic granulocytes, with a relatively normal amount of the lymphocytes, monocytes and acidophilic granulocytes (Table 1). The count of peripheral CD4 positive lymphocytes was 318-376/mL, which was not decreased even during the period of fever and in the presence of abnormal radiological change. His liver function and renal function was stable with a plasma creatinine level of 1.3 mg/dL and stool exam did not reveal ova, parasites or other pathogens. The serum immunoglobulins were also at the normal level. As he had no phlegm, the smear of throat was submitted and found to be normal. Anti-CMV immunoglobulin M and CMV pp65 antigens were negative, serum anti-tubercle bacillus (TB) antibody was also negative. The cultures of blood and urine during the hyperpyrexia stage were also negative. The possibilities of epidemic hemorrhagic fever, typhoid fever and ancylostomiasis were all excluded by relevant confirmatory diagnostic test. The pleural fluid was clear yellow and the lab test indicated exudative pleurisy, with negative anti-TB antibody and germ culture. Also there was no evidence of malignant pleural effusion.

After hospitalization, the MMF and tacrolimus were dis-
many polymorphonuclear lymphocytes and large numbers of alveolar lavage (BAL) fluid from the lower lobe showed without any endobronchial lesions. Analysis of the bronchoalveolar lavage fluid showed a few polymorphonuclear lymphocytes, plasma cells and monocytes, without any endobronchial lesions. BALF culture Negative. Cryptococcus Sputum culture Negative. Negative without oxygen inhalation. CRP (mg/L) 11~115.3 8~136.8

<table>
<thead>
<tr>
<th>Numeration of leukocyte (10^9/L)</th>
<th>Case 1</th>
<th>Case 2</th>
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<tbody>
<tr>
<td>Percents of neutrophil (%)</td>
<td>76.5~86.2</td>
<td>66.4~88.9</td>
</tr>
<tr>
<td>Percents of lymphocytes (%)</td>
<td>6.4~30.5</td>
<td>8.3~36.7</td>
</tr>
<tr>
<td>Percents of monocytes (%)</td>
<td>3.6~8.2</td>
<td>3.3~9.6</td>
</tr>
<tr>
<td>Percents of eosinophilic granulocytes (%)</td>
<td>0.1~0.6</td>
<td>0.1~0.5</td>
</tr>
<tr>
<td>peripheral CD4+lymphocytes (N/mL)</td>
<td>318~376</td>
<td>280~360</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>11~115.3</td>
<td>8~136.8</td>
</tr>
<tr>
<td>arterial partial pressure of oxygen (mmHg)</td>
<td>55~95</td>
<td>65~100</td>
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Figure 2. Lophomonas blattarum were found in Bronchoalveolar lavage (BAL) fluid from the case 1, it was about 20 μm in size, with a round or pear-shaped translucent body, a big and clear nucleolus, bars of short and thick flagellums on one-quarter end of its body (40×10).

continued and oral prednisone was replaced by intravenous methylprednisolone with a dosage of 40 mg/d. Anti-infection therapy was used in the combination of intravenous piperacillin / tazobactam, oral trimethoprim-sulfamethoxazole and oral fluconazole. Meanwhile, the expectorants, antitussives and drugs for relieving dyspnea were also used orally or by inhalation. The fever was controlled immediately, but it relapsed once when the dose of methylprednisolone was reduced to 20 mg/d. Repeat CT scan 17 days after hospitalization showed aggravating lower and middle lung field infiltration with more severe hydrothorax, the radiograph also indicated interstitial inflammation in the remaining lung fields (Fig. 1B).

The patient was submitted for diagnostic bronchoscopy, which revealed the presence of friable mucosa with bleeding without any endobronchial lesions. Analysis of the bronchoalveolar lavage (BAL) fluid from the lower lobe showed many polymorphonuclear lymphocytes and large numbers of rare living trichomonad like polypides, without any bacterium, acid fast bacillus, fungi, pneumocystis carinii, CMV (detection of cytomegalovirus antigen in lymphocytes by immunohistochemistry) or malignant cells. The polypide was about 20 μm in size, with a round or pear-shaped translucent body, a big and clear nucleolus, bars of short and thick flagellums on one-quarter end of its body (Fig. 2)). Its flagellums waved rhythmically when it was alive, when it was dead, its flagellums became silent and its body shriveled up. The unknown polypide was identified as Lophomonas blattarum according to its microscopic appearance in the Parasitology Department of Medical College of Zhejiang University. On investigation of the patient’s history again, he recalled cockroach contact during cleaning an old cabinet 3 weeks before the onset of this disease.

After the diagnosis of pulmonary L. blattarum infection, metronidazole was prescribed (1,000 mg, intravenous, two times/day) for ten days and then oral metronidazole (200 mg three times/day) for 14 days, without any other antibiotics. His temperature became normal just 3 days after metronidazole application, even with the intravenous methylprednisolone was discontinued. Phlegm was available 7 days after metronidazole application; repeated smear of phlegm specimens showed no L. blattarum, and repeated phlegm specimens culture were also negative. His pulmonary symptoms were gradually relieved day by day, and radiological evaluation was also improved 2 weeks after metronidazole treatment. Mycophenolate mofetil and tacrolimus were re-administered gradually to the normal doses. His plasma creatinine was still stable after discharge.

On follow-up, the serial lung radiological evaluation with CT scan was not recovered to normal state (Fig. 1C), but there was no recurrence of pulmonary symptoms or signs. Repeat evaluation with bronchoscopy 6 months after discharge still showed no sign of endobronchial lesions. BAL fluid showed a few polymorphonuclear lymphocytes, plasma cell and monocytes, without L. blattarum or other Microbes. Currently, this patient is receiving treatment of triple im-

Table 1. The Characteristics of Blood, Sputum and BALF Tests of These Two Patients Being in Hospital
munosuppressive agents with dosage reduced to a very low level, and his renal graft function is normal.

Case 2

A 55-year-old Chinese male presented with recurrent moderate fever for 7 days before admission. He had end-stage renal failure (ESRD) secondary to hypertensive nephropathy and accepted deceased donor renal transplantation 2 years prior to this presentation. His early stage maintenance immunosuppressive agents were microemulsified cyclosporine, MMF and prednisone, but the cyclosporin was then replaced with sirolimus for gingival hyperplasia and polycythemia 6 months before this admission. He did not experience any episode of acute rejection or infection after his transplantation. The trough concentration of sirolimus was 6-10 mg/L, MPA-AUC was 38-50 mg.h/L. He also had been given ganciclovir prophylaxis and trimethoprim-sulfamethoxazole prophylaxis as routine of our center. He was given ganciclovir prophylaxis and trimethoprim-sulfamethoxazole and fluconazole combined with tapered immunosuppressive agents, his symptoms did not diminish and the lung CT scan revealed that the lesion became more serious (Fig. 1D). He was then submitted for diagnostic bronchoscopy, and large numbers of L. blattarum were found in the BAL fluid, without any other pathogens. He also remembered cockroach contact 1 month before the onset of this disease. After the diagnosis, metronidazole was prescribed in the same method as in case 1. His body temperature became normal 2 days after metronidazole treatment, bronchoscopy was repeated 7 days after metronidazole treatment, and the BAL test showed large numbers of carcasses of L. blattarum (Fig. 3). The Cryptococcus humicola was also found in BAL culture, so intravenous fluconazole was added and the patient recovered rapidly. Lung CT scan returned to normal one month later. His pulmonary radiological evaluation and renal graft function both maintained stable at the 1-year follow-up.

Discussion

Human pulmonary L. blattarum infection is a rare disease with reports only in China (3, 4). There were total 15 cases L. blattarum infection reported prior to the present cases. All cases were in areas south of the Yangtze River in China. The environmental characteristic of this region is warm and moist, which favors the breeding of cockroaches and termites, who are the host of L. blattarum.

Analyzing those 15 reported cases, we found that L. blattarum not only infected the immunocompromised patients, including renal transplant recipients, but also infected those with normal immune function. Ten patients had no underlying chronic diseases (66.7%) (4). In both of the present cases the infection occurred more than 1 year after transplantation, which was not in the early post-transplant period common for opportunistic infection (5). Both patients were on regular follow-up, with normal graft function and relatively normal immune function, as indicated by the normal concentration of blood immunosuppressive agent concentration, a normal count of CD4+ lymphocyte and a normal level of serum immunoglobulins. The 4 cases pulmonary L. blattarum infection reported previously all occurred during the early post-transplant period, and the patients all had suppressed immune function (3). From our viewpoint, any healthy subject might be vulnerable to L. blattarum infection, but the infection in organ transplant recipient could be more serious.

Pulmonary L. blattarum infection had no specific symptoms, signs or radiological manifestation, especially in the early stage of the disease, a patient might only show pyrexia without any pulmonary symptoms or signs. Although L.
blattarum was one kind of parasites, only 50% of the patients had eosinophilia (4). Neither of the present two patients had eosinophilia. Because of the cellular immunity suppression, eosinophilia is generally scarce in parasitic infections of transplant recipients (6). L. blattarum could also be involved in infection mixed with other pathogens, such as: bacterium, CMV and TB (3). One of the present patients had mixed infection with fungi. The mixed infection in turn made the L. blattarum infection atypical. We suggest for those organ transplant recipients residing in regions suitable for the growth of cockroaches and termites, and presenting with fever and radiological abnormality irresponsible to regular antibacterium or anti-virus therapy, L. blattarum infection should be considered in the differential diagnosis. Timely bronchoscopy examination with BAL analysis is a useful and safe tool for the diagnosis of pulmonary L. blattarum infection and other pneumonia without definite pathogen (3, 7).

All of the articles reported that L. blattarum was sensitive to short-term metronidazole treatment (3, 4). The present case 1 was also sensitive to about one month of metronidazole treatment initially, but his lung radiological manifestation did not recover to normal, with the negative L. blattarum examination by bronchoscopy. It may be related to permanent lung damage with delayed metronidazole treatment, or an immune attack induced by the dead carcasses of L. blattarum. But due to the limited number of cases, we are still not certain about how long the metronidazole should be used to guarantee that all of the worms be killed and whether one time of L. blattarum infection can induce lifelong immunity. After all, it is very difficult for a lot of people to absolutely keep away from cockroaches in developing countries.

In conclusion, we reported 2 cases of late onset pulmonary L. blattarum infection in renal transplant recipients with normal graft function and relatively normal immune function. These cases suggest that all the organ transplant recipients might be vulnerable to L. blattarum infection. Any patient with pneumonia after transplantation in the correlative regions irresponsible to regular specific medication should be considered for possible L. blattarum infection. However, the duration of metronidazole treatment and whether and how L. blattarum prophylaxis should be introduced remain inconclusive.

The authors state that they have no Conflict of Interest (COI).

References