**Connecting the Dots: *Strongyloides stercoralis* and Chronic Urticaria with Angioedema**

**Abstract:**

Urticaria and angioedema are common in allergy clinics, but their association with parasitic infections is underexplored. A 70-year-old Puerto Rican woman with hypertension, diabetes, and asthma presented with chronic urticaria and angioedema. She had chronic eosinophilia (maximum 1600 cells/μL), elevated IgE (1417 IU/mL), and IL-5 (2.9 pg/mL). A parasitic workup confirmed *S. stercoralis* IgG. Ivermectin treatment resolved her angioedema and urticaria, led to mild improvement in her asthma, and resulted in normalized eosinophil and IL-5 levels, along with a decrease in IgE levels. Like our case, a few other studies have shown improvement in allergic conditions after treatment, though this area remains understudied. This case highlights the importance of parasite testing in chronic urticaria and angioedema, especially in eosinophilic patients from endemic regions. Antiparasitic treatment can significantly improve symptoms, underscoring the need for more research on the connection between parasitic infections and allergic diseases.

**Key Words:** *Strongyloides stercoralis* , Chronic Urticaria , Angioedema**,** allergy, eosinophilic patients

**Introduction:**

***Strongyloides stercoralis* is an intestinal roundworm that is often overlooked, but has a global prevalence that affects over one hundred million people worldwide.1 It can manifest from nonspecific symptoms to hyperinfection and disseminated disease that can be fatal. The human host is infected by direct skin penetration of the filariform larvae. Parasitic females reproduce, hatch their eggs, and release the rhabditiform larvae that are either excreted to start a free-living cycle or lead to autoinfection.2 It can also present with recurrent asthma exacerbations and hives, making proper recognition and workup important to prevent a delayed diagnosis and treatment.3**Urticaria and angioedema are frequently presenting complaints in allergy clinics. Although the immunomodulatory effects of helminths have been well documented, and many patients with allergic symptoms test positive for *Strongyloides*, there is a relative lack of literature on the association between parasites and allergic diseases.

**Case Presentation:**

Here, we present a case of a 70-year-old woman born in Puerto Rico, with a past medical history of hypertension, diabetes, and asthma. She presented with chronic diffuse urticaria characterized by generalized body itching and hives occurring almost daily since childhood. Additionally, she experienced occasional episodes of lip and tongue numbness and swelling every few months, leading to difficulty speaking. This required one emergency department visit and a few uses of Epinephrine injections at home. Laboratory tests revealed significant chronic eosinophilia for the last 16 years, with a maximum absolute eosinophil count of 1600 cells/μL.

To further evaluate her eosinophilia, a parasitic workup was performed, which was positive for *S. stercoralis* IgG. She also had elevated levels of serum IgE (1417 IU/mL) and serum IL-5 (2.9 pg/mL). Other laboratory tests including Trichinella and Toxocara antibodies, antinuclear antibody, ESR/CRP, and complement levels were normal. The patient was treated with two doses of Ivermectin 200 μg/kg. A few months post-treatment, she reported no episodes of angioedema and only experienced one mild episode of urticaria, which lasted for a few hours and was described by her as "much milder compared to before." She also reported mild improvement in her asthma symptoms, including subjectively slightly better breathing and reduced wheezing. Upon further inquiry, she reported her exercise tolerance, which was limited by her breathing, to a few blocks, did not change, and she had been using the same amount and frequency of her maintenance and rescue inhalers. Repeat lab tests six months after treatment showed a normal absolute eosinophil count of 300 cells/μL, a normal IL-5 level of 0.5 pg/mL, and a decreased serum IgE level of 562 IU/mL. She will be followed in the allergy clinic for monitoring of her symptoms including any recurrence of symptoms, absolute eosinophil count, and serum IgE and IL-5 levels.

**Discussion:**

*Strongyloides stercoralis* is a soil-transmitted nematode endemic to tropical and subtropical regions, including Southeast Asia, sub-Saharan Africa, South America, the Caribbean, the Southeastern United States, and Southern Europe*.*4 It is estimated that *strongyloidiasis* affects 100-370 million people worldwide.5, 6 Risk factors for contracting a *Strongyloides* infection include contact with soil from endemic areas, immunosuppressive diseases, such as diabetes, human immunodeficiency virus, human T cell-lymphotropic viruses, and alcoholism, as well as the use of immunosuppressive medications, such as corticosteroids.7, 8

The clinical presentation of *Strongyloides* infection can vary widely, ranging from asymptomatic cases to sepsis with organ damage due to hyperinfection.7 Hyperinfection syndrome denotes an acceleration of *S* *stercoralis’* normal life cycle, leading to an overwhelming worm burden within the traditional reproductive route (the skin, gut, and lungs), in the setting of immunosuppression.7 Skin involvement typically manifests as an itchy, serpiginous rash at the site of larval penetration, with "larva currens" or "running" larva being a pathognomonic dermatologic sign of *strongyloidiasis*.7 Some patients experience gastrointestinal symptoms, such as diarrhea, constipation, anorexia, and epigastric pain,9 while others may present with allergy-like symptoms, including angioedema, and chronic urticaria which affects nearly one-third of patients.9, 10, 11 *Strongyloides* can also mimic asthma, with its larvae triggering dry cough, dyspnea, and wheezing upon entering the lungs.7, 12, 13 Individuals from or who have visited endemic areas, presenting with larva currens rash, gastrointestinal symptoms, angioedema, urticaria, or asthma should undergo testing for *Strongyloides.* Since many patients may remain asymptomatic, *Strongyloides* should also be considered in cases of unexplained eosinophilia or elevated IgE levels. One systematic review and meta analysis found that almost 70% of patients had eosinophilia.13 Our patient had chronic eosinophilia for 16 years in addition to her symptoms, representing a missed opportunity for an earlier diagnosis.

Prompt diagnosis of *Strongyloides* infection is critical because corticosteroids, frequently used for allergic exacerbations, can precipitate hyperinfection syndrome, leading to end-organ damage.12 Hyperinfection can occur in the context of immunosuppression, with mortality rates exceeding 85%.14 Even brief courses of corticosteroids in non-immunocompromised patients have been linked to hyperinfection syndrome and death.15 Furthermore, other treatment options like antihistamines are limited due to side effects, especially in elderly patients like ours, underscoring the importance of addressing the underlying cause. There are no established gold standard tests for *Strongyloides* diagnosis. Since stool testing is not very sensitive, both stool and serologic evaluations are typically recommended to increase sensitivity.16 Multiple stool samples should be examined using concentration techniques to improve sensitivity although can still fail to yield a diagnosis.16 Serology testing is more sensitive than stool examination, particularly in chronic infections, although it may show cross-reactivity with other helminth infections.17In our case, the diagnosis was made based on serology testing. Once a diagnosis is made, appropriate treatment should follow.

Treatment aims to completely eradicate the parasite and is recommended for both symptomatic and asymptomatic individuals due to the risk of hyperinfection. Antiparasitic medications, such as Ivermectin, Thiabendazole, or Albendazole, can be used, with Ivermectin (200 micrograms/kg for two days) being preferred for its superior efficacy.7 Monitoring treatment response through serial stool or serologic testing for one to two years is crucial for all patients.7 ​​Our patient received Ivermectin, resulting in the resolution of her angioedema, significant improvement of her urticaria, and slight improvement of her asthma. Likewise, a few other retrospective observational studies have reported complete resolution or significant improvement in allergy symptoms (urticaria, angioedema, or rhinoconjunctivitis) in many patients post-treatment with minimal improvement in respiratory symptoms.10, 13, 18 Further research is necessary to delve into the relationship between parasite infections and allergic conditions.

**Conclusion:**

This case highlights the importance of considering parasite testing in the workup of chronic urticaria and angioedema, especially in patients from endemic regions and those with eosinophilia since antiparasitic treatment could potentially significantly alleviate the symptoms. Additionally, accurate diagnosis and treatment are important not only for symptom relief, but also to prevent the inappropriate use of steroids and mitigate the potential complications of hyperinfection.

**Consent**

As per international standards or university standards, patient(s) written consent has been collected and preserved by the author(s).

**Conference disclaimer:**

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Disclaimer (Artificial intelligence)

Option 1:

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

References:

1. Buonfrate D, Requena-Méndez A, Angheben A, et al. Severe strongyloidiasis: a systematic review of case reports. *BMC Infect Dis.* 2013;13:78. doi:10.1186/1471-2334-13-78
2. Buonfrate D, Angheben A, Requena-Méndez A, et al. Global prevalence of Strongyloides stercoralis infection in the general population: a systematic review and meta-analysis. *Lancet Infect Dis.* 2024;24(3):241-251. doi:10.1016/S1473-3099(23)00599-5
3. Nutman TB. Human infection with *Strongyloides stercoralis* and other related Strongyloides species. *Parasitology.* 2017;144(3):263-273. doi:10.1017/S0031182016000834
4. Lahari Rampur, Sunit P. Jariwala, Golda Hudes, David L. Rosenstreich, Gabriele de Vos, Effect of ivermectin on allergy-type manifestations in occult strongyloidiasis, Annals of Allergy, Asthma & Immunology, Volume 117, Issue 4, 2016, Pages 423-428, ISSN 1081-1206, <https://doi.org/10.1016/j.anai.2016.07.021>.
5. Mirzaei L, Ashrafi K, Atrkar Roushan Z, Mahmoudi MR, Shenavar Masooleh I, Rahmati B, Saadat F, Mirjalali H, Sharifdini M. Strongyloides stercoralis and other intestinal parasites in patients receiving immunosuppressive drugs in northern Iran: a closer look at risk factors. Epidemiol Health. 2021;43:e2021009. doi: 10.4178/epih.e2021009. Epub 2021 Jan 20. PMID: 33494130; PMCID: PMC8060525.
6. Eslahi AV, Badri M, Nahavandi KH, Houshmand E, Dalvand S, Riahi SM, Johkool MG, Asadi N, Hoseini Ahangari SA, Taghipour A, Zibaei M, Khademvatan S. Prevalence of strongyloidiasis in the general population of the world: a systematic review and meta-analysis. Pathog Glob Health. 2021 Feb;115(1):7-20. doi: 10.1080/20477724.2020.1851922. Epub 2021 Jan 12. PMID: 33433291; PMCID: PMC7850468.
7. Mora Carpio AL, Meseeha M. Strongyloidiasis. [Updated 2023 Sep 4]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK436024/>
8. Boggild A, Libman M, Greenaway C, McCarthy A. CATMAT statement on disseminated strongyloidiasis: Prevention, assessment and management guidelines. *Canada Communicable Disease Report*. 2016;42(1):12-19. doi:https://doi.org/10.14745/ccdr.v42i01a03
9. Tamarozzi F, Martello E, Giorli G, Fittipaldo A, Staffolani S, Montresor A, Bisoffi Z, Buonfrate D. Morbidity Associated with Chronic *Strongyloides stercoralis* Infection: A Systematic Review and Meta-Analysis. Am J Trop Med Hyg. 2019 Jun;100(6):1305-1311. doi: 10.4269/ajtmh.18-0895. PMID: 30963990; PMCID: PMC6553888.
10. Van Dellen RG, Maddox DE, Dutta EJ. Masqueraders of angioedema and urticaria. Ann Allergy Asthma Immunol. 2002 Jan;88(1):10-14; quiz 15, 41. doi: 10.1016/S1081-1206(10)63586-7. PMID: 11814272.
11. Dunlap, N. E., M. S. Shin, S. S. Polt, and K. J. Ho. "Strongyloidiasis manifested as asthma." *Southern Medical Journal* 77, no. 1 (1984): 77-78.
12. Salam R, Sharaan A, Jackson SM, Solis RA, Zuberi J. Strongyloides Hyperinfection Syndrome: A Curious Case of Asthma Worsened by Systemic Corticosteroids. Am J Case Rep. 2020 Dec 21;21:e925221. doi: 10.12659/AJCR.925221. PMID: 33347427; PMCID: PMC7767572.
13. Buonfrate D, Fittipaldo A, Vlieghe E, Bottieau E. Clinical and laboratory features of Strongyloides stercoralis infection at diagnosis and after treatment: a systematic review and meta-analysis. Clin Microbiol Infect. 2021 Nov;27(11):1621-1628. doi: 10.1016/j.cmi.2021.07.016. Epub 2021 Jul 26. PMID: 34325063.
14. Igra-Siegman Y, Kapila R, Sen P, Kaminski ZC, Louria DB. Syndrome of hyperinfection with Strongyloides stercoralis. Rev Infect Dis. 1981 May-Jun;3(3):397-407. doi: 10.1093/clinids/3.3.397. PMID: 7025145.
15. Ghosh K, Ghosh K. Strongyloides stercoralis septicaemia following steroid therapy for eosinophilia: report of three cases. Trans R Soc Trop Med Hyg. 2007 Nov;101(11):1163-5. doi: 10.1016/j.trstmh.2007.05.021. Epub 2007 Jul 26. PMID: 17662320.
16. Campo Polanco L, Gutiérrez LA, Cardona Arias J. Infección por Strongyloides stercoralis: metanálisis sobre evaluación de métodos diagnósticos convencionales (1980-2013) [Diagnosis of Strongyloides Stercoralis infection: meta-analysis on evaluation of conventional parasitological methods (1980-2013)]. Rev Esp Salud Publica. 2014 Oct;88(5):581-600. Spanish. doi: 10.4321/S1135-57272014000500004. PMID: 25327268.
17. Levenhagen MA, Costa-Cruz JM. Update on immunologic and molecular diagnosis of human strongyloidiasis. Acta Trop. 2014 Jul;135:33-43. doi: 10.1016/j.actatropica.2014.03.015. Epub 2014 Mar 28. PMID: 24686097.
18. Zubrinich CM, Puy RM, O'Hehir RE, Hew M. *Strongyloides* infection as a reversible cause of chronic urticaria. J Asthma Allergy. 2019 Feb 26;12:67-69. doi: 10.2147/JAA.S167292. PMID: 30881049; PMCID: PMC6396652.