Diagnostic Snapshot

A Patient With Gastrointestinal Symptoms and Eosinophilia

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Authors' disclosures of conflicts of interest are found at the end of this article.
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HISTORY

Mr. C, a 63-year-old Cape Verdean male, was referred to the hematology/oncology office for evaluation of eosinophilia in May 2017. The eosinophilia was first documented in December 2003 by his primary care provider. In March 2005, Mr. C underwent colonoscopy for mild rectal bleeding and was incidentally found to have eosinophilic colitis. Stool ova and parasite testing was negative. Because he was asymptomatic at the time, no treatment was initiated.

One year later (2006), Mr. C developed dyspepsia in the presence of continued eosinophilia. An upper endoscopy with biopsy was performed, revealing *Helicobacter pylori*–positive chronic active gastritis. He was treated with a 14-day course of triple therapy. Follow-up *H. pylori* antigen stool test was negative.

In April 2017, Mr. C developed recurrent abdominal pain for which an endoscopy and colonoscopy were performed. Biopsies of the cecum, splenic flexure, and sigmoid colon were significant for eosinophilic infiltrates. A complete blood count demonstrated eosinophilia with normal hemoglobin, white blood cell, and platelet counts. Stool testing using an extended gastrointestinal panel was unremarkable. It was at this time that Mr. C was referred to hematology/oncology.

Past medical history was significant for diabetes, hypertension, and hyperlipidemia. Mr. C did not have a history of asthma or food/drug allergies. His medications included amlodipine at 25 mg, aspirin at 325 mg, glipizide at 5 mg, metformin at 1,000 mg, and pravastatin at 80 mg. A review of systems revealed that Mr. C was negative for any fevers, night sweats, weight loss, rash/pruritus, dyspnea, or diarrhea. A physical exam showed normal vital signs, no palpable adenopathy, normal cardiopulmonary exam, no hepatosplenomegaly, no palpable masses, and no skin rashes or nodules. A computed tomography scan of the chest, abdomen, and pelvis was unremarkable. No adenopathy, masses, or hepatosplenomegaly were noted. Mr. C's labs are shown in Tables 1 and 2.

DIFFERENTIAL DIAGNOSIS

WHICH IS THE CORRECT DIAGNOSIS?

A. An underlying malignancy
B. Idiopathic hypereosinophilic syndrome
C. Helminthic infection
D. A drug hypersensitivity or other allergic disorder

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Table 1. Results of Bloodwork

Lab	Reference range	Value
WBC	3.5–11.0 x 10^9/L	9
RBC	4.2–5.5 x 10^{12}/L	4.87
Hemoglobin	13.5–16.0 g/dL	16
Hematocrit	37.0%–47.0%	46.1
Platelets	150–400 x 10^9/L	215
Neutrophils	1.5–7.5 x 10^9/L	1.3
Lymphocytes	1.0–4.0 x 10^9/L	2.3
Monocytes	0.2–0.8 K/µL	0.4
Eosinophils	0.0–0.5 K/µL	4.9
Basophils	0.0–0.2 x 10^9/L	0.1
IgE	3.0–209.0 IU/mL	481.1
JAK2	Negative	Negative
BCR-ABL	Negative	Negative
PDGFRα	Negative	Negative
Tryptase	Negative	Negative
Clonal T-cell gene rearrangement	Negative	Negative

Note. Red indicates value is out of reference range.
WBC = white blood count; RBC = red blood count; MPV = mean platelet volume; IgE = immunoglobulin E.

Table 2. Stool Cary-Blair Extended Gastrointestinal Polymerase Chain Reaction Panel

Micro-organism	Value
Campylobacter spp.	Negative
Clostridium difficile toxin A/B	Negative
Plesiomonas shigelloides	Negative
Salmonella spp.	Negative
Vibrio spp.	Negative
Vibrio cholerae	Negative
Yersinia spp.	Negative
Enteroaggregative *Escherichia coli* (EAEC)	Negative
Enteropathogenic *E. coli* (EPEC)	Negative
Enterotoxigenic *E. coli* (ETEC)	Negative
Shiga toxin	Negative
E. coli O157	Negative
Shigella/Enteroinvasive *E. coli* (EIEC)	Negative
Cryptosporidium spp.	Negative
Cyclospora cayetanensis	Negative
Entamoeba histolytica	Negative
Giardia	Negative
Adenovirus F 40/41	Negative
Astrovirus	Negative
Norovirus GI/GII	Negative
Rotavirus A	Negative
Sapovirus	Negative

DIFFERENTIAL DIAGNOSIS

A An Underlying Malignancy. Some cancer cells are capable of secreting factors that stimulate the proliferation of polyclonal eosinophils. This is more commonly seen in advanced stage solid tumor disease (lung, gastrointestinal, and ovarian), but it can also precede other clinical manifestations of an occult neoplasm, sometimes by many years (Falchi & Verstovsek, 2015; Klion, 2015). Eosinophilia may also be seen in myeloid and lymphoid disorders. The 2016 World Health Organization (WHO) classification system of hematopoietic and lymphoid tissues includes a special category for myeloid and lymphoid disorders with eosinophilia that is associated with specific molecular genetic rearrangements (Daniel et al., 2016; Table 3). Treatment of eosinophilia in these patients should follow disease-specific guidelines.

B Idiopathic Hypereosinophilic Syndrome. There are a number of autoimmune disorders that may be associated with hypereosinophilia (Table 4). Among these, idiopathic hypereosinophilia syndrome is a diagnosis of exclusion in patients with an absolute eosinophil count > 1,500/µL and evidence of end-organ damage. For most patients, corticosteroids remain the mainstay of treatment.

C Helminthic Infection. Various infections can cause eosinophilia, the most common being strongyloidiasis (Table 5). Infected patients treated with steroids are at increased risk of developing hyperinfection syndrome (gastrointestinal signs and symptoms attributable to increased larval migration); therefore, it is extremely important to rule out infection with *Strongyloides stercoralis* by serologic testing (Klion, 2015; O'Connell & Nutman, 2015).

D A Drug Hypersensitivity or Other Allergic Disorder. Eosinophilia is known to be associated

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Table 3. Molecular Attributes Associated With Myeloid/Lymphoid Neoplasms With Eosinophilia

- PDGFRA rearrangement
- PDGFRB rearrangement
- FGFR1 rearrangement
- PCM1-JAK2

with allergic disorders (Table 6). Generally, the eosinophil count is less than 1,500/µL in these settings (Curtis & Ogbogu, 2015).

CLINICAL MANAGEMENT

Given this patient's unremarkable workup, he was placed on a 10-day course of mebendazole to rule out chronic infestation of an intestinal nematode. Eosinophilia persisted posttreatment, and it was felt he most likely had low-risk eosinophilia syndrome. He was placed on prednisone at 30 mg twice daily for 1 month with a plan to taper after. When he returned to clinic 1 month later, he was found to be hyperglycemic, with reported blood sugars as high as 500 mg/dL. To compensate for this, Mr. C had reduced his prednisone to 20 mg twice daily and was self-titrating his oral diabetes medications. Management of his antiglycemic medications was relegated to his primary care provider. Once his sugars were controlled, the prednisone taper was initiated. Unfortunately, his eosinophilia began to rise. Serologic testing for strongyloidiasis was performed and found to be positive. Mr. C was treated with ivermectin at 18 mg once daily for 2 days, resulting in a complete resolution of eosinophilia.

Table 4. Autoimmune Disorders Associated With Eosinophilia

- Connective tissue disorders
- Inflammatory bowel disease
- Sarcoidosis

DISCUSSION

Strongyloidiasis is caused by infection with *Strongyloides stercoralis,* a helminth found primarily in the tropics and subtropics. Most patients are infected by exposure to contaminated soil when residing in endemic areas (Mejia & Nutman, 2012). In the United States, strongyloidiasis is often seen in socioeconomically disadvantaged persons, institutionalized populations, and rural communities. Risk factors for infection include walking with bare feet, contact with human sewage or waste, and occupations such as farming and coal mining (Centers for Disease Control and Prevention, 2019).

Manifestations of infection range from asymptomatic eosinophilia in the immunocompetent host to disseminated disease and septic shock in the immunocompromised host. Although corticosteroids remain the first line of therapy for most forms of hypereosinophilic syndromes (Klion, 2015), they have a particularly strong and specific

Table 5. Infections Associated With Eosinophilia

Type	Organisms
Helminth	*Strongyloides stercoralis; Ancylostoma duodenale; Ascaris lumbricoides; Toxocara canis; Toxocara cati; Trichinella; Schistosomiasis*
Ectoparasite	*Sarcoptes scabiei; Dermatobia hominis*
Protozoan	*Cystoisospora belli; Sarcocystis hominis*
Bacterial	*Mycobacterium tuberculosis; Streptococcus pyogenes*
Fungal	*Coccidioides; Aspergillus*

association with the development of hyperinfection syndrome and dissemination in strongyloidiasis. Oral ivermectin at 200 µg/kg for 2 days remains the treatment of choice for uncomplicated *Strongyloides* infection (Suputtamongkol, 2011). For symptomatic hypereosinophilia unrelated to strongyloidiasis, steroids should be initiated immediately to avoid end-organ damage.

Table 6. Allergic Disorders Associated With Eosinophilia

- Atopic dermatitis
- Allergic rhinitis
- Asthma
- Eosinophilic esophagitis
- Drug hypersensitivity

IMPLICATIONS FOR THE AP

As an advanced practitioner in oncology, familiarity with the phenomenon of eosinophilia is necessary. Eosinophilia is defined as an increase in the peripheral absolute eosinophil count (AEC). Eosinophilia is categorized as mild (AEC 500–1,500/µL), moderate (AEC 1,500–5,000/µL), and severe (AEC > 5,000/µL). Hypereosinophilia is defined as moderate to severe eosinophilia (Falchi & Verstovsek, 2015).

Although the underlying cause is not always hematologic/oncologic in nature, patients with isolated eosinophilia are frequently referred to the hematologist/oncologist's office for workup. While not an uncommon finding, eosinophilia can be difficult to diagnose due to its broad differential, ranging from allergic reaction to malignant neoplasm. As with the case described here, the eosinophilia may be present for years. In some cases, patients with eosinophilia may experience severe or life-threatening end-organ damage due to tissue eosinophil infiltration. Therefore, a broad differential diagnosis is critical to exclude an underlying malignancy.

If a hematologic malignancy is suspected, a bone marrow aspiration and biopsy should be performed as part of the workup. Appropriate scenarios include an acutely ill patient, an AEC > 1,500/uL or signs of eosinophilic organ involvement without an obvious cause identified from initial testing, and abnormal features on the peripheral blood smear (e.g., immature or dysplastic white blood counts, thrombocytopenia, or anemia). Patient demographics, travel history, symptoms, physical findings, duration of eosinophilia, and degree of eosinophilia must all be considered. For patients without an underlying malignancy, a referral should be made to the appropriate subspecialist. ●

Disclosure

The authors have no conflicts of interest to disclose.

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