Heliyon 10 (2024) e23484

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Pulmonary strongyloidiasis and hyperinfection in a Patient with idiopathic inflammatory myopathy : A case report

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ARTICLE INFO

Keywords:
Strongyloides stercoralis
Idiopathic inflammatory myopathy
Hyperinfection syndrome
Metagenomic next-generation sequencing
Case report

ABSTRACT

Pulmonary strongyloidiasis is a rare infection in patients with autoimmune diseases, and immunosuppression can lead to the development of hyperinfection syndrome with a high mortality rate. We present a case of a 78-year-old male with previous idiopathic inflammatory myopathy (IIM) with interstitial lung disease. He developed hyperinfection syndrome and respiratory failure, and diagnostic metagenomic next-generation sequencing (mNGS) of bronchoalveolar lavage fluid (BALF) confirmed the presence of *Strongyloides stercoralis*. After treatment with ivermectin, the patient's symptoms improved. Therefore, adequate screening and prophylactic treatment are needed for people at risk of immunosuppression, which can reduce the occurrence of the devastating *S. stercoralis* hyperinfection syndrome. It also highlights mNGS as a highly accurate test for the detection of difficult to atypical pathogens.

1. Introduction

The differential diagnosis of pulmonary infection in immunosuppressed patients is extensive and extremely complex. *Strongyloides stercoralis* is an intestinal nematode with endemic characteristics, and the prevalence of strongyloidiasis due to its infection is as high as 11–14 % in the subtropical region of South China [1,2]. Usually, it manifests as an asymptomatic chronic infection state, however, immune suppression can lead to its development into a hyperinfection syndrome. We report a patient with idiopathic inflammatory myopathy (IIM) and interstitial lung disease (ILD) who developed severe pulmonary strongyloidiasis after treatment with prednisone. Diagnostic metagenomic next-generation sequencing (mNGS) of bronchoalveolar lavage fluid (BALF) confirmed the presence of *Strongyloides* larvae.

2. Case report

A 78-year-old male farmer from rural southern China was admitted to the hospital after 2 weeks with cough, sputum, fever, and mild dyspnea. He had IIM combined with ILD since 2021. He started with myositis, symmetrical arthritis of the wrists and metacarpophalangeal joints, and chest computed tomography (CT) scan suggesting interstitial inflammation in the lower part of both lungs. The patient was treated with prednisone taper starting at 1 mg/kg/day and prednisone was reduced to 20 mg/day prior to admission. He did not receive any other immunosuppressive drugs for treatment.

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https://doi.org/10.1016/j.heliyon.2023.e23484
Received 25 June 2023; Received in revised form 3 December 2023; Accepted 5 December 2023
Available online 9 December 2023

On examination, he had a fever of 38.5 °C, and auscultation revealed moist crackles in the bilateral chest. His chest CT scan on admission showed interstitial changes in both lungs combined with a small amount of inflammation (Fig. 1A). The results of the first laboratory examination showed that C-reactive protein (CRP) increased to 37.29 mg/L. The serum concentration of Procalcitonin (PCT) increased to 0.065ng/ml. Blood cell analysis: leukocytes 5.08 × 10^9/L; neutrophil percentage 81.10 %; lymphocytes 14.20 %; eosinophils 0 %. Creatine kinase was normal. blood cultures were negative. The sputum smear examination was negative, but Aspergillus was found in the sputum culture. A fecal smear examination was negative. In addition, immunological tests such as antinuclear antibodies (ANA) were negative.

Therefore, the initial clinical diagnosis was IIM-ILD with invasive pulmonary aspergillosis. We started treatment with voriconazole, methylprednisolone, and broad-spectrum antibiotics for this patient. Seven days after admission, the patient's dyspnea continued to worsen and hemoptysis with decreased hemoglobin concentration was observed. His reexamined X-ray and chest CT showed rapid development of bilateral patchy pulmonary infiltrates (Fig. 1B–C). He was eventually mechanically ventilated for respiratory failure and then admitted to the intensive care unit (ICU). Bronchoscopy was performed through endotracheal intubation. The culture result of BALF was negative. Unbiased mNGS of the BALF identified 382 of 20310142 sequence reads corresponding to larvae of *S. stercoralis* (Fig. 2B–C), with 0.043 % coverage (Fig. 2A). mNGS was performed and reported by Wuhan Kangsheng Zhenyuan Medical Laboratory Co., Ltd. Methods and quality control of mNGS see in Supplementary Material. Subsequent fecal samples were sent for examination six times, of which live nematode larvae were detected on two occasions (Fig. 1E–F) and the larvae's pointed tails were seen at 1000x high magnification (Fig. 1G). Eosinophils in the patient's blood were normal. The patient began receiving ivermectin 15 mg daily and gradually reduced the dose of methylprednisone. The patient improved clinically and radiologically on the chest (Figure D). The patient's endotracheal tube was removed and transferred to the Rheumatology Department after 9 days of ivermectin treatment, and there were no side effects after treatment.

3. Discussion

Strongyloidiasis is prevalent mainly in rural areas with poor sanitation in tropical and subtropical climates [3,4]. The most common route of human infection with *S. stercoralis* is percutaneous [3,4]. Farmers often work barefoot in the fields. Filariform larvae in soil contaminated with feces can penetrate the skin of the barefoot people and migrate to the lungs, where they mature, are coughed up and swallowed. The larvae can mature into adult females in the small intestine, laying eggs that hatch into larvae, which are excreted in the feces [4,5]. The patient in this case was a farmer living in a rural area with a southern subtropical climate, thus having the potential for chronic infection.

S. stercoralis has three forms of infection: acute infection caused by primary parasitic invasion; chronic infection caused by auto-infection; and hyperinfection that occurs in an immunosuppressed state. Chronic *S. stercoralis* infections are mostly asymptomatic. When immunosuppression occurs in patients with chronic infection, a sharp increase in the rate of self-infection usually occurs,

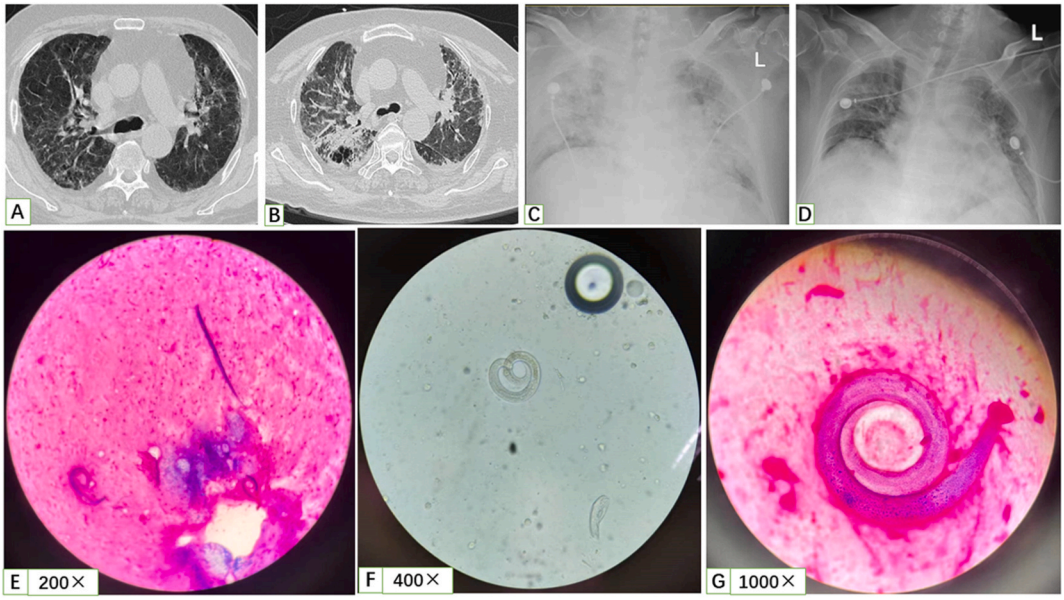

Fig. 1. A: Chest computed tomography (CT) scan on admission. Bilateral lung markings thickened, accompanied by a small amount of inflammatory exudate shadows. B–C: Reexamined X-ray and chest computed tomography 7 days after admission. Both lungs showed multiple inflammatory exudative shadows. D: Reexamined X-ray after 9 days of ivermectin treatment. Both lungs showed a decrease in inflammatory exudative shadows. E–G: Stool specimens were examined microscopically (E: Gram staining, 200 × ; F: 400 × ; G: Gram staining, 1000 ×) and larvae were found in the patient's stool.

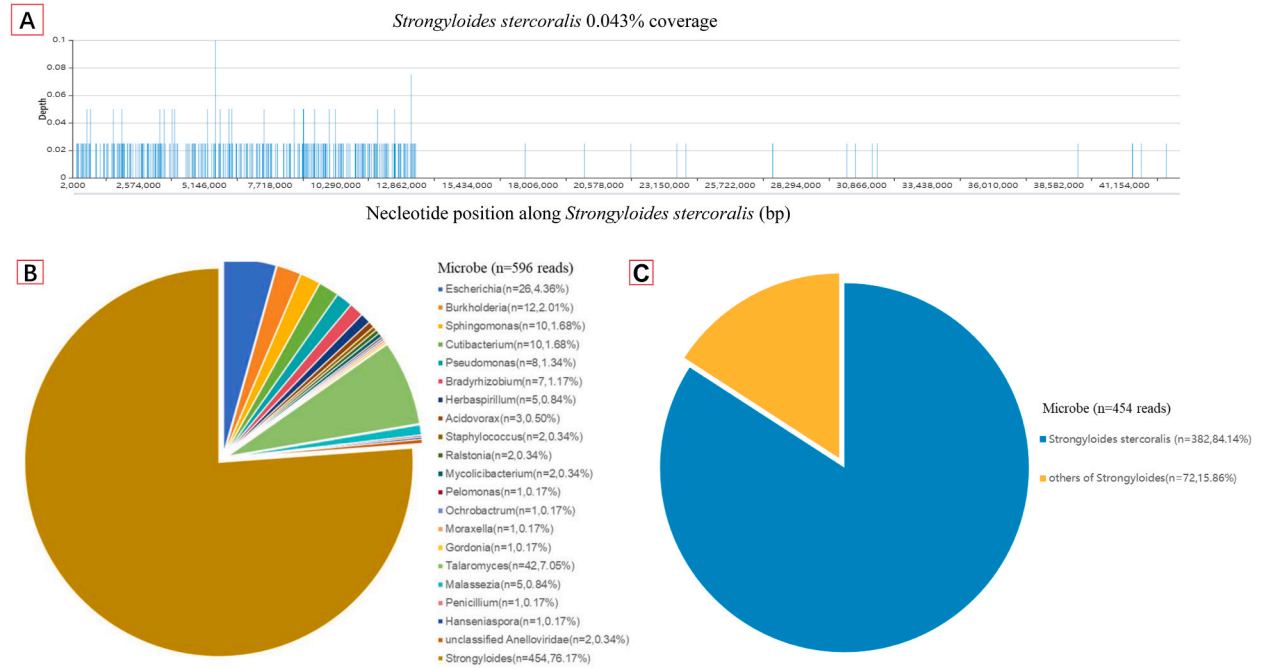

Fig. 2. A: The metagenomic next-generation sequencing (mNGS) results of this patient. The coverages of *S. stercoralis* by mNGS are shown in. B: There was a total of 20310142 reads in mNGS of BALF, and after 98.99 % of the reads were filtered to the human genome, 596 reads were mapped to the microbial genome genus level database. B and C: Of these, 454 reads (76.17 %) were sequenced in the genus *Strongyloides*, while the number of sequences of *S. stercoralis* in this genus was 382 reads (84.14 %).

resulting in the occurrence of *Strongyloides* hyperinfection syndrome [6]. According to reports, the use of prednisone with doses as low as 20 mg/day and a course of treatment as short as six days can induce *Strongyloides* hyperinfection syndrome [7]. Several cases of *Strongyloides* hyperinfection syndrome have been reported after the use of corticosteroids in the treatment of COVID-19 pneumonia [8,9]. The patient in this case may have initially been chronically infected with *S. stercoralis* in a rural area and later transformed into a putatively fatal pulmonary infection due to long-term treatment with corticosteroids for IIM disease. Glucocorticoid treatment can also lead to the fact that eosinophils are not significantly elevated. In severe cases, patients with *Strongyloides* hyperinfection syndrome develop hemoptysis and respiratory failure, with mortality rates fluctuating between 85 % and 100 % [10].

The gold standard for the diagnosis of *S. stercoralis* is the direct visualization of larvae in the specimen under the microscope. However, due to the intermittent excretion of larvae, the microscope sensitivity of a single fecal sample is as low as 21 % [11], and it is necessary to improve sensitivity by examining multiple samples obtained at different stages [5]. Also, sensitivity rises if fecal specimens are tested in triplicate. The method is labor intensive and dependent on the skill of the operator [10]. Real-time polymerase chain reaction (PCR) is highly sensitive, but results data are highly variable and nucleic acid probes are difficult to obtain [5]. As a next-generation sequencing technology, mNGS is a quantitative detection and identification of pathogens by counting sequence reads and calculating statistical significance of any DNA sequence information in patient specimens, and is independent of antibiotic application [12–14]. It has a short detection time, a wide range of applications, and higher sensitivity and specificity than traditional culture methods [12–14]. In this case, the initial fecal examination of the patient did not reveal the presence of *S. stercoralis*, making early diagnosis difficult. By taking advantage of mNGS, early identification of the pathogen gained time for the patient to obtain effective treatment.

Ivermectin is a broad-spectrum antiparasitic drug that is more effective in removing larvae than albendazole, similar in efficacy to thiabendazole, but with better tolerance [5]. Randomized clinical trials have confirmed that single-dose ivermectin treatment of strongyloidiasis can achieve similar efficacy as multi-dose regimens [15]. *Strongyloides* hyperinfection syndrome should be considered a medical emergency with a high mortality. Thus, treatment should be started immediately if this is being considered [10]. In highinfected patients, there is no standard treatment protocol, and most experts recommend treatment with ivermectin 200 μg/kg/day for at least two weeks and repeated examination of stool samples until no larvae are found in the stool specimen [10,16]. If the patient is also treated with immunosuppressive drugs, a reduction in the dose of immunosuppressive drugs should be considered if the risk of *S. stercoralis* hyperinfection syndrome outweighs the benefit of immunosuppression [10,16]. In this case, the patient's respiratory failure improved after nine days of ivermectin treatment.

4. Conclusion

Patients with chronic *S. stercoralis* infection in an immunocompromised state may develop life-threatening symptoms of

hyperinfection. So far, mNGS is a high-precision method for detecting pathogens that are difficult to culture, especially atypical pathogens. Ivermectin is the preferred drug for treating strongyloidiasis with well tolerance and high efficacy. Therefore, adequate screening and prophylactic treatment are needed for people at risk of immunosuppression, which can reduce the occurrence of the devastating *S. stercoralis* hyperinfection syndrome.

Consent

A written informed consent was obtained from the patient for publication of this article. Ethical approval was received from the institutional review board of Ren Ji Hospital, Shanghai Jiao Tong University School of Medicine.

Funding statement

This study is supported by Special fund for basic scientific research of Zhejiang University (226-2023-00100). Key Laboratory of Multiple Organ Failure (Zhejiang University), Ministry of Education, Zhejiang, China.

This study is also supported by open program of key laboratory of intelligent pharmacy and individualized therapy of Huzhou (HZKF-20240101).

Data availability statement

Data included in article/supp. Material/referenced in article.

Additional information

One additional information is available for this paper.

CRediT authorship contribution statement

Wei Fan: Writing – review & editing, Writing – original draft, Visualization, Validation, Software, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Qiong Fu:** Writing – review & editing, Conceptualization. **Yuetian Yu:** Writing – review & editing, Supervision, Project administration, Formal analysis, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

The authors are extremely grateful and thank the patient for the kind support.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2023.e23484.

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