INTRODUCTION
Due to corticosteroid therapy, several fungal and protozoal super infections, such as invasive pulmonary aspergillosis and lophomoniasis, post-COVID-19 have been reported. Here, we present a 68-year-old man with history of COVID-19 2 months ago. Monitoring of post-COVID-19 patients with prolonged cough and dyspnea is urgently necessary.

COVID-19, a disease with a wide variety of clinical signs, is caused by SARS-CoV-2 infection. While the majority of COVID-19 patients are asymptomatic or have mild-to-moderate symptoms of infection, high-risk individuals may develop severe illnesses that require hospitalization and support breathing. The effects of being older, as well as underlying comorbidities including hypertension, cardiovascular disease, and diabetes, have been recognized as risk factors for debilitating diseases.1

This infection can cause severe respiratory disease with an important rate of intensive care unit (ICU) admissions. Bacterial and fungal infections are complications of this viral pneumonia due to the severe damage of lung tissue, cytokine storm, and immune-paralysis caused by viral infection-induced acute respiratory distress syndrome (ARDS). Invasive pulmonary aspergillosis (IPA) has been reported in other respiratory viruses such as influenza viruses.2

Lophomonas is a neglected and emerging protozoan that infects the lower (primarily) and upper respiratory tracts of humans. It is commonly found as a commensal agent.
in the hind intestines of cockroaches.\textsuperscript{2,3} Lower and upper respiratory infections caused by \emph{Lophomonas} have been documented in various parts of the world in recent decades, notably in China and Iran. Iran has a reputation for having the largest number of lophomoniasis cases in the world.\textsuperscript{4–9}

Thus, only a few cases of lophomoniasis co-infection with other infectious illnesses have been documented throughout the world. There is some evidence that lophomoniasis co-occurs with HIV and TB.\textsuperscript{2,9,10} Several complications and super infections post-COVID-19 have been reported, such as fungal (mostly IPA) and bacterial infections,\textsuperscript{11} but there is no evidence regarding co-infection of \emph{Lophomonas} and IPA before and during the COVID-19 pandemic worldwide.

## 2 | CASE PRESENTATION

On December 22, 2020, an old man, 68 years old with history of diabetes mellitus (DM), hypertension (HTN), and coronary artery bypass graft (CABG) with symptoms of weakness and lethargy, dyspnea, fever, chills, and cough, was referred to Imam Khomeini hospital in Mazandaran Province, northern Iran. On examination, vital signs of the patient included RR: 28 breaths/min, BP: 140/95 mmHg, PR: 131 beats/min, Spo2: 88%, T: 37.5°C. With suspicion of COVID-19 pneumonia, a high resolution computed (HRCT) scan and real-time reverse transcriptase-polymerase chain reaction (RT-PCR) were performed on the patient to rule out COVID-19 infection. According to the HRCT and RT-PCR evidence, COVID-19 pneumonia infection was confirmed. Next, the patient was hospitalized in our infectious ward and, following severe dyspnea and loss of saturation, he was transferred to the ICU and intubated. Finally, after 15 days of hospitalization in the ICU and the current drug treatment, the patient was discharged with reduced symptoms and partial recovery.

Two months later, on February 20, 2021, the patient was referred to Imam Khomeini Hospital with symptoms of weakness and lethargy, weight loss (10–15 kg in 2 months), nausea, dyspnea, and productive coughing during the past week. The history of medications includes Losamix 25 mg, ASA 80 mg, Novomix 30, Metoral 50 mg, Atrovastatin 20 mg and Apixaban 2.5 mg. The results of laboratory tests on admission are shown (Table 1).

| Laboratory parameter | At admission | Reference range |
|-----------------------|-------------|----------------|
| Hemoglobin            | 11.3 g/dl   | 12–16          |
| White blood cells     | 19,200/mm³ | 4.5–11         |
| Platelet              | 391,000/mm³| 130–400        |
| Lymph                 | 4.9%        | 20–50          |
| Poly                  | 91%         | 37–72          |
| ESR                   | 86 mm/h     | 0–22           |
| NA                    | 133 mEq/L   | 135–145        |
| K                     | 4.8 mEq/L   | 3.5–5          |
| ALT                   | 54 IU/L     | 10–40          |
| AST                   | 24 IU/L     | 10–40          |
| ALP                   | 394 IU/L    | 20–140         |
| Bilirubin Total       | 0.7 mg/dl   | 0.1–1.2        |
| Bilirubin Direct      | 0.3 mg/dl   | <0.3           |
| LDH                   | U/L         | 100–500        |
| PT                    | 18 s        | 11–13          |
| PTT                   | 35 s        | 25–35          |
| INR                   | 1.2         | 1.1            |
| BUN                   | 68 mg/dl    | 8–20           |
| Creatinine            | 1.7 mg/dl   | 0.5–1          |

The patient was nominated for a bronchoscopy due to the recurrence of respiratory symptoms and a cough with sputum. On bronchoscopy, a black purulent discharge was seen up to the end of the trachea. Two BAL samples separately were subjected to the Iranian national registry center for lophomoniasis (INRCL), and tuberculosis reference laboratory, Mazandaran University of Medical Sciences, to rule out (R/O) lophomoniasis, and tuberculosis (smear and PCR) respectively. Furthermore, a serum sample of the patient was tested in the mycological laboratory for diagnosis of IPA using galactomannan (GM) enzyme immunoassay (EIA) test, as an antigen-based assay.

The obtained laboratory findings were as follows: in a wet smear prepared from the BAL sample, the live and motile protozoan parasite \emph{Lophomonas} was observed under a light microscope. The infection was also confirmed by a genus-specific small subunit ribosomal RNA (SSU rRNA) PCR.\textsuperscript{3} Additionally, GM antigenemia was detected in the patient serum and, consequently, IPA was confirmed. The BAL sample for BK (Bacillus of Koch) was also negative for both smear and PCR.

Based on the above-mentioned radiological and laboratory evidence, the patient was finally treated with intravenous amphotericin B (50 mg/day; 10 days) and oral...
voriconazole (200 mg/BD; 14 days) to treat IPA as well as metronidazole (500 mg/TDS; 2 weeks) to treat lophomoni-
asis. He was discharged in a good general condition from
the hospital. This research was carried out in accordance
with the principles outlined in the Helsinki Declaration.
Also, CARE guidelines and methodology were followed in
this study.

3 | DISCUSSION

Even though SARS-CoV-2 is primarily responsible for
severe pneumonia and ARDS, COVID-19 is associated
with a wide variety of extrapulmonary complications,
and, hence, it can be considered a systemic disease. 11 A
small percentage of COVID-19 patients have fungal or
bacterial co-infections, which are reportedly lower than in
the previous influenza pandemic. 12 A study showed that
among COVID-19 patients, those who were admitted to
the intensive care unit (ICU) had a higher probability (57% of
ICU cases) of acquiring a fungal or bacterial secondary
infection, which was higher than in an earlier study (only
14%). 12,13

All studies of COVID-19 fungal infections (Aspergillus) reported their occurrence during the
COVID-19 infection, mostly 14 days after the appear-
ance of COVID-19 symptoms. 12 The case in the current
study was a 68-year-old patient who was previously diag-
nosed with COVID-19 for a period of 2 months; after a
few weeks of his recovery, the patient developed weak-
ness, nausea, lethargy, weight loss, shortness of breath,
and productive coughing.

COVID-19-associated pulmonary aspergillosis
(CAPA) is difficult to diagnose since harmless replace-
ment of the airways by Aspergillus can spread and cause
pulmonary parenchymal injury when immunity is com-
promised. Patients with CAPA show more frequent pos-
tive serum Aspergillus GM EIA results when the fungal
infection is invasive beyond the airways into the blood.
In immunocompromised patients, IPA is a fatal oppor-
tunistic infection. As a result, early diagnosis of IPA is
critical for successful therapy, and Aspergillus GM is the
only non-invasive, reliable diagnostic test to monitor the
IPA. 12,13

Despite its high specificity, physicians seldom con-
sider direct sampling of the infection site through BAL in
COVID-19 patients due to the risk of increased COVID-19
transmission. In our patient, diagnostic bronchoscopy
was used to further investigation, and Lophomonas and
Aspergillus infections were detected. Lophomonas is a
neglected parasite reported in a few countries which still
remains unknown to many clinicians and laboratory
specialists. 14 In some parts of Iran, particularly northern
and eastern Iran, lophomoniases is endemic. 3,4,6,9 Our pa-
tient was from the Mazandaran Province, northern Iran,
where lophomoniases is relatively common. Furthermore,
the L. blattarum pathogen was recently isolated from the
cockroaches in the province. 3

Not only is this disease seen in immunocompromised
patients in other countries, 15 but it has also been seen in
Iran. 4-9 The symptoms of lophomoniases, such as cough,
fever, and shortness of breath, are common in
other respiratory infections. As a result, diagnosing and
treating this infection are challenging. For the treatment
of lophomoniases, metronidazole is the first line of ther-
apy. Recent studies have revealed that metronidazole
reduces the levels of inflammatory factors, such as IL8,
IL6, IL1B, TNFα, IL12, and IFNγ, as well as the levels of
CRP and neutrophil count, which were increased
during COVID-19 infection. Additionally, metronida-
azole has the potential to increase the number of circula-
tory lymphocytes. 15 Prescribing this drug, in addition to
eliminating the Lophomonas infection, may have accel-
erated the patient’s response to treatment for COVID-19
infection.

According to several studies, L. blattarum is consid-
ered an opportunistic infection in patients with kidney
and liver allograft transplantation, under corticoste-
roid therapy, HIV infection, and tuberculosis. 2 SARS-
CoV-2 infection impairs the immune system, making
individuals more susceptible to other infections and re-
activating latent infections. 16 Patients with chronic pul-
monary illness who have underlying lung diseases are
at risk of acquiring more severe instances of COVID-19,
according to a meta-analysis of research. Several problems occur from co-infection in a pregnant woman with COVID-19, which may be due to complications of COVID-19 itself that are caused by another infection. All infections may intensify each other's complications or drug reactions between medications used to treat certain infections. The *Lophomonas* parasite appears to be involved in the severity of the COVID-19 disease and can be considered as a risk factor. Hence, managing and diagnosing co-infections are crucial in clinical practice.

4 | CONCLUSION

Due to long corticosteroid therapy in patients with COVID-19, post-COVID-19 monitoring of them in the case of symptoms such as cough, shortness of breath and weight loss is urgently necessary. We recommended that diagnostic bronchoscopy, HRCT, and laboratory findings should be worked up for differential diagnosis to R/O IPA and lophomoniasis during COVID-19 pandemic.

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Declared none.

CONFLICTS OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

AS involved in the interpretation and collecting of data and editing of the manuscript. ZZ and ESB involved in writing, editing, and preparing the final version of the manuscript. MF and MN is involved in critically revising the whole manuscript. MS is responsible for collecting data and submitting the manuscript. All authors reviewed the paper and approved the final version of the manuscript.

ETHICAL APPROVAL AND CONSENT TO PARTICIPATE

This research was reviewed and approved by the research ethics committee of Mazandaran University of Medical Sciences (IR.MAZUMS.REC.1397.2969). Written informed consent was achieved from the patient to include the clinical details.

CONSENT

Informed consent for publication of this case report was taken verbally from the patient.

DATA AVAILABILITY STATEMENT

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

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