Eosinophilia, Hypereosinophilia and
Hypereosinophilic Syndrome: Diagnosis,
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Introduction

Definitions

**Blood eosinophilia** — >500 Eosinophils x 10^9/L blood

**Hypereosinophilia (HE)**

*HE >1500 Eosinophils x 10^9/L blood on 2 examinations (interval >1 month) and/or tissue HE defined by the following:

1. Percentage of eosinophils in BM section exceeds 20% of all nucleated cells and/or
2. Pathologist is of the opinion that tissue infiltration by eosinophils is extensive and/or
3. Marked deposition of eosinophil granule proteins is found (in the absence or presence of major tissue infiltration by eosinophils).

**Hypereosinophilic syndrome (HES)**

1. Criteria for peripheral blood HE fulfilled*
and
2. Organ damage and/or dysfunction attributable to tissue HE and
3. Exclusion of other disorders or conditions as major reason for organ damage.

*In the case of evolving life-threatening end-organ damage, the diagnosis can be made immediately to avoid delay in therapy.


**Current controversies in diagnostic criteria:**

1. Inclusion/exclusion of disorders of known etiology
2. What constitutes end organ damage attributable to eosinophilia
3. Sensitivity and specificity of the >1500 Eosinophils x 10^9/L cutoff

**Practical approach to the patient with HE**

1. **Assessment of acuity**

2. **Exclusion of secondary causes** that require treatment directed at underlying cause including, but not limited to:
   a. Infections
      i. Helminth
   b. Drug reactions (allergic or toxic)
   c. Neoplasms
   d. Allergic disorders (such as ABPA)
   e. Hypoadrenalism
   f. Immunodeficiency syndromes

3. **Classification**

   a. **Myeloproliferative**
      i. PDGFRA-associated
      ii. CEL-NOS
      iii. Idiopathic
   b. Lymphocytic variant
      i. Non-cyclic
      ii. Cyclic
   c. Idiopathic
   d. Hypereosinophilia of unknown significance (no evidence of end organ involvement)
   e. Familial
   f. Single organ involvement with or without peripheral eosinophilia >1500 x 10^9/L blood
   g. Associated (in setting of well-defined syndrome that can be associated with eosinophilia)

(Classification based on Simon et al. J Allergy Clin Immunol 126:45-49, 2010)
4. Treatment-based algorithm

A

- Presumed HES
- Documented* molecular or cytogenetic abnormality associated with imatinib-responsive HES?
  - Yes
  - Imatinib** (100-400 mg daily)
    - Response?
      - Yes: Continue imatinib indefinitely
      - No: Increase imatinib dose
        - Alternative tyrosine kinase inhibitors
        - Interferon-alpha
        - Consider allogeneic BMT
    - No: Presumed M-HES?
      - Yes: Go to panel B
      - No: Corticosteroid trial (1 mg/kg)
        - Response?
          - Yes: Go to panel C
          - No: Continue corticosteroid trial

B

- Presumed HES (except for M-HES)
- Symptomatic?
  - Yes: Consider no treatment with close monitoring
  - No: Presumed or documented eosinophilic vasculitis?
    - Yes: High-dose corticosteroids (1 mg/kg for at least 1 month) +/- cyclophosphamide
      - Clinical manifestations mild and restricted to a single organ?
        - Yes: Consider topical therapy
          - Response?
            - Yes: Go to panel C
            - No: Try alternative therapy*
        - No: Corticosteroid therapy
          - Response?
            - Yes: Go to panel C
            - No: Try alternative therapy*
    - No: Go to panel C

C

- Corticosteroid-responsive HES
- Slow corticosteroid taper
- Maintenance dose ≤10 mg prednisone daily?
  - Yes: Continue corticosteroids
  - No: Definite or presumed L-HES
    - Add interferon-alpha (1 μg daily)
      - Response?
        - Yes: Increase dose or try alternative therapy*
        - No: Continue for at least 6-12 months; consider pegylated

* or highly suspicious for and awaiting confirmatory testing
** with corticosteroids if evidence of cardiac involvement

(from Simon HU and Klion AD, Seminars in Hematology, 49:160-70, 2012)