

# Strongyloides Hyperinfection Syndrome Following Corticosteroid Therapy in a Patient with COVID-19 infection: A Case Report

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## ABSTRACT

*Strongyloides stercoralis* (*S. stercoralis*) is a helminth, which infects humans widely in tropical and subtropical countries. This parasitic infestation usually does not produce symptoms in humans; however, severe and life-threatening forms of this infection can occur in immunocompromised individuals. Patients with Coronavirus disease 2019 (COVID-19) with concurrent immunosuppressive therapy are at risk of developing *Strongyloides* hyperinfection syndrome (SHS). We present a 70-year-old male with a history of high-dose dexamethasone therapy due to severe COVID-19 who was referred to our hospital with chest discomfort, nausea, and anorexia. Histological assessment of the gastric and duodenal mucosae revealed numerous eggs and filariform larvae of *S. stercoralis* indicative of SHS. Ivermectin and albendazole were administered to the patient. Following the treatment, the patient's symptoms improved. Clinicians must be aware of the risk of SHS, especially in *S. stercoralis* endemic countries before and during corticosteroid therapy for COVID-19 because early diagnosis and appropriate treatment can significantly reduce mortality in these patients.

**Keywords:** COVID-19, Immunosuppression, Steroids, *Strongyloides stercoralis*

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## 1 Introduction

Coronavirus disease 19 (COVID-19) is a highly contagious pathogenic viral infection caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). COVID-19 has caused a global pandemic that led to a dramatic loss of human lives worldwide (1).

Administration of dexamethasone for management of COVID-19 has gained worldwide interest, particularly given the recent COVID-19 Treatment Panel guidelines released by the National Institutes of Health that recommends corticosteroid therapy for COVID-19 patients (2).

Dexamethasone reduces mortality in hospitalized patients with moderate and severe COVID-19 (3). Although clinicians are familiar with the most common adverse effects of dexamethasone usage, they may be

less familiar with *Strongyloides* hyperinfection or dissemination syndrome, which is less common, potentially severe, but preventable (2).

*Strongyloides stercoralis* (*S.stercoralis*) is a soil-transmitted helminth, widely distributed in tropical and subtropical countries, and is estimated to infect about 30 to 100 million people worldwide (4). According to a systematic review and meta-analysis published on July 23, 2021, the prevalence of *S. stercoralis* in immunocompetent and immunocompromised individuals was 2% and 4%, respectively, in Iran (5). Strongyloidiasis infection is often asymptomatic in immunocompetent adults but may present with mild gastrointestinal or respiratory symptoms or with larva currens, a rapidly moving pruritic linear skin

eruption. Eosinophilia and positive serology are seen in about 77% and 81% of patients with Strongyloidiasis infection. However, microscopy and culture assessments are frequently negative in patients with asymptomatic infection. Severe and life-threatening forms of this infection can occur in some patients, especially in immunocompromised individuals (4).

Strongyloidiasis hyperinfection syndrome (SHS) is defined as an acceleration in the parasite life cycle, which leads to excessive reproduction rates within the usual reproductive sites of the worm (skin, guts, and lungs). SHS is associated with an increased number of larvae in stool and/or sputum, along with clinical manifestations in the respiratory and gastrointestinal systems as well as the peritoneum. Disseminated Strongyloidiasis is a severe infection that results from massive dissemination of the parasite to other body organs, including the liver, heart, brain, and the urinary tract, where the parasite does not usually reach and colonize (6).

The mortality rate in untreated SHS is reportedly 100%, while treatment with ivermectin may reduce mortality to 47%. Fatal SHS has been reported following short courses of low-dose glucocorticoid treatment and a single high dose of dexamethasone (4).

COVID-19 patients with undiagnosed Strongyloidiasis who undergo immunosuppression are at risk of developing SHS (7).

## 2. Case Presentation

A 70-year-old man was admitted to the emergency ward of the Ayatollah Rouhani Hospital, Babol, Iran,

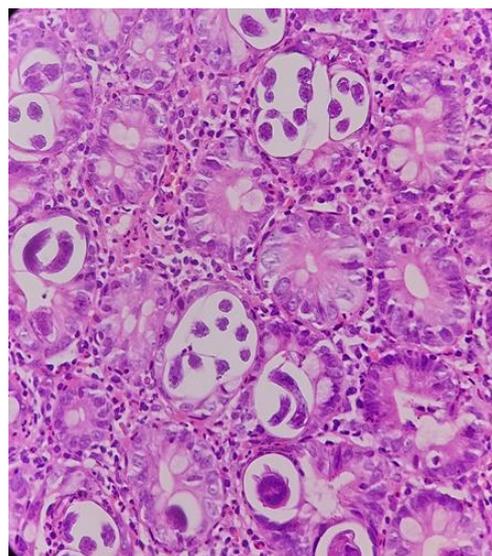
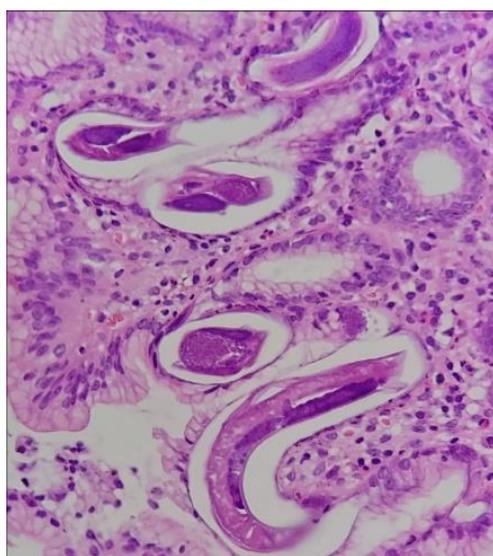
on September 1, 2020, with a history of chest discomfort, nausea, and loss of appetite for 10 days.

He had a history of mitral valve replacement and atrial fibrillation (AF) 13 years prior to his referral; and heart failure for 3 years. He was hospitalized due to severe COVID-19 about three weeks before the admission mentioned above, where he received 6 mg/day dexamethasone intravenously for 10 days. His vital signs were stable on admission, and oxygen saturation was 96% without supplemental oxygen. His physical examination was unremarkable except for AF arrhythmia.

Laboratory findings were as follows: white blood cell count (WBC): 17,600/ $\mu$ L (absolute neutrophil count: 7568/ $\mu$ L, absolute lymphocyte count: 2464/ $\mu$ L and absolute eosinophil count (EAC): 7040/ $\mu$ L), high sensitive C-reactive protein (h-CRP): 1 mg/L, ESR: 20 mm/h. Troponin I and CK-MB were negative. An electrocardiogram (ECG) showed AF rhythm with no ST-T wave changes.

After consultation with a gastroenterologist, a gastroduodenoscopy was performed. Gastroduodenoscopy revealed slight erythema in the gastric antrum, inflammation and few erosions in the distal part of the duodenum bulb, and a notable inflammation in D2. Multiple biopsies were taken from the gastric antrum and duodenal mucosae and sent for histopathologic examination.

Histopathologic examination of the biopsies showed numerous eggs and filariform larvae of *S. stercoralis* in the gastric and duodenal mucosae with increased eosinophilic infiltration in lamina propria (Figures 1).



**Figure 1.** A. H & E slides (400x) of gastric antral mucosa show many larvae of *S. stercoralis*. B. H & E slides (400X) of duodenal mucosa show a large number of larvae of *S. stercoralis*

These findings confirmed the diagnosis of SHS syndrome. Therefore, 200 µg/kg ivermectin was administered to the patient for two days. After 2 weeks, the patient's symptoms did not change, and the WBC: 10640/µL with EAC of 4117/µL were reported in the laboratory evaluation. Therefore, ivermectin was administered at a dose of 200 µg/kg for 5 days, accompanied by albendazole at a dose of 400 mg every 12 hours for 10 days.

Serial EAC revealed a decreasing trend in eosinophil count. The patient's symptoms, including chest discomfort, nausea, and anorexia, also disappeared.

#### Follow-up and Outcomes:

Currently, after about eight months, the patient is in good general condition without any complaints or adverse events.

### 3. Discussion

*Strongyloides* infection is common in tropical and subtropical regions and in passengers, migrants, and prisoners of war who have spent time in these areas. Strongyloidiasis is mainly an asymptomatic or mildly symptomatic disease (7). However, in the case of immunosuppression, strongyloidiasis can cause hyperinfection syndrome or disseminated infection with a mortality rate of 70 to 100% (9).

Asymptomatic *Strongyloides* infection in patients undergoing immunosuppression with dexamethasone should be considered to avoid precipitating SHS.

Clinical observational studies described improved clinical symptoms and oxygenation after steroid administration in patients with severe COVID-19 (10, 11, 12). We found two published case reports of SHS in COVID-19 patients who became immune-suppressed due to dexamethasone and tocilizumab administration.

For the first time, Marchese *et al.* reported a case of a 59-year-old Italian patient treated with high dose intravenous dexamethasone and two intravenous doses of tocilizumab for bilateral interstitial pneumonia associated with SARS-CoV-2 infection who developed itching, abdominal pain, and an increased eosinophil count. Stool examination confirmed the presence of *S. stercoralis* larvae. The patient was

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treated with a 4-day course of ivermectin that resulted in full recovery (13).

Furthermore, Lier *et al.*, on October 2020, reported a case of a 68-year-old man with COVID-19 infection who developed disseminated strongyloidiasis following treatment with high-dose corticosteroids and tocilizumab. The authors suggested *Strongyloides* infection be screened in individuals with COVID-19 who come from *S. stercoralis* endemic regions before initiating immunosuppressive therapy (14).

In this case presentation, we reported a 70-year-old man with SHS following a 10-day treatment with intravenous dexamethasone for severe COVID-19 who presented with a significantly increased EAC on admission.

In this context, the risk assessment should be performed for Strongyloidiasis in patients who live or have visited areas where the organism is endemic before and during corticosteroid therapy for COVID-19, and Strongyloidiasis should be considered in cases of unexplained hypereosinophilia.

### 4. Conclusion

Early diagnosis and appropriate treatment of SHS significantly reduce the mortality rate in SHS. Clinicians should be aware of the risk of SHS syndrome in COVID-19 patients undergoing corticosteroid therapy. Furthermore, unexplained hypereosinophilia in immunosuppressed patients should be an alarming sign of SHS, especially in *S. stercoralis* endemic areas.

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### Conflict of Interest

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