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## Case Report

# Differential diagnosis of lophomoniasis in patients with COVID-19 in northern Mexico: a case report

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## ABSTRACT

Pulmonary lophomoniasis is a rare infection produced by a multiflagellated and anaerobic pyriform or oval protozoan belonging to the family of Lophomonadidae. The study aimed learn the differential diagnosis of lophomoniasis in patients with COVID-19 in northern Mexico. Clinical case of a 37-years-old male patient diagnosed with pneumonia, respiratory syndrome, hemoptysis, and fever, which suggested pulmonary tuberculosis. Bronchial lavage was performed, and laboratory tests were requested, an RT-PCR test to search for SARS-CoV-2, which was positive. The results for TB and KOH for fungi were negative. In addition to the protocol, a fresh examination was performed by placing a drop from the sample on a glass slide and observing it with a 10X objective, then 40X searching for clinically structural elements. As a result, multiflagellated cellular elements in the continuous movement were observed that morphologically correspond to the genus *Lophomonas* spp concluding the bacteriological protocol of bronchial secretions should consider fresh examination to search for trophozoites of *Lophomonas* spp. Medical and laboratory personnel are unaware of the protozoa *Lophomonas* spp, since the fresh examination in the analysis protocol is not considered. This paper reports the first case of *Lophomonas* infection in a patient caused by chronic lung disease.

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## Diagnóstico diferencial de lofomaniasis en pacientes con COVID-19 en el norte de México: reporte de un caso

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### RESUMEN

La lofomoniasis pulmonar es una infección rara producida por un protozoo piriforme u ovalado multiflagelado y anaeróbico perteneciente a la familia de los Lophomonadidae. El estudio tuvo como objetivo conocer el diagnóstico diferencial de lofomoniasis en pacientes con COVID-19 en el norte de México. Caso clínico de un paciente masculino de 37 años con diagnóstico de neumonía, síndrome respiratorio, hemoptisis y fiebre, que sugería tuberculosis pulmonar. Se realizó lavado bronquial y se solicitaron pruebas de laboratorio, prueba RT-PCR para búsqueda de SARS-CoV-2, la cual resultó positiva. Los resultados de TB y KOH para hongos fueron negativos. Además del protocolo, se realizó un nuevo examen colocando una gota de la muestra en un portaobjetos de vidrio y observándola con un objetivo de 10X, luego 40X en busca de elementos clínicamente estructurales. Como resultado se observaron elementos celulares multiflagelados en movimiento continuo que morfológicamente corresponden al género *Lophomonas* spp, por lo que el protocolo bacteriológico de secreciones bronquiales debe considerar examen en fresco para búsqueda de trofozoítos de *Lophomonas* spp. El personal médico y de laboratorio desconoce la presencia del protozoo *Lophomonas* spp, ya que en el protocolo de análisis no se considera el examen en fresco. Este artículo reporta el primer caso de infección por *Lophomonas* en un paciente causado por una enfermedad pulmonar crónica.

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## 1. INTRODUCTION

Lophomoniasis is a disease caused by *Lophomonas* spp, a pyriform or oval multiflagellated anaerobic protozoan belonging to the family Lophomonadidae, order: Lophomonadida. They are considered parabasalids phylogenetically, of the same family as Trichomonas, currently, they are known as endocomensals of the digestive tract of some arthropods like termites and cockroaches. They have also been found in bustard birds [1]. These protozoans were found in the intestine of the synanthropic cockroach *Blatta orientalis* (Blattidae) in 1960 [1]. Have been documented Two types of *Lophomonas*, *L. blattarum* and *L. striata* They were considered harmless to humans for decades, but in 1993 the first case of pulmonary lofomoniasis was reported, and since then 163 cases have been identified worldwide [2]. About 95% of infections in China, other ones were documented in Turkey, Peru, India, and Mexico (a pediatric clinical case in 2017) [1]. In patients with coronavirus disease (COVID-19), a potentially fatal hyperinflammatory state called cytokine release syndrome occurs, which is characterized by rapidly worsening multiorgan dysfunction, which is why the use of early

immunosuppressive therapy is frequently used. Pulmonary lofomoniasis is a rare pathology that should be taken into account in immunocompromised patients with severe pneumonia who persist with fever and poor response to treatment, as is the case of patients with COVID-19 [3].

Lophomoniasis is caused by *Lophomonas* spp. A new emerging protozoan commonly affects the human lower respiratory tract [4]. *Lophomonas* infection is an emerging respiratory infection causing parasitic disease. Although it is common in immunocompromised patients, it has also been observed in some immunocompetent cases [5]. After China, Peru has the second place with the more occurrences [6]. Pneumonia is a common acute respiratory infection affecting the alveoli and distal airways; it is a serious health problem associated with high short- and long-term morbidity and mortality in all age groups worldwide [7]. Humans have witnessed three deadly pandemics in the 21st century, all associated with novel coronaviruses: SARS, Middle East respiratory syndrome, and COVID-19. All these viruses are responsible for causing acute respiratory tract infections. These are highly contagious because they have caused high mortality [8]. Multiple drugs used in the treatment of acute respiratory syndrome predispose the patient to infections by opportunistic microorganisms; in

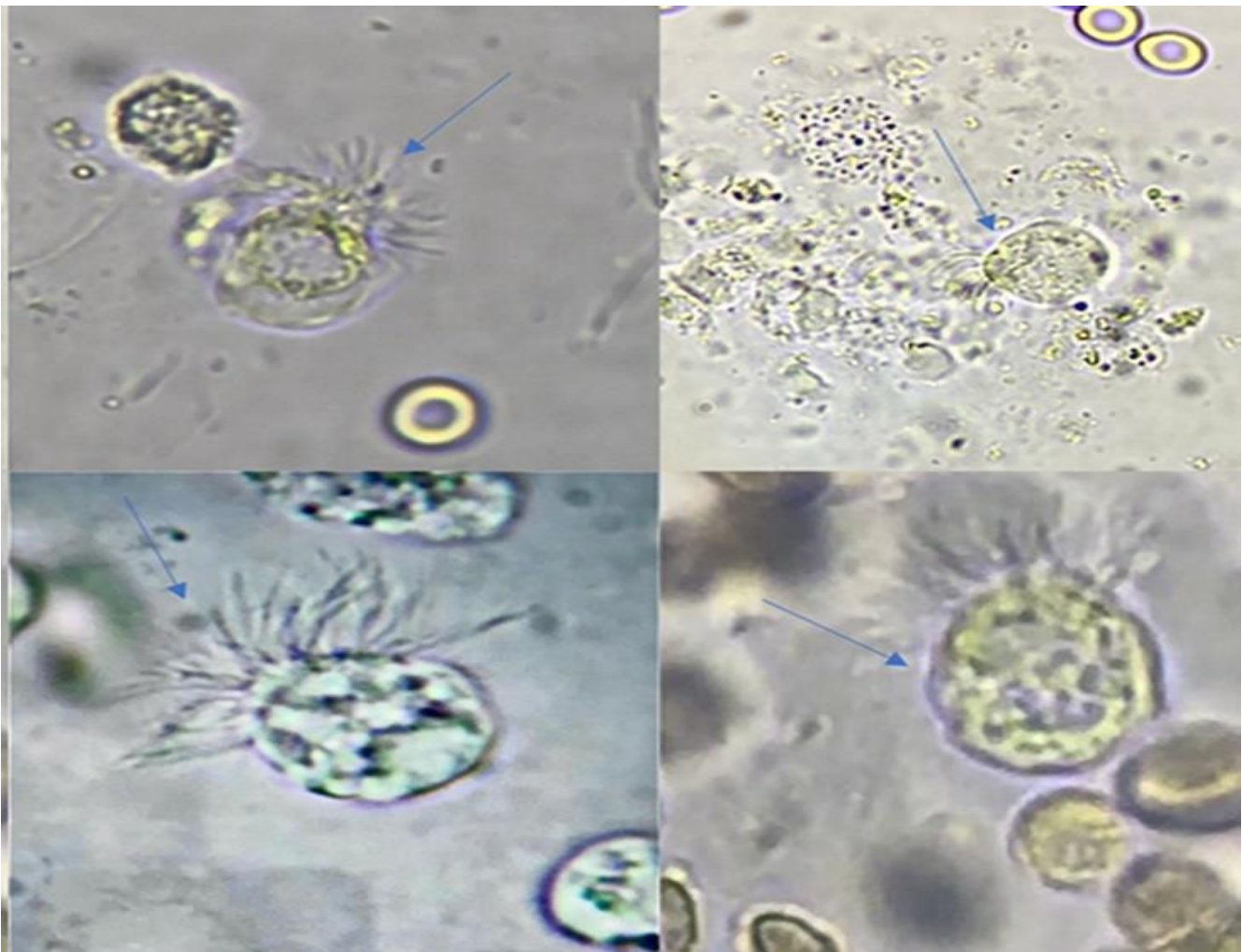
addition, patients with chronic obstructive pulmonary disease often suffer acute exacerbations and community-acquired pneumonia, referred to as non-pneumonic and pneumonic exacerbations of chronic obstructive pulmonary disease, respectively. Deficient host defense mechanisms may play a role in the specificity of the systemic inflammatory response [9]. Predisposition to lephomoniasis is higher in immunosuppressed patients or those with post-transplant infection, particularly those who do not respond to the usual antibiotic regimens [10]. It is necessary received attention to the relationship between *Lophomonas*, a genus of multiflagellate protozoa, and respiratory syndrome pathology. It is also necessary this infection should be recognized as a potentially important emerging field of study within respiratory medicine in addition, methodology must be included for the identification of this protozoan, either by phenotypic and molecular methods. In this study, we aimed to report a case of learn the differential diagnosis of lophomoniasis in patients with Coronavirus disease

(COVID-19) in northern Mexico.

## 2. CASE REPORT

A 37-year-old male patient diagnosed with pneumonia presented with productive cough, hemoptysis, and fever with the evolution of the disease for five months. The imaging result showed the sign of the tree in bud pattern, which is the non-specific tomographic manifestation of the disease of the small peripheral airway that causes dilatation and thickening of the walls of the centrolobulillary bronchioles, which have the lumen occupied by mucus, water, or pus, frequently associated with peribronchiolar inflammation.

The bronchial lavage sample was analyzed in the laboratory with the following results: In peripheral blood samples, laboratory results showed leukocytosis with the prevalence of polymorphonuclear and 12% of eosinophils (Medonic®



**Figure 1:** Trophozoites *Lophomonas* spp in bronchial lavage.

M32-Boule Diagnostics, Sweden), in clinical biochemistry glucose, urea, creatinine, and total protein (VITROS® 350, USA) parameters were normal. In microbiology, the RT-PCR test was performed to determine the presence of SARS-CoV-2, which was positive. Centrifugation smear microscopy (OPTSUM®, USB Digital camera OPT-14mp, Colombia) was accomplished with obtaining a negative result, the endpoint PCR test. For identification of strains of the *M. tuberculosis* complex, amplifying a sequence of 488 bp that includes part of the *murA* gene, the multiple hypervariable regions, V2 and the 16S rRNA gene of the *rrnA* operon, to determine the presence of *M. tuberculosis*, which was negative. The KOH test for fungi was negative. Sample quality was determined using the Murray and Washington criteria guideline establishing acceptable sputum quality for culture (greater than 25 leukocytes/100x field and < 10 squamous epithelial cells/100x). The sample was processed and seeded as quickly as possible on MacConkey agar, Biggy agar, and Casman agar with blood. A fresh examination was performed, the sample was homogenized, 50 µL was added on a slide, covered with a coverslip, and observed under a microscope with a 10X objective and later with a 40X objective for the purposeful search of structural elements of clinical importance. *Klebsiella pneumoniae* and *Streptococcus pneumoniae* were isolated in the growth media, but no fungi were isolated. However, in fresh examinations, multiflagellated cellular elements that morphologically correspond to *Lophomonas* spp were observed, according to the morphology and size of the trophozoites (Figure 1).

The patient presented with a general condition attack with acute respiratory syndrome and was treated with metronidazole 500 mg every 8 hours for three weeks. The physician had a presumptive diagnosis of tuberculosis (TB) due to the clinical conditions presented but had not considered that the patient had COVID-19. Finally, the patient developed pneumonia with pleural effusion and died. Since the study is a case report, there was no need to be approved by the ethics committee. Written consent was obtained from the patient regarding the use of his medical data.

### 3. DISCUSSION

In the clinical case under study, the finding is relevant for the medical field in the specialty of pneumology. The clinical case was associated with pulmonary disease but of unknown etiology, due to the clinical symptomatology such as chronic productive cough (cough with mucus, leukocytes, and epithelial cells), fever, and weight loss, which are

clinical features of TB and chronic pulmonary aspergillosis. It has been reported that TB and chronic pulmonary aspergillosis are progressive and debilitating parenchymal lung diseases with overlapping risk factors, symptomatology, and radiological findings often resulting in misdiagnosis of either [11]. The patient was diagnosed with COVID-19 due to RT-PCR testing for SARS-CoV-2 diagnosis; co-infection of COVID-19, TB and fungi is common. Koupaei *et al.* [12] state that TB patients are more likely to contract COVID-19 infection, furthermore, should TB patients be tested for COVID-19 and vice versa is a controversial issue in the scientific community. The physician had only TB as a diagnosis. However, the result for TB was negative. Our finding was relevant because in the fresh examination, we observed trophozoites of *Lophomonas* spp, which was diagnosed morphologically and by the anatomical site where it was observed, which coincides with the statements of Mokhtarian *et al.* [13] mentioned that lophomoniasis is still a mysterious disease with many unknown epidemiological aspects. In addition, Fernandes *et al.* [14] point out that nowadays; there are alternative analyses for diagnosis of lophomoniasis such as fresh examination with light microscopy or analysis of nucleic acids by PCR. However, some authors consider that false positive results can be obtained in PCR analysis. The patient presented five months of evolution with symptoms, mainly cough, he received multiple antibiotic treatments because the physician considered it was TB, but it only weakened the immune system and made him more vulnerable to other infections. Shields *et al.* [15] outcomes following SARS-CoV-2 infection in individuals with primary immunodeficiency or symptomatic secondary immunodeficiency remain uncertain. The prescription of metronidazole is consistent with that described by Sharifpour *et al.* [16] who prescribed metronidazole (500 mg/TDS; 2 weeks) to treat lophomoniasis. The patient later developed complications such as severe pneumonia four days after hospitalization and died. The clinical case leaves a relevant teaching since lophomoniasis had not been described in our country until today and is related to COVID-19 co-infection. As in other countries, in Mexico, *Lophomonas* spp is not epidemiologically associated with respiratory problems, and the diagnosis of differences between fungus, bacteria, viruses, and parasites is determinant for the correct and timely treatment. This paper reports the first case of *Lophomonas* infection in a patient caused by chronic lung disease. In addition, the observation of moving trophozoites in fresh examination is essential for differential diagnosis.

The protocol for bacteriological analysis (acid-fast bacillus,

Gram stain, and KOH) of bronchial lavage, bronchial brushing, bronchial secretion, or expectoration should include fresh examination of fungal structures (yeasts, hyphae, and mycelia), and parasites, especially trophozoites of *Lophomonas* spp. Lophomoniasis is not known by medical personnel because it is considered a problem only of vectors (cockroaches) unrelated to humans. It is not known in the clinical laboratory because medical requests for microbiological analysis the fresh examination is not considered in the analysis protocol. The fresh examination allows the analyst to find other microorganisms like protozoa of *Lophomonas* spp; it helps the physician establish the correct diagnosis and treatment when pulmonary problems are suspected, mainly mycobacteria and fungi.

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#### 5. CONFLICT OF INTERESTS

The authors have no conflict of interest to declare. The authors declared that this study has received no financial support.

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