MAYO CLINIC

65-Year-Old Woman With Chronic Eosinophilia

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A 65-year-old Cambodian woman presented to clinic for a general medical examination. Aside from chronic constipation associated with mild abdominal pain, she felt well. Review of her records revealed a 2-decade history of normocytic anemia and mild eosinophilia, both of unknown etiology, and 7 years of worsening kidney function, with her most recent creatinine suggesting chronic kidney disease stage 3. She had no other significant medical history. Labs were notable for normal electrolytes. Her medications included calcium, vitamin D, and vitamin B_{12} supplements for previous diagnoses of osteopenia and vitamin B_{12} deficiency.

Her median absolute eosinophil count (AEC) over the past 2 decades was 0.72 × 10^9/L (range, 0.24-1.33 ×10^9/L; normal range, 0.05-0.5 ×10^9/L), meeting the definition of mild eosinophilia. Seven years before her current presentation she had undergone a screening colonoscopy that revealed focal cecal erythema with biopsies showing increased eosinophil count. Given these findings and her peripheral eosinophilia, she was evaluated by hematology and gastroenterology. Over the course of 2 months, 2 separate stool ova and parasite examinations were obtained, both of which were negative. An esophagogastroduodenoscopy was performed, and biopsies showed numerous *Helicobacter pylori*, for which she completed triple therapy consisting of lansoprazole, amoxicillin, and clarithromycin. Because of concern for a hematologic malignancy, a computed tomography of the chest, abdomen, and pelvis was performed and was negative, and a JAK 2 test was obtained and was also negative. There were plans to send her to allergy clinic; however, she did not show up for that visit. She was lost to follow-up until 3 years before presentation, when she was seen again by hematology, and a serum protein electrophoresis was obtained to investigate the cause of her chronic normocytic anemia and worsening kidney disease. This showed reactive polyclonal hypergammaglobulinemia. No further evaluation of her eosinophilia was undertaken before her current presentation, at which time her AEC was 0.83 × 10^9/L (normal range, 0.05-0.5 × 10^9/L). She had no complaints and physical examination was unremarkable. She denied atopic symptoms.

1. Which *one* of the following is the next *best* step in managing this patient's eosinophilia?

a. Continue to monitor
b. Investigate for a primary (clonal) cause
c. Investigate for a secondary (reactive) cause
d. Diagnose her with idiopathic hypereosinophilic syndrome
e. Investigate for familial eosinophilia

Although patients with an AEC below 1.5 × 10^9/L and no signs or symptoms of organ involvement can be monitored, this patient has worsening kidney function with no clear cause.[1] In addition, she is an immigrant from an area where parasites are endemic, necessitating further evaluation.[2] Causes of eosinophilia can be defined as primary (clonal) or secondary (polyclonal, or reactive), a classification distinguished by whether eosinophils are central to the underlying disorder. Before investigating for primary causes, which generally involve a hematopoietic stem cell mutation, secondary causes should be investigated, with specific testing guided by details of the history and physical examination. Secondary causes commonly include drug reactions in the developed world and helminthic infections in the developing world. Diagnoses of idiopathic hypereosinophilic syndrome (HES) would not be accurate because it is a diagnosis of exclusion and her AEC does not meet the diagnostic criteria of being more than 1.5 × 10^9/L.[1] Familial eosinophilia is unlikely in this patient with no known family history, because it is a very rare typically autosomal-dominant condition,

See end of article for correct answers to questions.

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and should not be considered until primary and secondary causes have been excluded.[3] Because our patient had not yet been fully worked-up, and given that she had worsening creatinine of unknown cause and was an immigrant from Cambodia, she should be investigated for secondary causes.

2. Which *one* of the following is the *best* next step in the management of this patient?

a. Stop her calcium supplement and follow-up an eosinophil count in 1 month
b. Check troponins
c. Obtain echocardiogram
d. Obtain pulmonary function tests
e. Obtain skin biopsy

Obtaining a thorough medication history, including supplements and herbal therapies, is very important, because drugs are one of the most common causes of eosinophilia in the developed world. This patient is on a limited number of supplements, and calcium has not been found to cause eosinophilia. Therefore, stopping this supplementation would likely not impact her eosinophilia. Checking troponins would be the appropriate next step. Eosinophilia can cause end-organ damage, commonly in the cardiovascular system, and evaluating for this damage is important in approaching a patient with eosinophilia. The presence of organ damage can dictate urgency of therapy and evaluation. If troponins are elevated, an echocardiogram and electrocardiogram should be obtained. Our patient had recently undergone workup for lightheadedness that included a normal echocardiogram. Given this, suspicion for cardiac involvement was low and troponins were not checked. Other recommended tests to evaluate for end-organ damage include a chest x-ray and creatinine. Pulmonary function tests can also be used; however, they are indicated only in those cases in which there is suspicion for lung involvement, which was not the case for our patient. Although skin is a common target for eosinophil infiltration, a biopsy should only be obtained in the setting of symptoms or signs. With no indications of organ involvement, we felt comfortable starting off with more limited and targeted testing.

3. Which *one* of the following is the *most* likely etiology for her chronic mild eosinophilia?

a. Malignancy
b. Addison's disease
c. Helminthic infection
d. Allergies
e. Churg-Strauss syndrome

The answers listed above include secondary causes of eosinophilia. Investigation into specific secondary causes should be guided by the patient's history and physical examination. Although malignancy is a concerning possibility, the patient's stability and lack of symptoms over 2 decades makes this unlikely. Although there can be a delay in diagnosing Addison's disease, this patient does not have any symptoms, her vitals are stable, and her electrolyte panel is normal, making this disease unlikely. A helminthic infection is the most likely etiology, specifically *Strongyloides*, which is one of the few parasites that can establish a chronic, and sometimes lifelong, infection.[2,4] Chronic strongyloidiasis can be asymptomatic, and 10% to 70% of the cases have eosinophilia.[2] Allergies can also cause a chronic low-grade eosinophilia; however, this patient denied atopic symptoms. Churg-Strauss syndrome is unlikely because this typically causes, unlike in this patient, a higher grade eosinophilia. There was, therefore, a high suspicion that this patient had a helminthic infection, likely strongyloidiasis.

4. Which *one* of the following is the next *best* test to obtain?

a. *Strongyloides* serology
b. Colonoscopy
c. Stool ova and parasite examination
d. *Ascaris* serology
e. *Schistosoma* serology

Specific testing for various parasitic infections should be guided by the patient's exposures, symptoms, and history. All patients from areas where *Strongyloides* is endemic (such as Cambodia) should be tested with a *Strongyloides* serology. In addition, *Strongyloides* is one of the few parasites that could cause 2 decades of eosinophilia.[4] Serology is the preferred test in chronic infection, and has a high sensitivity and specificity for the