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Detection of *Lophomonas* in pericardial effusion sample in a COVID-19 patient with systemic sclerosis: An unusual case report

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Abstract

Systemic sclerosis is a connective tissue disorder that involves the skin and many other organs, such as the heart, skin, and gastrointestinal tract. Cardiac involvement is in the form of pericarditis, pericardial effusion, and pulmonary hypertension. Several complications and super infections post-COVID-19 have been reported, such as fungal, bacterial infections, and *Lophomonas blattarum*. Lophomoniasis is an emerging pulmonary infection that mainly involves the lower respiratory tract. Herein, we present an ectopic *Lophomonas* infection in an unusual location (pericardial effusion) in a COVID-19 patient who had systemic sclerosis.

Keywords

Systemic sclerosis, pericardial effusion, COVID-19, ectopic lophomoniasis

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Introduction

Systemic sclerosis (SSc) or scleroderma is a connective tissue disorder that affects the skin as well as many other organs, including the heart.[1] Scleroderma is derived from the Greek word "scleros," which means "hardened skin," and is a prominent feature of the disease.[2] This disorder is classified by the level of skin involvement and the pattern of internal organ involvement into four subtypes: limited cutaneous SSc, diffuse cutaneous SSc, SSc sine scleroderma, and SSc with overlap syndrome.[3] It can cause a variety of cardiac abnormalities, such as microvascular coronary artery disease, myocardial fibrosis, left ventricular (LV) systolic dysfunction, LV diastolic dysfunction, conduction abnormalities, and pericardial disease (including pericardial effusion).[4]

COVID-19 (coronavirus disease of 2019), a disease with a wide variety of clinical signs, is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. While the majority of COVID-19 patients are asymptomatic or have mild to moderate infection symptoms, high-risk individuals may develop serious infections that necessitate hospitalization and breathing support. Aging, as well as underlying comorbidities including hypertension, cardiovascular disease, and diabetes, have been identified as risk factors for severe diseases.[5] This virus has the potential to cause serious respiratory illness, with a high risk of intensive care unit (ICU) hospitalizations. Owing to the severe damage to lung tissue, cytokine storm, and immune-paralysis caused by viral infection-induced acute respiratory distress syndrome (ARDS), bacterial and fungal infections are comorbidities of this viral pneumonia.[6,7]

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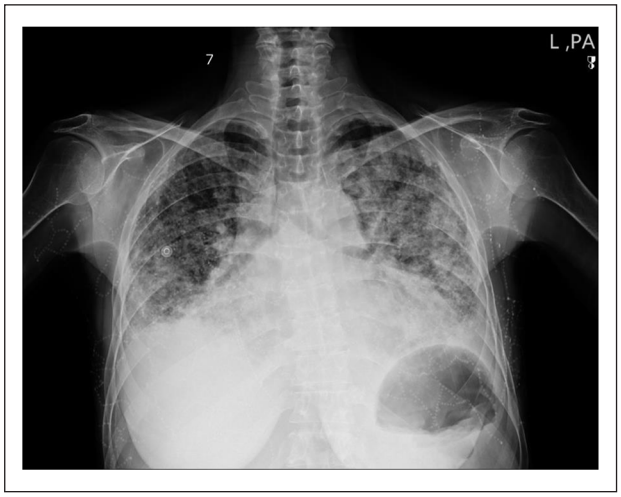

Figure 1. A chest X-ray showing cardiomegaly with widening of carinal angle and bilateral blunting of costophrenic angle, coarse reticular opacities in both lungs predominantly in the left lung.

Lophomoniasis is a chronic respiratory infection that affects both the upper and lower respiratory tracts, resulting in symptoms such as fever, cough, and pneumonia. The main causative agent of lophomoniasis is *L. blattarum*, which is found in the intestines of insects such as cockroaches. Inhaling cyst-containing aerosols mainly infects humans.[8–10] Herein, we report an unusual case of *Lophomonas* infection in a COVID-19 patient in which the parasite was detected in a pericardial effusion sample.

Case

On 3 April 2021, a 44-year-old woman, a known case of scleroderma and lung fibrosis, was referred to the emergency department (ED) of the Heart Center in northern Iran with a complaint of orthopnea and pleuritic chest pain that began a day before. She also complained of weakness, nausea, vertigo, and sweating. At ED triage, they recorded a blood pressure of 188/110 mmHg, a heart rate of 106 beats/min, a respiratory rate of 26 breaths per min, a temperature (T) of 37.8°C, and an oxygen saturation (SpO2) of 84%. Her drug history was mycophenolate mofetil 500 mg twice daily for her lung fibrosis, pantoprazole 40 mg daily and cisapride 10 mg q6h. At the physical examination, she had fine crackles in both lungs, decreased heart sounds, shiny skin, and both ankles were edematous. The rest of the organs had normal examinations. First, we obtained an electrocardiograph (EKG), which demonstrated sinus tachycardia, and low voltage waves. Next, a chest X-ray was requested for the patient (Figure 1), which revealed cardiomegaly with widening of the carinal angle and bilateral blunting of the costophrenic angle, along with, coarse reticular opacities in both lungs mostly in the left lung corresponding to pulmonary fibrosis.

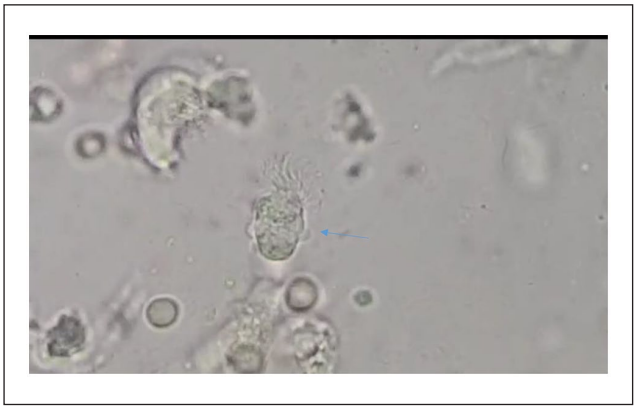

Figure 2. A direct smear of BALF specimen showing the *Lophomonas* trophozoite (arrow head) with tufted and irregular multiple flagella.

Her signs and symptoms and the chest X-ray's involvement led us to suspect community-acquired pneumonia, especially COVID-19 due to the pandemic. Therefore, immediate treatment was started for her as per local guidelines and a COVID-19 real-time reverse transcriptase-polymerase chain reaction (RT-PCR) was performed on the patient, which was positive. The patient was given oxygen through a non-rebreather mask at a rate of 10–15 L/min, prednisolone 0.5 mg/kg/d, remdesivir 200 mg on the first day, followed by 100 mg/d for 5 days, and medications for accompanying symptoms, such as cough, fever, and so on.

Next, because of the EKG findings, cardiomegaly and her symptoms, a cardiologist consultation was requested and recommended a transthoracic echocardiography (TTE). The result was a massive pericardial effusion with fibrotic stricture. Therefore, a pericardiocentesis was done for her, and 200 cc of pericardial fluid was obtained. Next, the sample was sent to a laboratory for pathology and bacteriology investigations, in which *Lophomonas* was detected within a wet direct smear under light microscopy. It was a motile ovoid-shaped protozoa with a granular cytoplasm and tufted flagella (Figure 2). Accordingly, metronidazole 500 mg every 8 h was added to her previous treatment for 2 weeks. Laboratory findings and details are described in Table 1.

After 48 h of her treatment, suddenly her SpO2 fell to 75% and she was immediately intubated. After the second day of intubation, the patient became bradycardia and a cardiac arrest followed. Immediately, advanced cardiac life support (ACLS) as per guidelines was started for her. Unfortunately, after 1 h of cardiopulmonary resuscitation (CPR), she died due to COVID-19 ARDS.

Written informed consent was obtained from the legally authorized representative of the subject, to publish this report in accordance with the journal's patient consent policy. This study was conducted according to the Declaration of Helsinki Principles. Also, CARE guidelines and methodology were followed in this study.

Table 1. Laboratory data results of the patient in the ICU ward.

Lab data parameter	Result	Normal range
Ph[a]	7.42	7.35–7.45
pCO2	53 mmol/L	35–45 mmHg
HCO3	33 mmol/L	22–28 mEq/L
FBS	72 mg/dL	90–110 mg/dL
Triglyceride	116 mg/dL	50–200 mg/dL
Cholesterol total	131 mg/dL	<200 mg/dL
AST	20 U/L	50–40 IU/L
ALT	21 U/L	<45 U/L
ALP	299 U/L	80–306 U/L
Troponin	<0.2 ng/dL	<0.01 IU/L
WBC	25,100 U/l	4000–10000/mm^3
RBC	$3.93*10^6$	4.2–5.4 cells/mcL
HB	9 g/dL	14–18 g/dL
PLT	700,000	145,000–450,000/mm^3
HCT	30	35.5%–44.9%
Neutrophils	86%	55%–70%
Lymphocyte	11%	20%–35%
Monocyte	3%	3%–8%
CRP	71 mg/L	Less than 6 mg/L
ESR	45 mm/h	0–20 mm/h
Urea	17 mg/dL	13–40 mg/dL
Cr	0.46 mg/dL	0.5–1.3 mg/dL
Na	129 mEq/L	135–145 mEq/L
K	4.5 mEq/L	3.5–5.5 mEq/L
Mg	2 mg/dL	1.8–2.5 mg/dL
Pericardial fluid analysis		
Color	Clear yellow	–
Total protein	3 mg/dL	2.8–3.8 mg/dL
LDH	100 U/L	84–168 U/L
Glucose	110 mg/dL	100–150 mg/dL
Acid-fast bacillus	Negative	–
COVID-19 PCR	Negative	–
Gram stain	No organisms seen	–
Cytology	*L. blattarum*	–

ICU: intensive care unit; WBC: white blood cell; RBC: red blood cell; HB: hemoglobin; PLT: platelets; PCR: polymerase chain reaction; FBS: Fasting Blood Sugar; AST: Aspartate Transaminase; ALP: Alkaline Phosphatase; HCT: Haematocrit; CRP: C-reactive protein; ESR: Erythrocyte Sedimentaion Rate; LDH: Lactate dehydrogenase..

[a]Note that PH, PCO2 and HCO3 results were obtained from venous blood gas (VBG), not arterial blood gas (ABG).

Discussion

Despite the fact that SARS-CoV-2 is generally responsible for severe pneumonia and ARDS, COVID-19 is associated with many extrapulmonary consequences, making it a systemic disease.[7] A low percentage of COVID-19 patients develop fungal or bacterial co-infections, compared with the previous influenza pandemic.[11] A study found that COVID-19 patients admitted to the ICU had a higher chance of developing a fungal or bacterial secondary infection (57 % of ICU cases), compared to only 14% in an earlier study.[11,12]

SSc is an immune-mediated disease that has a higher mortality rate than any other rheumatologic disease.[13] Pericardial effusion is one of the complications of SSc, whose pathophysiology remains unclear.[14] By the way, we assumed that our patient's pericardial effusion was due to her underlying disease, but what surprised us was the existence of *Lophomonas* in the pericardial fluid. Pericardial effusion can be caused by a number of infections and non-infection etiologies, but viral infection is more common.[15] Parasitic infections due to protozoa can involve the heart[16] and cause many cardiac complications, such as myocarditis, pericarditis, pericardial effusion, cardiac tamponade, or constrictive pericarditis.[17] There are no data that claim to show that *Lophomonas* is detected in pericardial fluid. We suspected that the source of infection was the lung, but it is not clear how *Lophomonas* was infiltrated and or arrived in the pericardial effusion. As a whole, we recommend considering heart involvement in lophomoniasis patients.

Due to the possibility of increased COVID-19 spreading, clinicians rarely consider direct samples of the infection site via bronchoalveolar lavage (BAL) in COVID-19 patients,

despite its high specificity. Sharifpour et al.[18] detected *Lophomonas* and invasive *Aspergillus* infection coexistence in a post-COVID patient utilizing bronchoscopic exploration. *Lophomonas* is a neglected parasite that has been identified in a few locations but is still unknown to many medical researchers worldwide.[19] Lophomoniasis is endemic in several parts of Iran.[8,20-23] Our patient was admitted from Mazandaran Province, northern Iran, where lophomoniasis is endemic.[8,9] In addition, the *Lophomonas* was recently isolated from cockroaches in the province.[21]

Pulmonary lophomoniasis with different clinical patterns has been reported from deferent parts of the world mainly Iran.[8–10,18,20,23,24] Cough, fever, and shortness of breath, which are all signs of lophomoniasis, are also frequent in other respiratory infections. As a result, identifying and treating this disease might be difficult. Metronidazole is the first drug of choice in the treatment of lophomoniasis.[8]

According to recent research, metronidazole decreases inflammatory cytokines including interleukin (IL)8, IL6, IL1B, tumor necrosis factor (TNF), IL12, and interferon (IFN), as well as C-reactive protein (CRP) and neutrophil count, which were all elevated after COVID-19 infection, according to recent research. Metronidazole has also been shown to increase the number of lymphocytes in the bloodstream.[25] Prescribing this medicine may have improved the patient's response to COVID-19 infection therapy.

Conclusion

To the best of our knowledge, this is the first report of ectopic lophomoniasis in a COVID-19 patient worldwide. Accordingly, extrapulmonary lophomoniasis should be considered in the differential diagnosis. As a whole, this case report and the detection of the parasite in an unusual location (pericardial effusion) could be important for understanding its potential pathophysiological aspects and lead us to new diagnostic and treatment challenges, particularly in COVID-19 co-morbidity.

Author contributions

Z.Z. and M.F. involved in the collecting of sample and data. A.S., M.F., Z.Z., and E.S.B. comprised in the interpretation writing and editing of the manuscript. M.F., M.S., and A.M.T. preparing the draft and final version of the manuscript. All authors reviewed and approved the final version of the manuscript.

Data availability statement

The data are available with the correspondence author and can be achieved on request.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethics approval

Ethical approval to report this case series was obtained from Mazandaran University of Medical Sciences (IR.MAZUMS.REC.1397.2969).

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Informed consent

Written informed consent was obtained from the legally authorized representative of the subject to publish this report in accordance with the journal's patient consent policy

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