

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 regions, 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 hyper_infection 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. The present study reports a case of latent strongyloidiasis diagnosis using a serological method. A 68-year-old female patient, originally from Guilan Province, residing in Tehran Province, with a medical history of asthma spanning over a decade, was admitted to the hospital and prescribed corticosteroid treatment for severe acute respiratory syndrome caused by the novel coronavirus (SARS-CoV-2). The patient exhibited symptoms including shortness of breath, constipation, skin itching and abdominal bloating. Following a referral to the Diagnostic Laboratory of Strongyloidiasis at the School of Public Health, Tehran University of Medical Sciences, the patient was found to be 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 imperative to consider strongyloidiasis in patients with a history of residing in endemic areas or immigration, and testing should be conducted before the initiation of immunosuppressive therapy. The ELISA method is a rapid and effective diagnostic tool for detecting *S. stercoralis* in suspected patients, particularly prior to corticosteroid treatment.

Keywords: Diagnosis, Strongyloidiasis, COVID-19, Corticosteroid, ELISA.

1. Introduction

Strongyloidiasis, a neglected disease caused by *Strongyloides stercoralis* contamination, poses a significant public health concern on a global scale (1). This parasitic infection is predominantly prevalent in tropical and subtropical regions, impacting approximately 370 million individuals worldwide (1-3). The nematode under consideration flourishes in habitats where temperature and humidity levels are optimal for its survival. It is endemic to the northern and southern provinces of Iran (4). Female *S. stercoralis* exhibit remarkable reproductive capabilities, characterized by a complex life cycle encompassing parasitic and free-living stages, thereby enabling prolonged infection of their hosts (2). It is noteworthy that individuals with compromised immune systems, or those undergoing corticosteroid therapy, are at elevated risk of developing hyperinfection syndrome, a severe complication with potentially fatal outcomes (5, 6). Conventional diagnostic methods for strongyloidiasis entail the use of parasitological techniques, including microscopic examination of stool samples to identify the presence of larval forms (3). The implementation of these methodologies necessitates the expertise of personnel with a high level of specialization, whilst also requiring a considerable investment of time. Conversely, serological tests have been utilised in epidemiological studies and screenings, providing a viable alternative for expeditious diagnosis (7). In recent years, molecular diagnostic approaches have emerged as a promising tool for enhancing the sensitivity of detecting *S. stercoralis* infection. Whilst the financial burden of these molecular methods may be prohibitive for routine clinical practice, they have been shown to 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 provides a detailed case example, offering valuable insights into the diagnosis and management of strongyloidiasis.

2. Case Presentation

The 68-year-old female patient, who comes from Guilan province but currently resides in Tehran with frequent visits to her hometown, has a complex medical history. For ten years, she had been managing asthma and diabetes, 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. The patient was admitted to the hospital with a diagnosis of acute respiratory distress syndrome (ARDS),

and a subsequent polymerase chain reaction (PCR) test confirmed the presence of the novel coronavirus (SARS-CoV-2) infection. Given the presence of pulmonary complications, dexamethasone was administered in conjunction with antiviral therapy prior to her discharge following a week-long hospital stay. After several weeks had elapsed, the patient began to manifest symptoms including gastrointestinal disturbances, exacerbated dyspnea, and intense pruritus. These symptoms prompted a medical evaluation based on the guidance of her physician. Subsequent comprehensive laboratory investigations yielded abnormal findings. The patient's FBS level was 173 mg/dl, TG level was 186 mg/dl, CHOL level was 130 mg/dl, ESR level was 65 (per 1 h), and RBC level was The patient's complete blood count (CBC) revealed a hemoglobin (Hb) level of 11.6 grams per deciliter (g/dL), with a hematocrit (Hct) level of 35.4% and a white blood cell (WBC) count of 9,000 cells per microliter ($\times 10^9/L$). Additionally, the Erythrocyte Sedimentation Rate (ESR) was determined, providing further diagnostic insights. 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. The diagnosis of strongyloidiasis was confirmed through the utilization of an enzyme-linked immunosorbent assay (ELISA) diagnostic kit (Novalisa, NovaTec, Germany), which exhibited an impressive 89.47% sensitivity and 94.12% specificity. The following guidelines have been established to facilitate the interpretation of normal ranges:

- 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 evaluation of the patient yielded a titer of 85.3 NTU on the initial day. Stool samples were examined through direct microscopic evaluation, formalin-ether concentration technique, and culture-based methodologies on agar plates. Following the implementation of subsequent culturing procedures, *S. stercoralis* larvae were identified after a two-day incubation period. As illustrated in Figure 1, parasitological observations from a 2-day stool culture of an individual affected by *S. stercoralis* infection are presented. It displays the second-stage rhabditiform larva of *S. stercoralis*, with a genital primordium (Gp) that is notably prominent. Following a consultation with her healthcare provider, the patient was administered Ivermectin therapy, comprising three doses on the same day, with the first dose administered at half-hour intervals, and four subsequent



Figure 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 .

doses on the following day, adhering to a comparable dosing schedule.

4. Discussion

Strongyloidiasis, a neglected soil-transmitted helminth, is distinguished by a distinctive life cycle (1, 2) and poses a risk of mortality in specific patients. In Iran, the northern regions, notably Mazandaran and Gilan 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 patient under consideration had a documented history of frequent travel to Guilan province. Furthermore, the patient had a background of corticosteroid therapy during a bout of severe acute respiratory syndrome (SARS-CoV-2). There have been numerous documented cases of hyperinfection syndrome and disseminated strongyloidiasis associated with various underlying conditions (6, 9, 11). It is noteworthy that corticosteroids have been observed to correlate with the emergence of these manifestations (6, 12), a phenomenon attributed to their capacity to markedly suppress eosinophilia and lymphocyte activation. Corticosteroids have been demonstrated to exert a direct impact on *S. stercoralis*, accelerating the transformation of rhabditiform larvae into invasive filariform larvae, thereby facilitating dissemination across all organs (13). Research has indicated a positive correlation between strongyloidiasis and certain comorbidities, including diabetes and HTLV1 (7, 14). The subject of this study had a medical history that included diabetes and had been receiving insulin therapy for a period exceeding ten years. 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). Furthermore, the patient in question demonstrated an increase in eosinophils of 8%. In light of the recent surge in hyperinfection syndromes and disseminated strongyloidiasis, both domestically and on a global scale (6, 9, 10), there is an imperative for medical laboratories to adopt rapid and highly sensitive diagnostic techniques for the timely detection of this disease. In this study, serological methods utilizing the ELISA technique are proposed as an effective preliminary screening tool for patients, which can be readily implemented in all medical diagnostic facilities. In light of the fact that strongyloidiasis should be recommended for patients with a travel history to endemic regions and symptoms before to the commencement of corticosteroid therapy, it is imperative to consider this condition when assessing patients.

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None

Authors' Contribution

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.

Ethics

It is evident that the manuscript under consideration adheres to the ethical recommendations stipulated within the

Declaration of Helsinki, a document promulgated by the World Medical Association (WMA).

Conflict of Interest

The authors hereby declare that there is no conflict of interest.

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Data Availability

The present article incorporates all data that has been generated.

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