ORIGINAL RESEARCH PAPER
Volume - 9 | Issue - 8 | August - 2020 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

BRONCHOPULMONARY INFECTION BY LOPHOMONAS BLATTARUM- AN EMERGING DISEASE OR A SPECULATIVE MYTH?

Microbiology

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ABSTRACT

Introduction: Lophomonas blattarum is a multi flagellated protozoan, which is the endocommensal of the intestinal tracts of termites and cockroaches. Human infections with Lophomonas blattarum are rare but the association of Lophomonas and respiratory pathology, especially in immunocompromised individuals has recently gained concern. **Aims & Objectives:** i)To determine the frequency of bronchopulmonary lophomoniasis in clinically diagnosed cases of respiratory tract infections. ii) To identify the risk factors associated with it. **Methods:** A retrospective data of three years was collected to study the number of bronchoalveolar lavage fluids showing the presence of Lophomonas blattarum, submitted to the Department of Microbiology. Lophomonas blattarum was identified in bronchoalveolar lavage fluid by direct microscopic examination of wet mount and / or Giemsa stained smear. **Results:** A total number of 1053bronchoalveolar lavage fluids were received fromclinically diagnosed / suspected cases of respiratory tract infections. the frequency of occurence of Lophomonas blattarum in BAL fluids was found to be 1.14% (12/1053). Amongst the positive cases, predominant age group affected was ≥ 61 years, followed by 31-40 years, and females outnumbered males with tje ratio of 4.5:1.Bronchopulmonary Lophomonas infection was most commonly associated with diabetes (41.7 %), followed by prolonged corticosteroid therapy (33.3 %), chronic smoking (16.7 %) and cytotoxic chemotherapy (8.3 %).**Conclusions:** The observation of Lophomonas blattarum, in BAL fluids, under light microscopy, in patients who donot respond to antibiotics, but show satisfactory improvement with antiprotozoal therapy, can be labeled as bronchopulmonary lophomoniasis. The development of molecular methods to resolve the issue regarding the confusion with other structures such as ciliated bronchial cells and other endocommensals of gut of the termites,would be promising.

KEYWORDS

BAL, Bronchopulmonary lophomoniasis, Lophomonas blattarum, Cockroaches

INTRODUCTION:

Lophomonas blattarum is a multiflagellated protozoan, which inhabits the hindgut of termites and cockroaches, belonging to the Lophomonassub order, Hypermastigida order, phylum Parabasalia.[1,2,3,4]The first case of pulmonary infection by L. blattarum was identified in 1993 in China by Chen and Mengsin, and thereafter more than 100 cases of bronchopulmonary lophomoniasis have been reported since 1993. [5,6,7] The cockroaches, such as Periplaneta Americana and Blattellagermanica, excrete the parasite in the feces and once eliminated, it forms cyst that remains in the environment. [3,8]Although the human infection by L. blattarum is rare, it could cause pulmonary infection in susceptible patients through the inhalation of dust containing the cyst.[8,9]As far as its pathogenic mechanisms are concerned, certain proteases have been identified that are involved in cyto-adherence, epithelial barrier rupture, apoptosis.[10]

Pulmonary protozoal infections are increasingly being recognized in this current scenario.[11]This rise may be due to an increasing proportion of the population having compromised immune status. Immunocompromised function in the respiratory tract could be due to infection with the human immunodeficiency virus, long-term use of steroids and other immunosuppressive drugs, malignancies, systemic illness, or chronic respiratory pathology.[12]A proportion of the rise in protozoal infections is due to multiflagellate Lophomonas blattarum.[13,14] Although L. blattarum is uncommon but has a potential to cause pulmonary infections and respiratory symptoms.[14-17]The most common symptoms are fever, cough, expectoration, and shortness of breath, and the radiological findings may show pneumonia, bronchiectasis, pulmonary abscesses, and pleural effusion.[18]The protozoan has been also reported in patients with severe pulmonary disease [18] and asthma[19,20]. The identification of L. blattarumis based on the morphological features under light microscopy using fresh and stained samples including sputum, bronchoalveolar lavages, bronchial brushings and tracheal aspirates. Multiflagellate protozoa are difficult to differentiate from ciliated bronchial epithelial cells, under light microscopy, and their misidentification is an important issue.[21]. L. blattarum is round to oval, [20-60]um in diameter, and has an double tuft of flagella at the anterior end.[22,23] Electron microscopy provides ultrastructure of L. blattarum and its differentiation from bronchial ciliated epithelial cells.The funnel shaped calyx, axial filament, and perinuclear tubules are special structures of L. blattarum.[24]

To the best of our knowledge, limited data is available on pulmomary lophomoniasis in western Uttar Pradesh, which has prompted us to carry out the present study in this belt.

Materials And Method:

The retrospective study was conducted in a tertiary care hospital, from April 2016 to March 2019. Our laboratory receives bronchoalveolar lavage fluids for microbiological investigations, from patients with a clinical diagnosis of lower respiratory infections.

The study group included all the patients irrespective of age and gender, whose BAL fluids had been received in the laboratory.

Sample Processing:

BAL fluids were processed for direct microscopy and for culture as per standard techniques :[25,26]

BAL fluids were centrifuged at 3000 rpm for 15minutes and the deposits obtained were processed as follows as per the requisition such as :

1. Wet mount/10% Potassium hydroxide (KOH) mount
2. Gram Staining
3. Ziehl Neelsen(ZN) staining- Smears were stained by Ziehl Neelsen(ZN) staining to look for beaded acid-fast bacilli.
4. Bacterial culture aerobic- Samples were inoculated on to Bloodagar, Chocolate agar, MacConkey agar. Plates were incubated at 37º C for 24 hours. Any growth obtained was identified as per standard protocol, If there was no growth, culture plates were reincubated for another 24 hours.
5. Culture for Mycobacterium tuberculosis by automated liquid culture (BacT/ALERT 3D, BioMerieux):
6. Fungal culture- Samples were inoculated onto Saboraud dextrose agar (SDA) with antibiotics but without cycloheximide, and incubated at 25°C and 37°C. The culture tubes were examined at 3-4days interval for growth.The isolates were identified by as per the standard mycological techniques.

RESULTS:

A total number of 1053 bronchoalveolar lavage fluids received from clinically diagnosed cases of lower respiratory tract infections were subjected to microbiological investigations. Out of 1053 cases, 220 were found to be negative for bacterial/ tubercular/ fungal etiology. Among the remaining 833 cases, 754 BAL fluids were positive for

bacterial growth, 71 showed fungal growth and 8 cases were positive for Mycobacterium tuberculosis.

Out of total of 220 culture sterile BAL fluids, in 12 samples multiflagellated protozoan Lophomonas blattarum was identified as an incidental finding in wet mount, which was further subjected to identification by Giemsa staining. Thus, the frequency of occurrence of Lophomonas blattarum in BAL fluids in clinically diagnosed cases of lower respiratory tract infections was found to be 1.14%(12/1053).

Amongst the positive cases,(n=12). predominant age group affected was ≥ 61 years, followed by 31-40 years, and females outnumbered males with 4.5:1 (Table 1).

Bronchoulmonary Lophomonas infection was most commonly associated with diabetes (41.7 %), followed by prolonged corticosteroid therapy (33.3 %), chronic smoking (16.7 %) and cytotoxic chemotherapy(8.3 %)(Table 2).

Computed axial tomography-high resolution (HRCT) chest findings in all the cases of bronchopulmonary lophomoniasis were consistent with either consolidation or brochiectatic changes, predominantly consolidation. Bilateral pulmonary consolidation was found in 50% cases of brochopulmonary lophomoniasis, followed by right lobe consolidation (25% cases), left lobe consolidation (16.7% cases) and right lobe bronchiectasis (8.3% cases)(Table 3).

Table 1:Age and gender wise distribution of cases of brochopulmonary lophomoniasis (n= 12)

Age (in years)	Positive cases		
	Number of positive cases	Male	Female
41-50	1	1	0
51-60	5	3	2
≥ 61	6	4	2
Total	12	8	4

Table 2: Risk factors associated with cases of bronchopulmonary lophomoniasis (n= 12)

Risk factor	Positive cases (n=12)	Percentage (%)
Diabetes mellitus	5	41.7
Prolonged steroid therapy	4	33.3
Chronic smoking	2	16.7
Cytotoxic chemotherapy for underlying breast carcinoma	1	8.3

Table 3: Radiological findings associated with cases of bronchopulmonary lophomoniasis (n= 12)

Chest computed tomography findings	Number of cases	Percentage of cases (%)
Bilateral pulmonary consolidation	6	50
Right lobe pulmonary consolidation	3	25
Left lobe pulmonary consolidation	2	16.7
Right lobe bronchiectasis	1	8.3

DISCUSSION:

Lophomonas blattarum(LB) is being considered and recognized an emerging parasite that can cause respiratory tract infection. L. blattarum is a multiflagellated protozoan parasite living in the intestinal tracts of termites and cockroaches.[1]More than 100 cases of L. blattarum infection have been reported since the first case emerged in 1993.[7] The vast majority of studies reported L. blattarum infection based on morphology under a light microscope.[15,27,28]

In the present study the frequency of bronchopulmonary lophomoniasis in clinically diagnosed cases of lower respiratory tract infections was found to be 1.14%.

Infection caused by the multiflagalled protozoon L. blattarum has been reported by various authors and its presence in respiratory secretions, has been identified.[15,27,28]

L. blattarum can be detected in sputum smears, BAL, or biopsy smears.[8]There are reports on lophomonas pulmonary infection from China,[12,13,15] Turkey,[16] Spain,[17] Peru, [19]India[20] and Iran,[4,30,31]As per the literature, 137 cases have been reported from 1993 to 2014.[8] Human pulmonary infection with L. blattarum has been also reported in patients with bronchopneumonia, severe pulmonary disease [7]and adult patients with asthma[3-9,32]

In our set up, amongst the positive cases of bronchpulmonary L. blattarum infection (n=12), predominant age group affected was ≥ 61years, followed by 31-40 years. The occurrence of Lophomonas infection in elderly patients reflects its association with weakened immune system in aging process. Females outnumbered males with the ratio of 4.5:1 (Table 1).

Bronchoulmonary Lophomonas infection, in the present study was most commonly associated with diabetes (41.7 %), followed by prolonged corticosteroid therapy (33.3 %), chronic smoking (16.7 %) and cytotoxic chemotherapy (8.3 %).(Table 2).

The majority of these Lophomonas pulmonary infections have been reported in immunocompromised patients in China.[12,13,15]A case of a patient having dual infection with tuberculosis has been reported from India.[33]

Although, most of the cases been reported in immunocompromised patients,[6,7] a case has been reported in immunocompetent young male in Mumbai, India by Tyagi R et al. in [2016.34]

Clues to L. blattarum infection include patients who are immunocompromised or have history of prolonged use of immunosuppressants due to underlying disease, marked peripheral eosinophilia, clinical features of a pulmonary infection, and poor response to antibiotics.[8] Authors have also reported that patients subjected to solid organ or hematopoietic cell transplants developed the pulmonary L. blattarum infection, during the course of illness. [17,22]

In our study, computed tomography chest findings in all the cases of bronchopulmonary lophomoniasis were consistent with either consolidation or brochiectatic changes. Bilateral pulmonary consolidation was found in 50% cases of bronchopulmonary lophomoniasis, followed by right lobe consolidation (25% cases), left lobe consolidation (16.7% cases) and right lobe bronchiectasis (8.3% cases).

The clinical signs and symptoms of L. blattarum pulmonary infection are generally nonspecific in majority of the cases, and the clinical findings of pneumonia are the same as with other etiological agents.[35]

Under light microscopy, it is difficult to differentiate Lophomonas blattarum from ciliated bronchial epithelial cells. L. blattarum was first described in 1860 by S. Stein from the gut of the cockroach Blattaorientalis. It was, also observed in the hindgut of the other cockroaches such as Periplaneta Americana and Blatella Germanica.[5]

A detailed morphologic description of L. blattarum under a light microscope was undertaken by Brugerolle and Lee in 1911.[36] The presence of L. blattarum could be determined for being motile with a tuft of flagella extending from the anterior end It possesses about 50 or more flagella of different lengths. It has a piriform structure with diameter ranging from 20 to 60 μ depending on the number of vacuoles it possesses. Golgi body, mitochondria and other organelles are present in its cytoplasm .[18,37]

Ciliated epithelial cells are conical or columnar in shape, having round-oval nucleus at the basal end and a marked terminal bar at the apical end of the cell with regular, unidirectional tuft of cilia inserted into the terminal bar.[23,37]

Because many of these flagellates cannot be cultivated, their identification by light and electron microscopy is important.The development of molecular methods for identification of L. blattarum becomes essential[38]

In our study, all the cases of bronchopulmonary lophomoniasis did not show any clinical improvement with broad spectrum antibiotics. All these cases had responded well to metronidazole . Metronidazole was administered intravenously with the loading dose of 15mg/kg, followed by oral metronidazole 500mg thrice a day for ten days. All the cases showed good clinical response.

Metronidazole have been reported in various studies as the most

effective treatment for the Lophomonas infection worldwide.[18,33,34,39-41]

CONCLUSION:

We consider that the finding of Lophomonas blattarum, a multiflagellated protozoon, under light microscopy, in symptomatic patients, who do not respond to antibiotics, but show satisfactory improvement with antiprotozoal therapy,can be described as bronchopulmonary lophomoniasis. This infection should be recognized as a potentially important, especially in the patients with compromised immunity and risk factors.We would emphasize the need of the development of a technique to culture the organism or the use of molecular methods to resolve the issue regarding the confusion with other structures such as ciliated bronchial cells, and other endocommensals of gut of the termites.

LIMITATION:

Development of molecular techniques would have helped distinguish between ciliated bronchial cells and the protozoa. The findings under electron microscopy would have also been noteworthy.

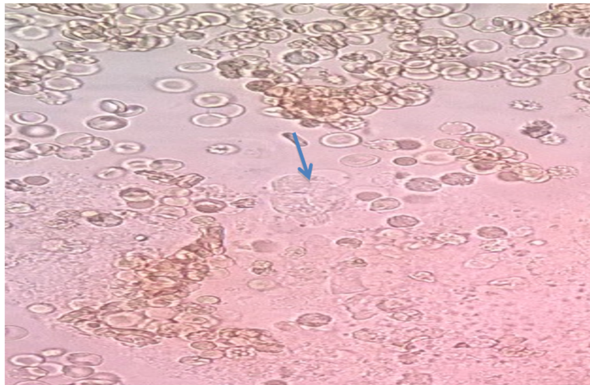

Image 1: *Lophomonasblattarum* in wet mount of BAL fluid (blue arrow)

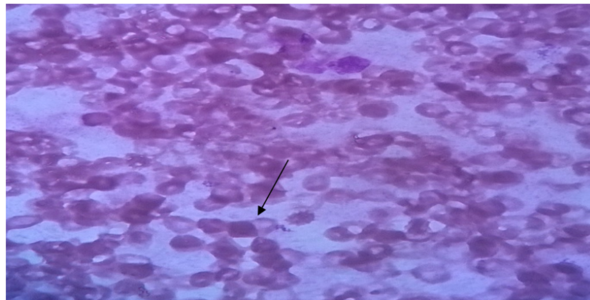

Image 2: Lophomonasblattarum in Giemsa stained smear of BAL fluid (black arrow)

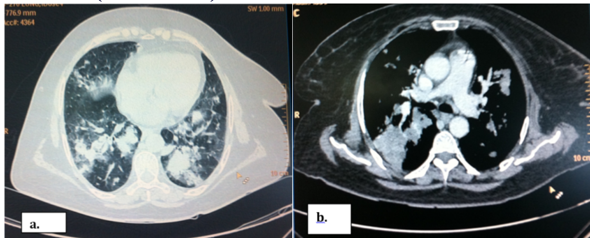

Image 3: CT chest a) Lung window and b) Mediastinal window axial images reveal bilateral lung consolidations

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