Eosinophilia

Anna Kovalszki, MD[a,*], Peter F. Weller, MD[b]

KEYWORDS

• Eosinophilia • Asthma • Eosinophilic gastrointestinal disease • Drug allergy
• Parasitic disease • Hypereosinophilic syndromes

KEY POINTS

- Eosinophilia is an elevation in the total number of bloodstream eosinophils, can be transient or sustained, and can exist in milder versus more significant levels.
- Sustained and significant eosinophilia in the 1500 cells/μL or above range, without clear cause, should prompt evaluation.
- Processes known to cause modest eosinophilia include allergic disease, parasitic disease, drug allergy, and mastocytosis.
- More significant eosinophilia is often caused by drug allergy, aspirin exacerbated respiratory disease, sustained and significant atopic dermatitis, and some parasitic disorders.
- If no apparent cause of the eosinophilia is known and levels above 1500 cells/μL exist for greater than 1 month, an exhaustive search guided by clinical presentation should ensue.

INTRODUCTION

Eosinophilia represents an increased number of eosinophils in the tissues and/or blood. Although enumeration of tissue eosinophil numbers would require examination of biopsied tissues, blood eosinophil numbers are more readily and routinely measured. Hence, eosinophilia is often recognized based on an elevation of eosinophils in the blood. Absolute eosinophil counts exceeding 450 to 550 cells/μL, depending on laboratory standards, are reported as elevated. Percentages generally above 5% of the differential are regarded as elevated in most institutions, although the absolute count should be calculated before a determination of eosinophilia is made. This is done by multiplying the total white cell count by the percentage of eosinophils.

Eosinophils are bone marrow–derived cells of the granulocyte lineage. They have an approximate half-life of 8 to 18 hours in the bloodstream, and mostly reside in tissues[1] where they can persist for at least several weeks. Their functional roles are

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[a] Allergy and Inflammation, Beth Israel Deaconess Medical Center, Harvard Medical School, One Brookline Place Suite 623, Brookline, MA 02445, USA; [b] Allergy and Inflammation, Department of Medicine, Beth Israel Deaconess Medical Center, Harvard Medical School, CLS Building, Room 943, 330 Brookline Avenue, Boston, MA 02215, USA
* Corresponding author.
E-mail address: akovalsz@bidmc.harvard.edu

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multifaceted and include antigen presentation; the release of lipid-derived, peptide, and cytokine mediators for acute and chronic inflammation; responses to helminth and parasite clearance through degranulation; and ongoing homeostatic immune responses. They can be part of the overall cellular milieu in malignant neoplasms and autoimmune conditions, and connective tissue disorders, and are also found in less well characterized entities as described elsewhere in this paper.

The approach to eosinophilia is largely based on clinical history. Often, a few aspects of a case alert the clinician as to the likely underlying cause of abnormally elevated eosinophils. However, at times, more significant investigations need to occur to more clearly define the cause of their presence and possible role in disease presentation.

Eosinophilia → 450 to 550 cells/μL in the blood stream

Allergic Sensitization

Mild eosinophilia is present often in patients with allergic disease (<1500 cells/μL will be used for the definition of mild, whereas hypereosinophilic syndromes, defined elsewhere in the article, are generally considered with sustained eosinophilia > 1500 cells/μL[2]). Allergic rhinitis and asthma often produce a mild eosinophilia. Atopic dermatitis may produce a more significant eosinophilia if affecting a large part of the body and if associated with significant atopy. Eosinophilic esophagitis as well as other eosinophilic gastrointestinal diseases can cause a mild peripheral eosinophilia.

Chronic sinusitis, especially of the polypoid variety seen in aspirin-exacerbated respiratory disease, produces a more robust eosinophilic response that can be in the mild to moderate range. Often these patients start with nasal allergies and asthma, but then develop abnormal arachidonic acid metabolizing cascades and hence have a more dramatic presentation both of their disease entity and of the eosinophilia.[3,4]

Allergic bronchopulmonary aspergillosis, related both to a fungus (Aspergillus) and to sensitization in an allergic/asthmatic host, can also produce varied and sometimes significant degrees of eosinophilia and also elevated total immunoglobulin (Ig)E.[5]

Chronic eosinophilic pneumonia often starts in a sensitized, asthmatic host. Although these patients may have milder peripheral eosinophilia at disease onset, they often have more moderate range eosinophilia later in the course. They also have bronchoalveolar lavage fluid that contains at least 40% eosinophils in up to 80% of cases.[6] This form of eosinophilic pneumonia can be premonitory to the later development of the eosinophilic vasculitis, eosinophilic granulomatosis with polyangiitis (EGPA), previously known as Churg-Strauss vasculitis.

Drug allergy can cause anywhere from mild to severe eosinophilia and often waxes quickly and wanes in a slower fashion; it can take months for eosinophilia from drug allergy to clear. There is usually, although not always, an associated drug rash of the diffuse/maculopapular variety. Patients can also present with asymptomatic eosinophilia owing to drugs, especially penicillins, cephalosporins, or quinolones.[7] Pulmonary infiltrates and peripheral eosinophilia have been associated with varied medications, including nonsteroidal antiinflammatory drugs, sulfa drugs, and nitrofurantoin.[7] Drug-induced diseases of other organs can also elicit tissue and blood eosinophilia (eg, drug-induced interstitial nephritis). **Box 1** summarizes causes of allergen-induced eosinophilia.

The drug rash with eosinophilia and systemic symptoms (DRESS) syndrome often produces significant eosinophil elevations in addition to liver function abnormalities, temperature dysregulation and lymphadenopathy. In reviews of 2 large,

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