Gruber SF, Gallagher MA, Malik MS, Hall MAK. More Than Just Stool: Hypereosinophilic Syndrome Presenting as Persistent Diarrhea in a Patient With Ulcerative Colitis. *Brown Hospital Medicine*. 2024;3(4):9-12. doi:10.56305/001c.122954

Case Reports

More Than Just Stool: Hypereosinophilic Syndrome Presenting as Persistent Diarrhea in a Patient With Ulcerative Colitis

Sarah F Gruber[1], Michael A Gallagher, MD[2,3], Manpreet S Malik, MD[2,3], Mary Ann Kikconnell Hall, MD, MPH[2]

[1] Emory University School of Medicine, Atlanta, GA, USA,
[2] Division of Hospital Medicine, Emory University School of Medicine, Atlanta, GA, USA,
[3] Grady Health System, Atlanta, GA, USA

Journal of Brown Hospital Medicine
Vol. 3, Issue 4, 2024

Article Information

Keywords: Case report, Hypereosinophilic syndrome, Acute diarrhea, Persistent diarrhea, Eosinophilic colitis, Strongyloidiasis, Ulcerative colitis, Primary sclerosing cholangitis

https://doi.org/10.56305/001c.122954

Submitted: May 06, 2024 EST

Accepted: August 24, 2024 EST

Abstract

We highlight a case of non-infectious diarrhea that progressed despite supportive care, prompting further workup. A 50-year-old man presented with 1 week of voluminous diarrhea, nausea, emesis, and abdominal pain. His history included ulcerative colitis, primary sclerosing cholangitis, *Clostridioides difficile* treated via total colectomy with ileoanal pouch, treated disseminated *Mycobacterium avium* complex, and international travel. On physical exam he had normal vital signs, diffuse abdominal tenderness without peritoneal signs, and a rash. Lab work revealed leukocytosis with eosinophilia, hyponatremia, and elevated creatinine. Lactate, inflammatory markers, stool studies, and computed tomography of his abdomen were normal. Tissue biopsies of the duodenum, ileum, and rectal pouch collected during colonoscopy and push enteroscopy revealed prominent mucosal eosinophilia, confirming the diagnosis of hypereosinophilic syndrome (HES). Treatment with steroids led to significant improvement in all symptoms and blood eosinophilia. This case highlights the importance of aggressive workup of diarrhea with peripheral eosinophilia, especially in patients with ulcerative colitis: waiting 6 months to confirm the diagnosis via blood work would delay treatment. Notably, infection with *Strongyloides stercoralis* was ruled out in this case prior to treatment. This is an important step in the workup and management of HES to prevent progression of Strongyloidiasis.

BACKGROUND

Acute diarrhea is exceedingly common, averaging 0.72 cases per person per year in the United States.[1] The most common etiology is viral gastroenteritis, which is generally self-limiting.[2] Diagnostic investigation of infectious diarrhea with stool cultures, stool ova, and parasites, or molecular testing is typically reserved for patients with persistent fever, bloody stool, or immunosuppression.[2,3] Less commonly, acute diarrhea may have a non-infectious etiology such as autoimmune disease, dietary factors, medication effects, or a systemic condition, either common or rare.[3,4] Systemic conditions presenting with gastrointestinal manifestations present a diagnostic challenge for clinicians due to the lack of specificity of these symptoms. Persistent diarrhea, defined as lasting more than 14 days, coupled with a negative infectious workup, may indicate further workup, including careful consideration of systemic conditions.[1,5] Further, the presence of a rash and non-specific laboratory findings such as peripheral eosinophilia, with or without a history of ulcerative colitis, may prompt specific investigation of hypereosinophilic syndrome (HES) as the etiology of non-infectious, persistent diarrhea.[6-8] HES is a rare, underdiagnosed group of closely related blood disorders, each characterized by peripheral eosinophilia and organ damage secondary to eosinophilic infiltration.[6,9] The skin, heart, lungs, and central and peripheral nervous systems are affected in over half of all cases.[6] However, the extent of damage to specific organs varies among patients, leading to numerous clinical phenotypes.[6] Eosinophilic gastroenteritis and colitis are common complications, leading to abdominal pain, diarrhea, nausea, and vomiting.[6,9]

CASE PRESENTATION

A 50-year-old man presented with one week of diarrhea. He reported 10 voluminous, watery bowel movements each day, nausea, and frequent non-bloody, non-bilious emesis. Additional symptoms included progressive right-sided abdominal pain, generalized pruritus, and diffuse weakness in all extremities. Eating meat exacerbated both his abdominal discomfort and pruritus. His medical and surgical history included type 2 diabetes mellitus, hypertension, hyperlipidemia ulcerative colitis, primary scleros-

ing cholangitis, *Clostridioides difficile* treated via total colectomy with ileoanal pouch, and treated disseminated *Mycobacterium avium* complex. His home medication regimen consisted of only oral aspirin 81 mg daily and oral atorvastatin 40 mg daily. He had no known allergies. Notable travel history included trips to rural Indonesia and Bermuda within the past five years.

Despite normal vital signs, he appeared uncomfortable. The physical exam was remarkable for diffuse abdominal tenderness to palpation without peritoneal signs, and a blanching erythematous rash overlying his sternum. Laboratory data revealed an elevated white blood cell count of 17.7 K/μL (range 4.5 – 11 K/μL) with an absolute neutrophil count of 11,830 K/μL (range 2,500 – 6,000 K/μL), and an elevated absolute eosinophil count (AEC) of 3,510 K/μL (range 30 – 350 K/μL). Low sodium, 132 mEq/L (range 135 – 145 mEq/L) and elevated creatinine, 2.0 μmol/L (0.6 – 1.2 μmol/L) were also noted on blood work; lactate, erythrocyte sedimentation rate, and c-reactive protein were all within normal limits. Stool studies, including *Clostridioides difficile* toxin, common bacteria and viruses associated with diarrhea, and ova and parasites, were all negative. Computed tomography scan of the abdomen and pelvis revealed no acute processes. Further labs revealed low immunoglobulin G (IgG), normal tryptase, normal T-, B-, and natural killer cell levels, negative immunoglobulin E alpha-gal, and negative *Strongyloides* IgG. Despite supportive treatment, his abdominal pain intensified, diarrhea became more frequent and newly bloody, rash spread across his chest wall, and AEC rose to 7,900 K/μL. Gastroenterology performed colonoscopy to investigate potential causes and push enteroscopy to obtain tissue biopsies of the duodenum, mid-ileum, and rectal pouch which revealed prominent mucosal eosinophilia, confirming the diagnosis of hypereosinophilic syndrome (HES).

Treatment commenced with 1 mg/kg intravenous methylprednisolone daily for 3 days, followed by transition to oral prednisone with a slow taper. Significant improvement was noted in abdominal pain, rash, and peripheral eosinophilia with treatment, and his diarrhea completely resolved.

DISCUSSION

HES, while uncommon, is a clinically significant and potentially lethal multi-system disorder.[10,11] Historically, HES has been defined as the presence of blood eosinophilia >1500 K/μL for at least six months, the exclusion of secondary causes of blood eosinophilia, and signs and symptoms of organ involvement.[1-3,12] In 2010, Simon et al. proposed new criteria, which allowed marked tissue hypereosinophilia combined with associated symptoms and blood eosinophilia to substitute for 6 months of persistent blood eosinophilia.[12]

Each presentation of HES is unique and dependent upon both the organ systems affected and the degree of severity.[6] Interestingly, the AEC does not always correlate with the degree of symptom severity.[10] The skin, heart, lungs, and both the peripheral and central nervous systems are affected in more than half of all cases of HES.[6] Involvement of the skin leads to cutaneous manifestations, including rash, as was seen in this case.[10] The gastrointestinal system is also commonly affected in HES, leading to effects that include gastroenteritis and colitis.[10] Notably, HES is known to be associated with inflammatory bowel disease, and blood eosinophilia has been linked to increased disease severity and incidence of primary sclerosing cholangitis in patients with ulcerative colitis.[7,8]

While acute diarrhea is most often infectious in origin, this patient's negative infectious workup and lack of clinical improvement with supportive care prompted a more comprehensive evaluation, including critical analysis of the white blood cell differential and unexplained rash.[2] Further, his history of ulcerative colitis with primary sclerosing cholangitis increased suspicion of HES as the cause of his constellation of symptoms and peripheral eosinophilia.[7,8] Given the potential for severe consequences secondary to eosinophil-mediated organ damage, waiting six months to repeat blood work to confirm persistent eosinophilia and prove the diagnosis of HES is not practical.[11] Rather, an aggressive and comprehensive workup must be undertaken at the time of initial presentation when HES is suspected, as per the recommendations of Simon et al.[10] Following the exclusion of alternative etiologies to explain blood eosinophilia and organ dysfunction, tissue biopsy of the affected organs should be completed.[13] The presence of hypereosinophilia in the affected tissue confirms the diagnosis of HES.[11,12]

Once the diagnosis of HES is made, the clinician's presumptive reaction may be to initiate treatment immediately with steroids, the most common first-line agent.[10,13] However, it is imperative first to ensure that Strongyloidiasis has been excluded by ELISA testing before initiating treatment with steroids.[14,15] If not, introducing an immunosuppressed state would enable *Strongyloides* to progress, causing a potentially life-threatening infection.[9,12] If clinical severity due to HES does not afford time to await ELISA results, such as in cases of cardiac, neurologic, or pulmonary involvement with hypoxia, urgent treatment with steroids and empiric ivermectin is indicated.[10,13] Fortunately, in this case, Strongyloidiasis had been ruled out prior to the diagnosis of HES via colonoscopy and tissue biopsy.

In conclusion, this atypical case of diarrhea had a negative infectious workup and progressed with supportive care, prompting further investigation. The diagnosis of HES was suspected, given the history of persistent, non-infectious diarrhea coupled with peripheral eosinophilia,

unexplained rash, and history of ulcerative colitis; the diagnosis was confirmed via tissue biopsy of the small intestine and rectal pouch. This case highlights the importance of aggressive workup of diarrhea with peripheral eosinophilia, especially in patients with ulcerative colitis: waiting six months to confirm the diagnosis via repeat blood work would have delayed treatment and might have allowed severe complications secondary to eosinophilic infiltration of the bowel. Notably, Strongyloides infection was ruled out in this case prior to initiation of treatment of HES with steroids. This is an important step in the workup and management of all patients diagnosed with HES to prevent the potentially life-threatening progression of Strongyloidiasis.

Author Contributions

All authors have reviewed the final manuscript prior to submission. All the authors have contributed significantly to the manuscript, per the International Committee of Medical Journal Editors criteria of authorship.

- Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND
- Drafting the work or revising it critically for important intellectual content; AND
- Final approval of the version to be published; AND
- Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Disclosures/Conflicts of Interest

The authors declare they have no conflicts of interest

Corresponding Author

Sarah F Gruber
Department of Medicine
Emory University School of Medicine
Email: sarah.gruber@emory.edu

REFERENCES

1. Drancourt M. Acute Diarrhea. *Infectious Diseases*. 2017:335-340.e332. doi:10.1016/B978-0-7020-6285-8.00038-1

2. Barr W, Smith A. Acute diarrhea. *Am Fam Physician*. 2014;89:180-189.

3. Aranda-Michel J, Giannella R. Acute diarrhea: a practical review. *Am J Med*. 1999;106:670-676. doi:10.1016/s0002-9343(99)00128-x

4. Panigrahy A, Srinivasan S. Gastrointestinal Manifestations of Systemic Diseases in Critically Ill. *Indian J Crit Care Med*. 2020;24:s190-s192. doi:10.5005/jp-journals-10071-23610

5. Arasaradnam R, Brown S, Forbes A, et al. Guidelines for the investigation of chronic diarrhoea in adults: British Society of Gastroenterology, 3rd edition. *Gut*. 2018;67:1380-1399. doi:10.1136/gutjnl-2017-315909

6. Roufosse F, Goldman M, Cogan E. Hypereosinophilic syndromes. *Orphanet J Rare Dis*. 2007;2:37. doi:10.1186/1750-1172-2-37

7. Ramos DV, Dotta DD, Barros LL. Hypereosinophilic Syndrome Secondary to Ulcerative Colitis and Primary Sclerosing Cholangitis. *Case Rep Gastroenterol*. Published online 2023. doi:10.1159/000527380

8. Barrie A, Mourabet M, Weyant K, et al. Recurrent blood eosinophilia in ulcerative colitis is associated with severe disease and primary sclerosing cholangitis. *Dig Dis Sci*. 2013;58:222-228. doi:10.1007/s10620-012-2329-7

9. Freeman H. Adult eosinophilic gastroenteritis and hypereosinophilic syndromes. *World J Gastroenterol*. 2008;14(9):6771-6773. doi:10.3748/wjg.14.6771

10. Roufosse F, Weller P. Practical approach to the patient with hypereosinophilia. *J Allergy Clin Immunol*. 2012;126:39-44. doi:10.1016/j.jaci.2010.04.011

11. Valent P, Klion A, Horny H, et al. Contemporary consensus proposal on criteria and classification of eosinophilic disorders and related syndromes. *J Allergy Clin Immunol*. 2012;130:601-612.e609. doi:10.1016/j.jaci.2012.02.019

12. Simon H, Rothenberg M, Bochner B, et al. Refining the definition of hypereosinophilic syndrome. *J Clin Microbiol*. 2010;126:45-49. doi:10.1016/j.jaci.2010.03.042

13. Klion A. How I treat hypereosinophilic syndromes. *Blood*. 2015;126:1069-1077. doi:10.1182/blood-2014-11-551614

14. Krolewiecki A, Nutman T. Strongyloidiasis: A Neglected Tropical Disease. *Infect Dis Clin North Am*. 2019;33:135-151. doi:10.1016/j.idc.2018.10.006

15. van Doorn H, Koelewijn R, Hofwegen H, et al. Use of enzyme-linked immunosorbent assay and dipstick assay for detection of Strongyloides stercoralis infection in humans. *J Clin Microbiol*. 2007;45:438-442. doi:10.1128/jcm.01735-06