

Hypereosinophilic Syndrome With Eosinophilic Gastritis

Global Pediatric Health
Volume 4: 1–3
© The Author(s) 2017
Reprints and permissions:
sagepub.com/journalsPermissions.nav
DOI: 10.1177/2333794X17705239
journals.sagepub.com/home/gph



Vignesh Hebri Nayak, MD¹, Nesrin Yurttutan Engin, MD¹,
James Joseph Burns, MD, MPH¹, and Priyanka Ameta, MD¹

Received March 7, 2017. Accepted for publication March 21, 2017.

Introduction

Hypereosinophilic syndrome (HES) is a heterogeneous group of disorders characterized by sustained overproduction of eosinophils. The term *hypereosinophilic syndrome* was first coined in 1968 by Hardy and Anderson.¹ Chusid et al in 1975 defined the diagnostic criteria for HES, which includes (1) absolute eosinophil count (AEC) >1500 cells/μL persisting for 6 months or longer, or on at least 2 occasions; (2) absence of another diagnosis to explain the eosinophilia; and (3) signs and symptoms of organ involvement.²

In 2011, the Working Conference on Eosinophil Disorders and Syndromes proposed a new classification. As per the panel, hypereosinophilia (HE) was defined as persistence of peripheral blood eosinophilia (AEC >1500/μL) on at least 2 occasions with a minimal interval of 4 weeks, and/or with evidence of marked tissue eosinophilia. HE was classified into hereditary (familial) HE variant, primary (clonal/neoplastic) HE produced by clonal/neoplastic eosinophils (HE_N), secondary (reactive) HE (HE_R), and HE of undetermined significance (HE_{US})/Idiopathic variant. The HES term was used for any patient with HE with clear evidence of HE-related organ damage.³

Any organ system can be affected by persistent eosinophilia. However, the most commonly affected organ systems include skin, lungs, gastrointestinal system, cardiovascular system, and nervous system.⁴

Case Report 1

A 16-year-old female presented to the emergency department (ED), while she was on a band trip, with abdominal pain for 2 days, over umbilicus, without any history of vomiting or fever or change in the pattern of stools. She was evaluated in the ED for the concerns of appendicitis, but the workup was negative. Her complete blood count at that time showed white blood cells (WBC) of 15000 with 42% eosinophils (AEC 6300). She was diagnosed to have HE, was started on albendazole for 2 weeks, and

was instructed to follow-up with her primary care physician. Her subsequent labs done at 2 weeks, 2 months, and at 5 months, following the ED visit, are as follows: WBC 12.2 with 45% eosinophils (AEC 5490), 14.3 with 43% eosinophils (AEC 6150), and 17.2 with 34% eosinophils (AEC 5854), respectively. She denied any history of fever or weight loss or passage of worms in her stool or any recent travel. As she had persistent eosinophilia, intermittent abdominal pain, and vomiting, she was referred to our hospital for workup on eosinophilia and further management.

Her physical examination was unremarkable. Her labs during hospitalization are as follows: WBC count was 17200 with 34% eosinophils (AEC 5854). C-reactive protein, erythrocyte sedimentation rate, immunoglobulin (Ig) E levels, and stool OP were negative. Parasitic workup for *Trichinella*, *Toxocara*, *Strongyloides*, *Ascaris*, and *Entamoeba* all were negative. Echocardiogram, creatinine kinase MD, and troponin levels were normal. Computed tomography scan of chest, abdomen, and pelvis for occult malignancy was negative. A bone marrow aspirate and biopsy was performed, which showed marked eosinophilia in the absence of blasts. Cytogenetic studies showed a translocation between chromosomes 1, 5, and 14. Fluorescence in situ hybridization studies were positive for PDGFRB (5q33.1) consistent with myeloproliferative variant of HES. Flow cytometry was normal.

Case Report 2

A 3-year-old female presented with intermittent abdominal pain and vomiting for 6 weeks. Vomiting, initially

¹Sacred Heart Children Hospital, University of Florida, Pensacola, FL, USA

Corresponding Author:

Vignesh Hebri Nayak, Department of Pediatrics, University of Florida, Sacred Heart Children Hospital, 5151 N 9th Ave, Pensacola, FL 32504, USA.

Email: nayakv86@ufl.edu



started as once per day, then progressed to 2 to 3 times per day, nonbilious, nonbloody, clear, containing food particles. She also had abdominal pain for 6 weeks, diffuse, dull aching, at least once in a day, lasting for several minutes and used to resolve on its own. There is no history of weight loss, loss of appetite, cough, loose stools, photophobia, rash, focal respiratory symptoms, or cardiovascular symptoms. Patient's mother also reports that the child's grandmother is an animal rescuer, who visits animal care with her granddaughter every now and then. They have 3 pet dogs and family denies any history of recent travel.

On physical examination, the patient had nonfocal examination findings, pertinently negative for any lymphadenopathy, rash, abnormal pigmentation, masses or lumps, or evidence of malnutrition, and her systemic examination was within normal limits.

Laboratory findings include WBC count 30900/ μL , with 12% neutrophils, 20% lymphocytes, and 64% of eosinophils (AEC 19770), with normal hemoglobin and platelets. Erythrocyte sedimentation rate was normal, antibodies for celiac disease were negative, complete metabolic panel was normal, mildly elevated amylase 160 U/L, lactate dehydrogenase and uric acid was normal, Pro-Brain natriuretic peptide was normal, electrocardiogram and echocardiogram were normal without any evidence of eosinophilic myocarditis. Stool was negative for ova, cyst, and parasites, antibodies for *Toxocara* and *Strongyloides* were negative, ruling out parasitic causes. Wheat allergen IgE, cow milk allergen, and egg allergen were negative, ruling out allergic causes. Bone marrow biopsy showed marked eosinophilia, absent iron stores, and absent blasts, and flow cytometry was normal, ruling out neoplasms. Immunoglobulins IgA, IgG, IgM, and IgE were normal.

Upper esophagogastroduodenoscopy showed nodularities over antrum and body of the stomach. Stomach biopsy revealed superficial gastric erosions with focal eosinophilia. Ultrasound abdomen was normal and chest X-ray revealed minimal atelectasis at lung bases. She was diagnosed to have Idiopathic HES.

Discussion

Both of our patients presented in a similar way, had gastrointestinal symptoms, and met the diagnostic criteria for HES. However, one of them was diagnosed with idiopathic variant of HES, who was managed supportively, and the other with myeloproliferative variant of HES, who was treated with imatinib. Hence, identifying the type of HE is very important, as treatment and prognosis depend on the disease process.

Eosinophilia has been categorized into mild (AEC 500-1500/ μL), moderate (AEC 1500-5000/ μL), and

severe (AEC >5000/ μL).⁵⁻⁷ Eosinophilia can also be categorized into primary, secondary, and idiopathic. Primary eosinophilia is related to clonal or neoplastic abnormalities of the bone marrow (myeloproliferative/lymphocytic); secondary eosinophilia is caused by infectious (parasitic/fungal infections) or allergic disorders, immunological disorders, or is medication induced; and idiopathic is a diagnosis of exclusion. Hence, whenever a patient presents with HE, keeping a broad differential in mind and ruling out all possible causes are very important.

The exact pathogenesis of HES is not well known. In myeloproliferative form, increased production of eosinophils is a result of mutation in hematopoietic multipotent precursor cells, and in the lymphocytic form, it is due to increased production of at least one eosinophil hematopoietin (IL-3 and/or IL-5).⁸ No matter what the cause for peripheral eosinophilia is, tissue infiltration with eosinophils is next step in the disease process and is responsible for clinical consequences.

Eosinophilic tissue infiltration of gastrointestinal tract can produce various symptoms, which are usually nonspecific. Involvement of mucosal layer can cause nausea, vomiting, diarrhea, malabsorption, protein losing enteropathy; involvement of muscularis layer can cause intestinal obstruction (especially of pylorus); and involvement of serosal layer can cause ascites, abdominal distention.^{9,10}

Reduction of the eosinophil load is the major goal of treatment. Current treatment is based on the pathogenic variant and disease severity. For patients with secondary eosinophilia, treatment is directed toward the causative agent. For patients with idiopathic HES, who are asymptomatic or have no evidence of organ dysfunction, despite high AEC, will not need any treatment, but has to be under a close follow-up for every 3 to 6 months. In patients with organ involvement, initial therapy is with prednisone (1-2 mg/kg/day). If the patient does not respond to steroids or for corticosteroid sparing purposes, other immunomodulating agents can be tried, which includes hydroxyurea, interferon alpha, and imatinib.^{11,12}

For patients with myeloproliferative variant of HES, imatinib is the recommended initial treatment. For lymphocytic variant of HES, corticosteroids are first-line therapy. For patients who do not respond to corticosteroids, second-line drugs such as interferon-alpha, hydroxyurea, and imatinib are recommended.^{4,13,14}

Our patient with idiopathic HES was managed supportively with pantoprazole and zofran. She was followed-up with monthly complete blood count. Her eosinophil counts gradually decreased and returned to normal in 4 months; and for the patient with myeloproliferative HES, she was started on imatinib, initially, 400

mg PO once a day but had to be decreased to 100 mg over a period of time, as she had severe neutropenia. Her eosinophil counts returned to normal in a month. She had a bone marrow aspiration and biopsy done recently, which showed no evidence of PDGFRB mutation, but had 1/20 cells showing translocation of 1, 5, and 14. She continues to take imatinib, is on close follow-up, and her eosinophil counts are within normal limits.

Conclusion

As eosinophilia can be an incidental finding in many of our patients, identifying hypereosinophilia and hypereosinophilic syndrome is key in early diagnosis and management, as it can affect almost all the organs and if missed can prove fatal to the patient.

Author Contributions

VHN: Contributed to conception and design; contributed to acquisition, analysis, and interpretation; drafted manuscript; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.

NYE: Contributed to design; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.

JJB: Contributed to design; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.

PA: Contributed to design; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

References

- Hardy WR, Anderson RE. The hypereosinophilic syndrome. *Ann Intern Med.* 1968;68:1220-1229.
- Chusid MJ, Dale CD, West BC, Wolff SM. The hypereosinophilic syndrome: analysis of fourteen cases with review of the literature. *Medicine (Baltimore).* 1975;54:1-27.
- Valent P, Klion AD, Horny HP, et al. Contemporary consensus proposal on criteria and classification of eosinophilic disorders and related eosinophilic disorders and related syndromes. *J Allergy Clin Immunol.* 2012;130:607-612.
- Gotlieb J. World Health Organization-defined eosinophilic disorders: 2014 update on diagnosis, risk stratification, and management. *Am J Hematol.* 2014;86:325-337.
- Brigden M, Graydon C. Eosinophilia detected by automated blood cell counting in ambulatory North American outpatients. Incidence and clinical significance. *Arch Pathol Lab Med.* 1997;121:963-967.
- Rothenberg ME. Eosinophilia. *N Engl J Med.* 1998;338:1592-1600.
- Pardnani A, Patnaik MM, Tefferi A. Eosinophilia: secondary, clonal and idiopathic. *Br J Haematol.* 2006;133:468-492.
- Simon HU, Rothenberg ME, Bochner BS, et al. Redefining the definition of hypereosinophilic syndrome. *J Allergy Clin Immunol.* 2010;126:45-49.
- Heine RG. Pathophysiology, diagnosis and treatment of food protein induced gastrointestinal disease. *Curr Opin Allergy Clin Immunol.* 2004;4:221-229.
- Ngo P, Furuta G, Burks W. The pathobiology of eosinophilic gastroenteritis of childhood: is it really the eosinophil, allergic mediated, or something else. *Curr Gastroenterol Rep.* 2004;6:436-440.
- Fauci AS, Harley JB, Roberts WC, Ferrans VJ, Gralnick HR, Bjornson BH. NIH conference. The idiopathic hypereosinophilic syndrome. Clinical, pathophysiologic, and therapeutic considerations. *Ann Intern Med.* 1982;97:78-92.
- Rothenberg ME, Klion AD, Roufousse FE, et al. Treatment of patients with the hypereosinophilic syndrome with mepolizumab. *N Engl J Med.* 2008;358:1215-1228.
- David M, Cross NC, Burgstaller S, et al. Durable responses to imatinib in patients with PDGFRB fusion-gene positive and BCRABL: negative chronic myeloproliferative disorders. *Blood.* 2007;109:61-64.
- Muller AM, Martens UM, Hofmann SC, Bruckner-Tuderman L, Mertelsmann R, Lubbert M. Imatinib mesylate as a novel treatment option for hypereosinophilic syndrome: two case reports and a comprehensive review of the literature. *Ann Hematol.* 2006;85:1-16.