



## Pulmonary Infection with *Lophomonas blattarum*

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Received: 30 October 2019 / Accepted: 15 April 2020 / Published online: 26 June 2020  
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### Abstract

**Objective** To describe the characteristics of *Lophomonas blattarum* infection in children based on a retrospective review of medical records data from Beijing Children's Hospital, Capital Medical University, China.

**Methods** This study included 53 cases from July 2014 through December 2016. The data were tabulated and statistically analysed in a Microsoft Excel spreadsheet and SPSS 17.0.

**Results** The average age of the 53 patients was  $7.10 \pm 0.56$  years, and the male/female ratio was 3:2.3. The most common clinical manifestation was cough, and almost half of the patients had fever. Furthermore, all patients were treated with metronidazole and recovered.

**Conclusions** For children who have had long-term respiratory symptoms, the possibility of *Lophomonas blattarum* infection should be ruled out. Metronidazole is effective in treating *L. blattarum* infection in children.

**Keywords** *Lophomonas blattarum* · Pulmonary infection · Children

### Introduction

The global climate has changed in recent years; physicians, especially pediatricians, are confronted with many parasitic lung infections, including protozoal and helminthic infections [1]. Protozoal infection is always associated with individual states of suppressed immunity, which can be caused by acquired immunodeficiency syndrome (AIDS), transplants, malignant hemopathies, and corticosteroid therapy. Visiting endemic areas, keeping pets, and exposure to a filthy environment could also increase the possibility of inviting the disease.

Some pulmonary protozoans, such as *Babesia* and *Balantidium coli*, have been reported to rarely exist in patients' lungs [2], but *Lophomonas blattarum* (*L. blattarum*) is a relatively rare protozoal infection, and most infections occur in China, with more than 90% cases [3]. *L. blattarum* is a multiflagellated protozoan belonging to the suborder

Lophomonadina (Hypermastigida order). It is considered an endocommensal parasite in the gut of cockroaches, such as *Periplaneta americana* and *Blattella germanica* [4]. It is a rare but potentially valuable cause of infection in a variety of tissues and organs, including the maxillary sinus and other sinuses and reproductive and respiratory systems. Adults with bronchopneumonia and asthma and pediatric in-patients with severe pulmonary disease [5] were also found to be related to *L. blattarum* [6]. Coughing, expectoration, breathlessness, pneumonia, bronchiectasis, pulmonary abscesses, and pleural effusion are the most common symptoms [4]. Chest X-rays and lung CT scans are helpful imaging techniques that reveal the illness by showing patchy nodular or linear infiltrating scatter opacities, which may be migratory and associated with a degree of bronchial obstruction. Bronchoscopy can be used to indicate affected airways that are narrowed with obstruction of the bronchial orifices and the bronchial mucosa that appears congested and edematous, with foci of hyperplasia and inflammation and white necrotic matter on the mucosa [7]. Analysis of blood samples showed that eosinophils were raised in approximately one-third of patients [7]. Bronchoscopic brush smear or alveolar lavage fluid is usually used for the diagnosis of protozoan parasites. Clinically, almost all patients were treated with metronidazole or tinidazole and had a good prognosis.

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Most of the cases were adults or immunosuppressed patients; there are few reports of *L. blattarum* infection in children. However, due to the complexity of the living environment and the nature of the activity, children are consequently susceptible to *L. blattarum* infections. Therefore, this study aimed to analyse the current clinical features and trends of *L. blattarum* in Chinese children. All 53 cases presenting to the Beijing Children's Hospital, Capital Medical University, China, from July 2014 through December 2016 were included.

## Material and Methods

This study is a retrospective review of *L. blattarum* cases gathered from July 2014 through December 2016 based on medical records data from Beijing Children's Hospital, Capital Medical University, China. Data included demographic information and clinical information, including age, gender, address, and diagnosis.

The inclusion criteria was as follows: First, the diagnosis of pneumonia meets the guidelines for the management of community-acquired pneumonia in Chinese children (revised in 2013). Second, patients' bacterial and fungal examinations were performed using the Vitek (R) MS system, and the results were negative. The results of tests for routine respiratory viruses (respiratory syncytial virus, parainfluenza virus, 2009 H1N1 influenza virus, H3 subtype influenza virus, seasonal H1 subtype influenza virus, influenza B virus, human enterovirus, human coronavirus, human metapneumovirus, and human bocavirus), mycoplasma, and chlamydia were also negative; and third, all cases were negative for the HIV antibody. Fourth, protein purified derivative (PPD) examination was completed for all instances to exclude tuberculosis infection. All the results were negative. Fifth, *L. blattarum* was found in alveolar lavage fluid using a bronchoscope and was not observed after metronidazole treatment.

All the data analysed were anonymized. Data for continuous variables were presented as mean  $\pm$  standard deviation (SD) or median. For categorical variables, the relative numbers of patients in each category were calculated. Non-normally distributed dates were reported with medians and 25th and 75th interquartile ranges (IQR). The data were tabulated and statistically analysed in a Microsoft Excel spreadsheet and Statistical Product and Service Solutions (SPSS) 17.0.

The study protocol was approved by the Ethical Review Committee of Beijing Children's Hospital. This study is a retrospective analysis of pre-existing data, and informed consent from parents or guardians was not required.

## Results

The 53 cases were distributed in 12 provinces/municipalities/autonomous regions. A total of 69.81% (37/53) of cases occurred in four provinces/municipalities (namely, Beijing, Hebei, Henan, and Shandong). The highest infection rate (28.30%) was in Hebei province ( $n = 15$ ), followed by Beijing (15.09%,  $n = 8$ ), Henan (15.09%,  $n = 8$ ) and Shandong (11.32%,  $n = 6$ ) (Table 1). Patients from northern China accounted for 81.1% ( $n = 43$ ), and the others ( $n = 10$ ) came from the southern area. Northern China refers to Heilong Jiang, Liaoning, Hebei, Shanxi, Shandong, Henan, Beijing, and Inner Mongolia municipality. Southern China refers to Zhejiang, Jiangxi, Hubei, Sichuan, and Yunnan provinces.

A total of 53 *L. blattarum* cases were admitted to the hospital from July 2014 through December 2016 (Table 2). The number of cases reported ranged from 10 to 27 every year, with a mean of 18 cases per year. Among the children, 30 cases were male, and 23 cases were female, with ages ranging from 1 to 17 years. The median course of the disease was 3.5 months.

As shown in Table 3, cough was the most common symptom, followed by breathlessness, expectoration and hemoptysis. In addition, 25 (47.17%) children had fever. Thirty-nine of 53 cases were inoculated with the influenza vaccine, and only one was not inoculated for the Bacillus Calmette–Guerin (BCG) and diphtheria pertussis tetanus (DPT) vaccines.

Forty-five of 53 cases had their CD4<sup>+</sup>, CD8<sup>+</sup>, B cells, and NK cells checked. Only one child's number of CD4<sup>+</sup> T cells was normal (55.0% - 57.0%), and in 44 cases, number of CD4<sup>+</sup> T cells were lower than 55.0%. The number of CD8<sup>+</sup> T cells in 20 cases was normal (11.0% - 25.0%), but the number in 25 cases was higher than 25.0%. The CD4<sup>+</sup>:CD8<sup>+</sup> ratio was abnormal in 16 cases (<1.1 or >2.0). B cells were normal in 39 cases (11.0% - 45.0%), and those of the others were lower than 11.0%. Regarding NK cells, in 27 cases they were normal (7.0% - 40.0%), with 18 cases having lower than 7.0% NK cells (Table 4).

Among 53 cases, in 51 cases eosinophils were checked, but one case lacked this value (Table 4). Nine of them (9/50) exceeded the standard amounts ( $>0.50 \times 10^9/L$ ), and eleven of them (11/51) exceed the standard values ( $>5\%$ ). In 45 cases blood CD3<sup>+</sup> T cells were detected; in 41 cases they were normal (55.0–82.0%), 3 cases had lower than 55.0%, and only one case had higher than 82.0%.

Lung imaging tests were performed in 50 of 53 children, including lung CT (47 cases) and X-ray examination (3 cases). Five of the fifty lung imaging examinations prompted two main kinds of imaging abnormalities, and the rest showed only one. The most common features of these abnormalities appeared as patchy local shadowing on radiography (Table 4).

After taking oral metronidazole (the dose of metronidazole was 10 mg/kg/d, taken orally 3 times), no *L. blattarum* was

**Table 1** *L. blattarum* cases distribution between 2014 and 2016

Year	China Total no. of cases	Hubei No. of cases	Jiangxi No. of cases	Henan No. of cases	Hebei No. of cases	Shandong No. of cases	Beijing No. of cases	Zhejiang No. of cases	Yunan No. of cases	Sichuan No. of cases	Inner Mongolia No. of cases	Liaoning No. of cases	Heilong Jiang No. of cases	Shanxi No. of cases
2014	27	1	4	6	5	2	2	1	1	1	2	1	1	0
2015	16	0	1	2	4	3	4	0	0	0	1	0	0	1
2016	10	0	0	0	6	1	2	1	0	0	0	0	0	0
Total	53	1	5	8	15	6	8	2	1	1	3	1	1	1

found on re-examination (bronchoscopy). After treatment, the temperature of 49 cases was normal, except 3 cases who had a transient fever. Twenty-one patients had expectoration, 6 of whom have had bronchiectasis before.

**Discussion**

*L. blattarum* is a rare and host-specific protozoan found in muggy environments [8], and many insects found in domestic environments are the hosts. *L. blattarum* can be spread by termites and cockroaches, is shed in the dust during crawling of the host, which could be related to an increased risk of inhalation and subsequent human infection. The most likely route of transmission for *L. blattarum* is airborne. *L. blattarum* infection has only been found in the respiratory system to date.

All 53 children in this study experienced prolonged pulmonary infection but showed negative results for tests for common clinical pathogens (bacteria, viruses, mycoplasma, chlamydia, fungi). The authors tried administering antibiotics and antiviral drugs without any success. They then used a bronchoscope to check the alveolar lavage fluid, leading to the detection of *L. blattarum*. Metronidazole was used to treat this disease. After treatment, most pulmonary-related symptoms disappeared, and the protozoan could no longer be detected. Although *L. blattarum* infections are rare, bronchoscopy results together with the effectiveness of the treatment, suggest that these children were indeed infected by it.

Under the microscope, the morphology of *L. blattarum* can be challenging to distinguish from that of pulmonary cilia, which can lead to misdiagnosis. However, Fakhar et al.

recently reported the first tool for the molecular diagnosis of *L. blattarum*, which will help identify this protozoan infection in the future [9].

Although immunosuppression is an essential factor in a considerable number of cases, it was not present in the majority of the case reports identified in other statements, which is the same as the results of present study, with 26 cases without any previous underlying diseases. In contrast, clinical manifestations of the respiratory system were generally present either as a concomitant condition or after the infection [10]. Although the guardians of these children could not confirm whether their children had a history of insect contact, considering the characteristics of poor self-control and hyperactivity, children have a high risk of contracting it from dirt and insects. This study also reveals that even healthy children can be infected by *L. blattarum* when living with cockroaches and termites.

Pediatricians paid little attention to *L. blattarum* previously; especially in those children who failed to receive antibiotic treatments and had prolonged fever (especially children with long-term low temperature) and cough. After the authors

**Table 2** Number of *L. blattarum* cases reported between 2014 and 2016

Year	Cases	%	Gender (M:F)	Age (year)	Course (month)
2014	27	50.9	16:11	8.33 ± 0.71	5.00 (2.00–12.00)
2015	16	30.2	9:7	4.86 ± 1.02	2.25 (0.88–12.00)
2016	10	18.9	5:5	7.36 ± 1.28	2.00 (0.42–14.00)
Total	53	100	30:23	7.10 ± 0.56	3.50 (1.00–12.00)

**Table 3** Clinical features of infection in the 53 patients

Index	Present at admission No./Total no. (%)	Median (IQR)
Temperature	53 (100)	37.00 (36.40–38.85)
36.0–37.0 °C	28 (52.8)	36.40 (36.03–36.50)
37.1–38.0 °C	5 (9.4)	37.80 (37.55–37.80)
38.1–39.0 °C	9 (17.0)	38.50 (38.45–38.85)
39.1–40.0 °C	11 (20.8)	39.50 (39.30–39.80)
Cough	41 (77.4)	–
Breathlessness	10 (18.9)	–
Expectoration	8 (15.1)	–
Hemoptysis	3 (5.7)	–
Vaccine inoculation		
Influenza vaccine	39 (73.58)	–
Bacillus Calmette - Guerin	52 (98.11)	–
Diphtheria pertussis tetanus	52 (98.11)	–

**Table 4** Laboratory and radiographic findings on admission

Variable	Value (IQR)
Leukocyte count (per mm <sup>3</sup> )	8.95 (6.63–12.85) × 10 <sup>9</sup> (n = 52)
CD3 <sup>+</sup> T lymphocyte count (percentage)	68.37 ± 1.45 (n = 45)
CD4 <sup>+</sup> T lymphocyte count (percentage)	36.97 ± 1.20 (n = 45)
CD8 <sup>+</sup> T lymphocyte count (percentage)	27.13 (22.01–30.00) (n = 45)
CD4 <sup>+</sup> :CD8 <sup>+</sup> ratio < 1.1 [no./total no. (%)]	9/45 (10.00)
CD4 <sup>+</sup> :CD8 <sup>+</sup> ratio > 2.0 [no./total no. (%)]	7/45 (15.56)
B lymphocyte count (per mm <sup>3</sup> )	18.09 ± 1.17 × 10 <sup>9</sup> (n = 45)
Natural killer cells (per mm <sup>3</sup> )	8.70 (5.30–13.40) × 10 <sup>9</sup> (n = 45)
Hemoglobin (g/L)	129 (118.00–142.50) (n = 52)
Platelet count (per mm <sup>3</sup> )	327.92 ± 11.29 × 10 <sup>9</sup> (n = 52)
C-reactive protein >10 mg/L [no./total no. (%)]	13/49 (26.53)
Eosinophil count (per mm <sup>3</sup> )	0.21 (0.07–0.37) × 10 <sup>9</sup> (n = 50)
Eosinophil count (percentage)	2.20 (1.00–4.70) (n = 51)
Abnormalities on lung imaging test [no./ total no.(%)]	
Local patchy shadowing	18/50
Flocculent shadow	10/50
Lung nodules	10/50
Ground-glass opacities	5/50
Interstitial abnormality	2/50
Substantial abnormality	2/50
Interstitial and Substantial abnormality	1/50
Pulmonary atelectasis	2/50
Pleural effusion	1/50

searched the relevant papers, they found that the majority of these cases were from China, with a few cases being reported in Spain [6] and Peru [7]. One case of a patient having a dual infection with tuberculosis has been reported in India [11]. Unfortunately, *L. blattarum* infection presents with atypical symptoms, such as cough, sputum, and dyspnea [12]; all of these symptoms are common in other respiratory infections. Therefore, there is some difficulty in differential diagnosis and treatment. To prevent and minimize the consequences of *L. blattarum*, a deeper understanding of the clinical features and epidemiology of *L. blattarum* is imperative.

In general, diagnostic clues to *L. blattarum* infection include patients who are immunocompromised or have a history of prolonged use of immunosuppressants, marked peripheral eosinophilia, clinical features of a pulmonary infection, and inadequate response to antibiotics [13]. In the present study, 27 children had underlying diseases, 10 cases had bronchiectasis, one had favism, one had congenital ciliated immobility, and one had infection combined with bronchial asthma. One girl had a long history of taking glucocorticoids and tacrolimus for her nephrotic syndrome (NS). Five cases were bronchiolitis obliterans (BO); among them, one child was also diagnosed with asthma. Nine cases were diagnosed with asthma alone. One case had congenital developmental delay and

bronchiolitis, and the father of one child had a long history of drug use. Even though the symptoms of *L. blattarum* infection are common in other respiratory diseases, the authors observed that cough, breathlessness, expectoration, and hemoptysis should be noted more. Moreover, as a biomarker, eosinophilia is a central feature of the host response to helminth infection [14]. It can be detected in sputum smears, bronchoalveolar lavage (BAL), or biopsy smears. When patients do not have any condition causing immunosuppression, some marked blood eosinophilia can also reveal the possibility of protozoan infection [15]. As reported [16], there is an imbalance of CD8<sup>+</sup> and CD4<sup>+</sup> T cells in the protozoan infection, which is similar to the present result. In the present study, the number of CD4<sup>+</sup> T cells in most patients was abnormal. More than half of them had a higher number of CD8<sup>+</sup> T cells, and the CD4<sup>+</sup>:CD8<sup>+</sup> ratio of almost half of them was unusual.

Regarding the abnormalities on a lung imaging test, patchy local shadowing, flocculent shadow, and lung nodules were the top three imaging features. In 2011, after summarizing 32 adult cases of *L. blattarum* infection, Zhou et al. found that in adults, the chest image is mainly composed of exudative patches and solid changes, which are very different from children's chest imaging [17]. There are some limitations to the present study. First, most of the patients came from northern

China as the study site hospital is located in Beijing, which is in northern China. In addition, there was an analyst bias because of the lack of some patients' inspection results.

## Conclusions

Although *L. blattarum* infection is rare and mostly reported in immunocompromised adults, children can also be infected by it; even those without any underlying disease. Metronidazole is effective in treating *L. blattarum* infection in children. Furthermore, for children with long-term pulmonary disease, the possibility of *L. blattarum* infection should be ruled out.

**Authors' Contributions** QD reviewed the medical records, analyzed and interpreted the data, and drafted the manuscript. KLS designed and oversaw the study, interpreted the data, and revised the manuscript. Both the authors have read and approved the final manuscript for publication. KLS will act as Guarantor for this paper.

## Compliance with Ethical Standards

**Conflict of Interest** None.

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