Diagnosis of latent strongyloidiasis following Corticosteroid Therapy in a Patient with COVID-19 infection

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Abstract

Strongyloidiasis, classified as a neglected tropical disease (NTD), is predominantly prevalent in tropical and subtropical areas, impacting an estimated 100-370 million individuals globally. The northern and southern provinces of Iran are recognized as endemic areas for this disease, characterized by environmental conditions such as optimal temperature and humidity conducive to the survival of the causative agent. Although this disease commonly presents no symptoms, individuals with compromised immune systems or those undergoing corticosteroid treatment face an elevated risk of developing hyperinfection syndrome, a serious complication with potentially fatal outcomes. In the case of immunocompromised patients, especially those receiving corticosteroid therapy, the timely diagnosis of strongyloidiasis is imperative as the infection can lead to life-threatening outcomes. This study reports a case of latent strongyloidiasis diagnosis using a serological method. A 68-year-old woman, originally from Guilan Province, living in Tehran Province, with a history of asthma for over a decade, was hospitalized and received

corticosteroid treatment for COVID-19. She exhibited symptoms such as shortness of breath, constipation, skin itching, and abdominal bloating. Upon referral to the Diagnostic Laboratory of Strongyloidiasis at the School of Public Health, Tehran University of Medical Sciences, the patient tested positive for Strongyloides stercoralis using an enzyme-linked immunosorbent assay (ELISA) kit (Novalisa, NovaTec, Germany). The infection was successfully treated with anthelmintic drugs. It is crucial to consider strongyloidiasis in patients with a history of residing in endemic areas or immigration, and testing should be conducted before initiating immunosuppressive therapy. The ELISA method is a rapid and effective diagnostic tool for detecting S. stercoralis in suspected patients, particularly before corticosteroid treatment.**Keywords**: Diagnosis, Strongyloidiasis, COVID-19, Corticosteroid, ELISA.

Introduction

Strongyloidiasis, a neglected disease caused by *Strongyloides stercoralis* contamination, poses a significant public health concern globally (1). This parasitic infection predominantly prevails in tropical and subtropical regions, impacting approximately 370 million individuals worldwide (1–3). The nematode thrives in habitats with ideal temperature and humidity levels that promote its survival, and it is endemic to the northern and southern provinces of Iran (4).

Female *S. stercoralis* demonstrate impressive reproductive abilities with an intricate life cycle that includes parasitic and free-living stages, facilitating long-term infection of the hosts (2). Notably, immunocompromised individuals or those undergoing corticosteroid therapy are at heightened risk of developing hyperinfection syndrome, a severe complication with potentially fatal outcomes (5, 6).

Traditional laboratory diagnosis of strongyloidiasis relies on parasitological techniques, such as microscopic examination for larval identification in stool samples (3). These methods demand highly skilled personnel and are time-consuming. In contrast, serological tests have found utility in epidemiological studies and screenings, offering a viable alternative for rapid diagnosis (7).

In recent years, advancements in molecular diagnostic approaches have emerged as promising tools for enhancing sensitivity in detecting *S. stercoralis* infection. These molecular methods, albeit cost-prohibitive for routine clinical practice, exhibit superior accuracy, particularly in research settings (8).

The increasing prevalence of immune-suppressing conditions emphasizes the critical importance of enhanced vigilance against Strongyloides infections in different regions of Iran (9, 10). This study showcases a specific case, elucidating the diagnosis and management of strongyloidiasis.

Case presentation

The 68-year-old female patient, originally from Guilan province but now residing in Tehran with frequent visits back to her hometown, presented a complex medical history. She had been managing asthma and diabetes for a decade, relying on insulin glargine (Lantus; 32 units nightly), NovoRapid insulin (8 units in the morning and 10 units at night) for diabetes, and salbutamol spray for asthma-induced dyspnea. She was hospitalized due to acute respiratory distress syndrome (ARDS), and a subsequent PCR test confirmed her COVID-19 diagnosis. Given pulmonary complications, dexamethasone was administered alongside antiviral therapy before her discharge following a week-long hospital stay.

Several weeks later, she experienced gastrointestinal disturbances, exacerbated dyspnea, and intense pruritus, prompting a medical evaluation based on her physician's guidance.

Comprehensive laboratory investigations ensued, revealing abnormal findings: FBS: 173 mg/dl, TG: 186 mg/dl, CHOL: 130 mg/dl, ESR: 65 (per 1 h), RBC: 3.99 (Cell/µl), Hb: 11.6 g/dl, Hct: 35.4%, WBC: 9000 (x 109/L), and EOS: 8%.

In light of these findings, the healthcare provider made a referral to the Strongyloidiasis Laboratory at Tehran University of Medical Sciences for additional specialized diagnostic testing. Strongyloidiasis diagnosis was confirmed utilizing an enzyme-linked immunosorbent assay (ELISA) diagnostic kit (Novalisa, NovaTec, Germany), boasting an impressive 89.47% sensitivity and 94.12% specificity. The normal range interpretation guidelines are as follows:

- *Results > 11 NTU: Indicates a positive serology result*
- *Results ranging from 9 to 11 NTU: Considered doubtful*
- *Results < 9 NTU: Indicates a negative outcome*

The initial serological test on the patient yielded a titration of 85.3 NTU on the first day. Stool samples were examined through direct microscopic evaluation, formalin-ether concentration technique, and culture-based methodologies on agar plates. Following subsequent culturing procedures, *S. stercoralis* larvae were identified after a two-day incubation period. Figure 1 shows parasitological observations from a 2-day stool culture of the individual affected by *S. stercoralis* infection. It showcases the second-stage rhabditiform larva of *S. stercoralis*, with a notably prominent genital primordium (Gp). Upon consulting her healthcare provider, the patient received Ivermectin therapy, consisting of three on-day, one with half-hour intervals, and four doses on a subsequent day following a similar dosing schedule.

Fig 1. The rhabditiform larva of *S. stercoralis* was acquired from a rinsed agar plate culture and treated with Lactophenol stain for observation. The scale bar represents 20 µm.

Discussion

Strongyloidiasis is a neglected soil-transmitted helminth characterized by a distinctive life cycle (1, 2) and poses a risk of mortality in specific patients. In Iran, the northern regions, notably Mazandaran and Guilan provinces along the southern coast of the Caspian Sea, exhibit a subtropical humid climate and are endemic areas for strongyloidosis in the country (11). The case under consideration had a history of frequent travel to Guilan province.

Furthermore, the patient had a background of corticosteroid therapy during a bout of COVID-19. There have been numerous documented cases of hyper infection syndrome and disseminated strongyloidosis associated with various underlying conditions (6, 9–11). Notably, corticosteroids showed a correlation with the development of these manifestations (6, 12), due to their acute suppression of eosinophilia and lymphocyte activation. Corticosteroid can directly impact *S.*

stercoralis by hastening the transformation of rhabditiform larvae into invasive filariform larvae, leading to dissemination in all organs (13).

Studies have indicated a positive correlation between strongyloidiasis and certain comorbidities such as diabetes and HTLV1 (7, 14). The patient in this study had a history of diabetes and had been on insulin therapy for over a decade.

Eosinophilia is frequently observed in the clinical manifestation of *S. stercoralis* infection in both asymptomatic and symptomatic cases, indicating the predominant rationale for strongyloidiasis suspicion (11). Our patient also exhibited 8% eosinophilia.

Given the prevalence of hyperinfection syndromes and disseminated strongyloidiasis in recent years in Iran and globally (6, 9, 10), it is crucial to incorporate rapid and highly sensitive diagnostic techniques in medical laboratories for the timely detection of this disease. In this study, serological methods utilizing the ELISA technique are proposed as an effective initial screening tool for patients, which can be easily implemented in all medical diagnostic facilities. Considering strongyloidiasis should be recommended for patients with a travel history to endemic regions and symptoms before starting corticosteroid therapy.

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Ethics

The manuscript complies with the ethical recommendations of the Declaration of Helsinki of the World Medical Association (WMA).

Authors' contributions

E.D: Investigation, manuscript writing. E.B.K: study design, critically revised the manuscript. R.D: contributed to data collection and provided the materials. M.A.S: contributed to data collection and provided the materials. Z.F.K: supervised the project, and edited the manuscript.

Conflict of Interest

The authors declare no conflict of interest.

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Availability of data and materials

All data generated are included in the current article.

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