

A 68-year old woman with asymptomatic hypereosinophilia

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ABSTRACT

Eosinophilia is known to have a wide variety of etiologies including atopic diseases, infections, endocrine abnormalities, hematologic/neoplastic causes, and certain immunodeficiency disorders. In contrast, hypereosinophilic syndromes refer to a group of heterogeneous disorders with persistent eosinophilia and organ involvement. The treatment of eosinophilia varies widely based on its etiology and therefore should be evaluated thoroughly at onset. We present the case of a 68-year-old woman with isolated asymptomatic hypereosinophilia.

(Allergy Asthma Proc 35:495–497, 2014; doi: 10.2500/aap.2014.35.3775)

CASE PRESENTATION

Chief Complaint

Hypereosinophilia noted on complete blood count.

History of Present Illness

A 68-year-old woman was seen and evaluated for new-onset hypereosinophilia. The patient had a history of anemia of chronic kidney disease with stage 2 chronic renal failure. She had monthly complete blood counts drawn for routine monitoring of her anemia and was told that her two most recent evaluations were significant for hypereosinophilia. She denied any history of allergic rhinitis, asthma, food allergies, or eczema. She also denied any new symptoms of rhinorrhea, nasal congestion, conjunctival erythema, or epiphora. She denied any recent international travel. She had recently developed constipation and had started a natural supplement to treat this symptom. None of her prior medications had changed in color or size to suspect a change in manufacturer. On review of systems she denied any joint pains, skin changes, fevers, night sweats, shortness of breath, orthopnea, chest pain, edema of the extremities, weight loss, or lymphadenopathy.

Physical Examination

Vital signs were within normal limits. The patient was a healthy-appearing woman with clear conjunctivae and nasal passages with normal pink turbinates.

Her lungs were clear without wheezes, rales, or rhonchi. There was no lymphadenopathy or hepatosplenomegaly. Cardiac exam revealed regular rate and normal rhythm. Skin examination did not show any urticaria, dermatitis, or angioedema.

Laboratory Findings

Regular blood counts showed a progressive eosinophilia beginning with an absolute eosinophil count of 497 rising steadily over several weeks to its peak of 6413 cells/ μ L (Fig. 1). Hemoglobin was 10.2 g/dL and hematocrit was 29.8%. Serum creatinine was found to be 1.3 mg/dL. In addition, fluorescence in situ hybridization analysis of serum was performed with 0% deletion for CHIC2.

QUESTION 1

What is the differential diagnosis of these symptoms?

- a. Atopic disease
- b. Parasitic infection
- c. Hypereosinophilic syndrome
- d. Drug hypersensitivity
- e. Hematologic disorders

QUESTION 2

What additional laboratory data or investigations would be helpful in arriving at a diagnosis in this patient?

Given the patient's denial of constitutional symptoms, organomegaly, and otherwise normal complete blood count and metabolic panel, further investigation of all current medications should be sought, prescription as well as nonprescription. In addition, studies to assess organ function should be performed including liver function tests, renal function tests, urinalysis, and

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The authors have no conflicts of interest to declare pertaining to this article

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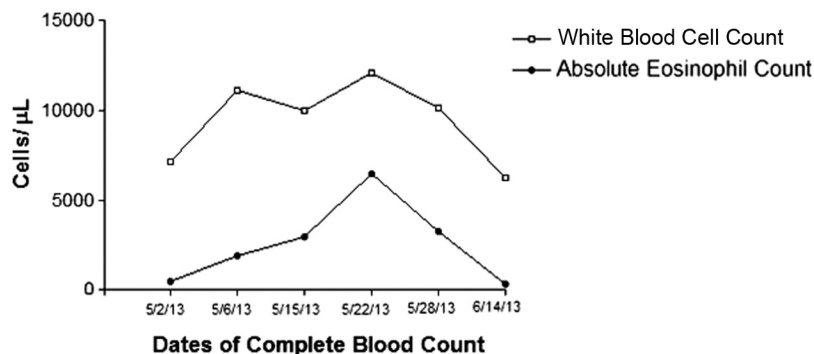


Figure 1.

chest radiograph. If no other cause for eosinophilia can be determined, bone marrow aspirate and biopsy may need to be performed to fully assess the underlying etiology. Analysis should also be performed for FIP1L1-PDGFRα fusion transcript to assess for chronic eosinophilic leukemia, which is highly responsive to tyrosine kinase inhibitors.¹

Clinical Course

During the course of the initial patient interview, she disclosed that she felt that the newest formulation of the supplement “was different.” Although she had been on this supplement for a few months, on starting a new bottle, it began to cause diarrhea rather than normal bowel movements. Therefore, the patient was advised to stop using the natural supplement “Gentle Senna,” (Health Concerns, Oakland, CA) which she had used to treat her constipation. “Gentle Senna” is a product made by Health Concerns and is advertised as being helpful for constipation and digestion. Serial blood counts showed a prompt reduction in eosinophilia, which ultimately returned to the normal range.

The patient’s anemia remained present and appeared to be unrelated to her eosinophilia.

DISCUSSION

Complementary and alternative medicine (CAM) includes multiple categories of which herbal supplements are a subset.² The use of CAM has increased in recent years and it is estimated that ~42% of adults use some form of CAM. Considering that the majority of CAM is paid out-of-pocket, annual spending for CAM is estimated at >\$30 billion.³ Herbal supplements specifically are being used for a myriad of ailments ranging from osteoarthritis to side effects from chemotherapy.

Per the Dietary Supplement Health and Education Act of 1994, herbs are classified as dietary supplements and therefore can be marketed and sold without first establishing safety and efficacy. An analysis of 25 commercially available ginseng products found significant variation in the concentration of two ingredients thought to be biologically active.⁴ When DNA barcoding was used to verify the presence of active ingredi-

ents in dietary supplements, it was found that only 2 of 12 companies had products without any substitution or fillers and that most products contained additional ingredients not listed on the label.⁵ A much more concerning report looked at contamination with heavy metals and pesticides in samples of Chinese herbal medicines. This study found that pesticides were detectable in 36.7% of samples and at least one metal was found in all samples.⁶ The poorly regulated nature of this industry makes it likely that alternative treatments could contribute to otherwise unexplained eosinophilia. A prior study had found that up to 70% of patients who use unconventional therapies did not inform their medical doctor, which reinforces the need to take a thorough history when evaluating patient eosinophilia.⁷ If there is suspicion for an adverse event that occurs as the result of a contaminated dietary supplement, a voluntary report should be filed with the U.S. Food and Drug Administration through their online website.

Eosinophilia is defined as >450 eosinophils/μL measured in peripheral blood. Eosinophils are found predominantly in peripheral tissues with a mucosal–environmental interface, such as those seen in the respiratory, gastrointestinal, and lower genitourinary tracts. Worldwide, the most common cause of eosinophilia is helminthic infection, followed by drug hypersensitivity and atopic diseases.⁸ It is known that there are instances of eosinophilic syndrome occurring with supplements or their contaminants. Examples of these include L-tryptophan, which led to eosinophilia–myalgia syndrome as well as Spanish toxic oil syndrome.⁹ There have also been reports of eosinophilia (without evidence of end organ damage) with use of echinacea.¹⁰ More recently, there have been two case reports of eosinophilia with mononeuritis multiplex and necrotizing vasculitis in association with use of nonprescription probiotics.¹¹

It is crucial in eosinophilia to immediately evaluate the presence of end-organ involvement, the most serious consequence of hypereosinophilic syndrome.¹² If suspected, the patient needs rapid multidisciplinary evaluation and initial treatment with systemic steroids. If there is concern about strongyloidiasis, which is

endemic in the southeastern United States, then an empiric single dose of ivermectin should also be considered because *Strongyloides* hyperinfection caused by systemic steroids can be fatal.

To our knowledge, this is the first reported case of eosinophilia occurring with the combined herbal supplement, sold under the name "Gentle Senna." It is unknown which herbal component led to the eosinophilia or whether a contaminant in the product was the culprit. This case exemplifies the importance of taking a thorough history when evaluating cases of isolated eosinophilia and educating patients on potential adverse effects of nonregulated herbal supplementation.

Final Diagnosis

Hypereosinophilia is associated with an herbal supplement.

SUMMARY

Seemingly harmless health supplements can be the rare cause of eosinophilia and should be fully evaluated for when approaching a patient with new-onset, isolated eosinophilia.

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