Published in final edited form as:

J Allergy Clin Immunol Pract. 2015 ; 3(2): 304–305. doi:10.1016/j.jaip.2014.09.024.

Difficult Cases: Hypereosinophilic Disorders

Princess Ogbogu, MD and

The Ohio State University Wexner Medical Center, 473 W. 12th Avenue, 201 DHLRI, Suite 201,
Columbus, OH 43210, (614) 293-7546

Amy D. Klion, MD

Laboratory of Parasitic Diseases, NIAID, NIH, Bethesda, MD

Princess Ogbogu: Princess.ogbogu@osumc.edu

Keywords

eosinophil; hypereosinophilic syndrome; FIP1L1-PDGFR α

A 36 year old man presented to his local emergency department with complaints 19 of acute onset vertigo and chest discomfort. He underwent evaluation which was remarkable for a normal electrocardiogram, negative serum troponin levels, and abnormal complete blood count revealing an absolute eosinophil count (AEC) of 12,400 (nl <500 cells/ μ l). He was admitted to the hospital for evaluation of pre-syncope and hypereosinophilia. His hospital evaluation revealed a normal repeat EKG, echocardiogram with normal ejection fraction (65%) and mild diastolic dysfunction. A cardiac stress test was normal. Bone marrow biopsy revealed hypercellularity with marked eosinophilia, eosinophil dysplasia, and no increase in blasts. No cytogenetic abnormalities were detected, and evaluation for mutations in *PDGFRA*, *PDGFRB*, and *JAK2* were negative. Stool examinations were negative for ova and parasites. Repeat laboratory evaluation confirmed an elevated AEC of 12,000 cells/ μ l and did not identify any other significant abnormalities. He was discharged home with no specific therapy. He presented 3 months later with worsening chest discomfort and pressure. His AEC remained elevated at 11,380 cells/ μ l. His EKG now revealed T wave inversions in the anterior leads. CT scans of the chest, abdomen, and pelvis were obtained and were remarkable for interstitial lung changes, bilateral lung nodules, mediastinal lymphadenopathy, and splenomegaly. Pulmonary function tests showed a restrictive pattern with diffusion defect, and transbronchial biopsies showed patchy interstitial fibrosis without evidence of vasculitis. Cytology was negative for malignancy. Further laboratory evaluation revealed unremarkable peripheral blood lymphocyte immunophenotyping, polyclonal T cell receptor rearrangement, elevated serum vitamin B12 (1725, (nl 180-914 ng/L), and elevated serum tryptase level 17.1 (nl <11.5 ng/ml). He was treated with high dose steroids (1mg/kg

© 2014 Published by American Academy of Allergy, Asthma and Immunology.

Correspondence to: Princess Ogbogu, Princess.ogbogu@osumc.edu.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

solumedrol) and referred for further evaluation. On repeat evaluation, the AEC was 8640/ μ l. He was started empirically on imatinib 400 mg daily and a prednisone taper was initiated. Within 1 week of starting imatinib, his AEC normalized. Repeat testing for *FIP1L1-PDGFR*A returned positive. After 6 months, his imatinib dose was tapered to 100 mg daily, and the patient has remained stable since that time.

Discussion

This patient presented with marked eosinophilia and cardiac complaints. His clinical manifestations (cardiac involvement, pulmonary fibrosis, and splenomegaly) coupled with his laboratory findings (elevated serum vitamin B12 and tryptase levels and a hypercellular bone marrow with dysplastic eosinophils and spindle-shaped mast cells) were most consistent with myeloproliferative variant hypereosinophilic syndrome (MHES).¹ The most common cause of MHES is an interstitial deletion in chromosome 4 leading to the imatinib-sensitive fusion tyrosine kinase, *FIP1L1-PDGFR*A.² Although prednisone is the first line therapy for most forms of HES, *PDGFR*A-positive disease is typically steroid-refractory and should be treated with imatinib.^{1–4} Since MHES with cardiac involvement is life threatening, imatinib therapy should be initiated irrespective of results of testing for *FIP1L1-PDGFR*A if this diagnosis is strongly suspected. Concomitant steroids should be given in the setting of an elevated serum troponin or other evidence of eosinophilic myocarditis to prevent myocardial necrosis, a rare complication of imatinib therapy in patients with HES.⁵

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

This work was funded by the Division of Intramural Research, NIAID/NIH

References

1. Klion AD, Noel P, Akin C, et al. Elevated serum tryptase levels identify a subset of patients with a myeloproliferative variant of idiopathic hypereosinophilic syndrome associated with tissue fibrosis, poor prognosis, and imatinib responsiveness. *Blood*. 2003; 101(12):4660–6. [PubMed: 12676775]
2. Cools J, DeAngelo DJ, Gotlib J, et al. A tyrosine kinase created by fusion of the *PDGFR*A and *FIP1L1* genes as a therapeutic target of imatinib in idiopathic hypereosinophilic syndrome. *N Engl J Med*. 2003 Mar 27; 348(13):1201–14. [PubMed: 12660384]
3. Ogbogu PU, Bochner BS, Butterfield JH, et al. Hypereosinophilic syndrome: a multicenter, retrospective analysis of clinical characteristics and response to therapy. *J Allergy Clin Immunol*. 2009 Dec; 124(6):1319–25. [PubMed: 19910029]
4. Simon HU, Klion A. Therapeutic approaches to patients with hypereosinophilic syndromes. *Semin Hematol*. 2012 Apr; 49(2):160–70. [PubMed: 22449626]
5. Ogbogu PU, Rosing DR, Horne MK 3rd. Cardiovascular manifestations of hypereosinophilic syndromes. *Immunol Allergy Clin North Am*. 2007 Aug; 27(3):457–75. [PubMed: 17868859]