Loeffler's Syndrome Secondary to Hyperinfection by *Strongyloides stercoralis* Associated with Methotrexate in a Patient with Rheumatoid Arthritis

Sir,

Strongyloidiasis is endemic in tropical and subtropical regions. The overall prevalence may exceed 25%, especially in the southeastern areas of the United States and in people who have recently traveled to endemic areas.[1,2] It is estimated to affect at least 60 million people.[3] Herein, we present the first case of Loeffler's syndrome secondary to *Strongyloides stercoralis* hyperinfection in a patient with rheumatoid arthritis on methotrexate therapy who was successfully treated with ivermectin.

A 74-year-old Hispanic female with a history of breast cancer in clinical remission for 10 years, rheumatoid arthritis on weekly methotrexate presented to the emergency department with complaints of a 1 week history of dark bloody and mucoid diarrhea, with frequency of 8–9 times of bowel movements daily associated with nausea and nonbloody nonbilious vomiting. She also complained of poorly localized upper colicky abdominal pain. She traveled to Puerto Rico 2 months ago. On physical examination, she had a bilateral tender erythematous rash on the shin surfaces of her legs and sides of the ankles. Laboratory testing was significant for white blood cell count (WBC) of 16,000 with eosinophils of 27%. On day 3, the WBC subsequently increased to 26,000 of which 60% wereeosinophils and the absolute eosinophilic count was 15,800. The patient started to experience cough, wheezing, and shortness of breath. Arterial blood gases revealed severe hypoxia. Chest X-ray showed bilateral increased interstitial infiltrates in the lung fields. Doppler ultrasound of the lower extremities showed a common femoral vein deep vein thrombosis and was managed with inferior vena caval filter due to the fact that the patient had continuous bloody bowel movements. On day 4, stool analysis revealed microscopic evidence of *S. stercoralis* larvae. She was started on ivermectin 15 mg daily for 2 days, the WBC trended down from 26 to 16.3 over 48 h, and absolute eosinophils trended down from 15.6 to 5.2, diarrhea stopped, and the rash resolved completely over 4 days with complete resolution of the erythema that started to develop into a desquamative pattern. Her respiratory status also improved dramatically. Human T-cell leukemia virus type 1 and 2 antibodies were negative. The patient clinically improved and was subsequently discharged from the hospital. *S. stercoralis* was not detected in the subsequent follow-up stool examinations thereafter.

S. stercoralis is a parasitic nematode that affects gastrointestinal, cutaneous, pulmonary systems. The infection occurs after the parasite (filariform larvae form), which is usually found in the soil and human feces, penetrates the human skin, and from there, the parasite migrates to the lungs hematogenously.[4,5] The larvae migrates from the lung alveolar sacs to the tracheobronchial tree and subsequently will be ingested to the gastrointestinal tract. In the gastrointestinal tract, it transforms into the adult worms which will reside in the duodenojejunal mucosa and produce eggs that transform into the rhabditiform (noninfectious form) which are passed with feces and mature into filariform larvae. These larvae then penetrate the intestinal mucosa and the perianal skin. In the case we presented, the patient had Loeffler's syndrome which manifested as pulmonary symptoms of wheezing in the setting of hypereosinophilia and diarrhea. The pulmonary symptoms were severe enough to cause hypoxia. The pulmonary symptoms, the radiographic findings, and the hypereosinophilia supported the diagnosis of Loeffler's syndrome which is a very rare manifestation of Strongyloides infection.[5] This, to our knowledge, is the first reported case of Loeffler's syndrome secondary to methotrexate-related hyperinfection syndrome related to *S. stercoralis* that clinically responded to ivermectin therapy. Methotrexate

was most likely the trigger for Strongyloides hyperinfection in our patient. In addition to immunosuppression, which is associated with the pulmonary and hyperinfection syndrome, other factors such as hematopoietic stem cells, HTLV viral infections, and glucocorticoids have also been implicated.[6,7] The hyperinfection/Loeffler's syndrome is believed to occur when chronic Strongyloides infection in immunocompromised host results in more egg-laying nematodes in the intestines and more migration.[8,9] The diagnosis of Strongyloides is confirmed with stool microscopy. Stool samples are negative in up to 70%, especially in uncomplicated cases where intestinal worm load is low.[10-12] The treatment of choice is 2 days of ivermectin therapy. Albendazole can also be used although it has lower efficacy.[10,11]

In conclusion, Strongyloidiasis is an infection that can involve gastrointestinal, pulmonary, and cutaneous systems. The infection can result in Loeffler's syndrome which can be fatal. The definitive diagnosis can be challenging, and the treating physician has to pay attention to the important clues of eosinophilia and history of travel to endemic areas.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

Moayad Al Hadidi, Hamid Shaaban, Khalid Hani Jumean, Paloma Peralta

Department of Internal Medicine, St Michael's Medical Center, Newark, NJ, USA

Address for correspondence: Dr. Hamid Shaaban, Department of Internal Medicine, St Michael's Medical Center, 111 Central Avenue, Newark, NJ, USA.
E-mail: hamidshaaban@gmail.com

References

1. Posey DL, Blackburn BG, Weinberg M, Flagg EW, Ortega L, Wilson M, *et al.* High prevalence and presumptive treatment of schistosomiasis and strongyloidiasis among African refugees. Clin Infect Dis 2007;45:1310-5.
2. Gyorkos TW, Genta RM, Viens P, MacLean JD. Seroepidemiology of *Strongyloides* infection in the Southeast Asian refugee population in Canada. Am J Epidemiol 1990;132:257-64.
3. Gotuzzo E, Terashima A, Alvarez H, Tello R, Infante R, Watts DM, *et al. Strongyloides stercoralis* hyperinfection associated with human T cell lymphotropic virus type-1 infection in Peru. Am J Trop Med Hyg 1999;60:146-9.
4. Nwokolo C, Imohiosen EA. Strongyloidiasis of respiratory tract presenting as "asthma". Br Med J 1973;2:153-4.
5. Keiser PB, Nutman TB. *Strongyloides stercoralis* in the immunocompromised population. Clin Microbiol Rev 2004;17:208-17.
6. Marty FM. *Strongyloides* hyperinfection syndrome and transplantation: A preventable, frequently fatal infection. Transpl Infect Dis 2009;11:97-9.
7. Jamil SA, Hilton E. The *Strongyloides* hyperinfection syndrome. N Y State J Med 1992;92:67-8.
8. Koosha S, Fesharaki M, Rokni MB. Comparison of enzyme-linked immunosorbent assay and indirect immunofluorescence assay in the diagnosis of human strongyloidiasis. Indian Soc Gastroenterol 2004;23:214-6.
9. Kishimoto K, Hokama A, Hirata T, Ihama Y, Nakamoto M, Kinjo N, *et al.* Endoscopic and histopathological study on the duodenum of *Strongyloides stercoralis* hyperinfection. World J Gastroenterol 2008 21;14:1768-73.
10. Zaha O, Hirata T, Kinjo F, Saito A, Fukuhara H. Efficacy of ivermectin for chronic strongyloidiasis: Two single doses given 2 weeks apart. J Infect Chemother 2002;8:94-8.
11. Muennig P, Pallin D, Challah C, Khan K. The cost-effectiveness of ivermectin vs. albendazole in the presumptive treatment of strongyloidiasis in immigrants to the United States. Epidemiol Infect 2004;132:1055-63.
12. González-Ramos J, Alonso-Pacheco ML, Mora-Rillo M, Herranz-Pinto P. Need to screen for Chagas disease and Strongyloides infestation in non-endemic countries prior to treatment with biologics. Actas Dermo-Sifiliográficas (English Edition) 2017;108:373-5.

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

Access this article online

Quick Response Code:

Website: www.jgid.org

DOI: 10.4103/jgid.jgid_69_17

How to cite this article: Al Hadidi M, Shaaban H, Jumean KH, Peralta PA. Loeffler's Syndrome Secondary to Hyperinfection by *Strongyloides stercoralis* Associated with Methotrexate in a Patient with Rheumatoid Arthritis. J Global Infect Dis 2018;10:29-30.