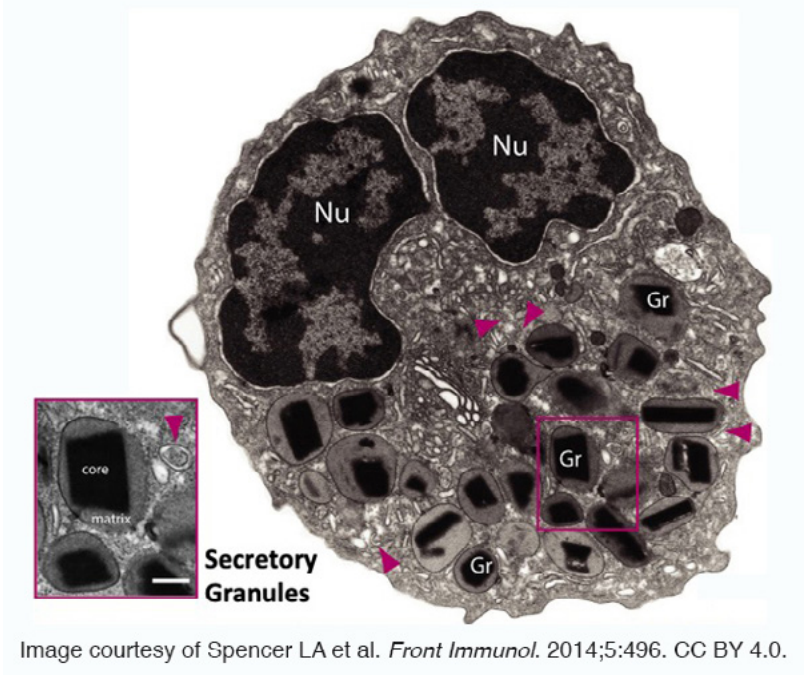
CLINICAL INSIGHT

1. Eosinophils Overview

Eosinophils are white blood cells with multifunctional roles, including protection from parasitic infections, modulation of innate and adaptive immunity, and tissue homeostasis. Eosinophils contain multilobed nuclei and large cytoplasmic secretory granules that house cytotoxic proteins. When overactive, eosinophils can lead to pathogenic states through cytotoxicity caused by degranulation or through recruitment or activation of inflammatory cells via the secretion of proinflammatory mediators. Eosinophil regulation is dependent on many signaling molecules, including the cytokine IL-5.



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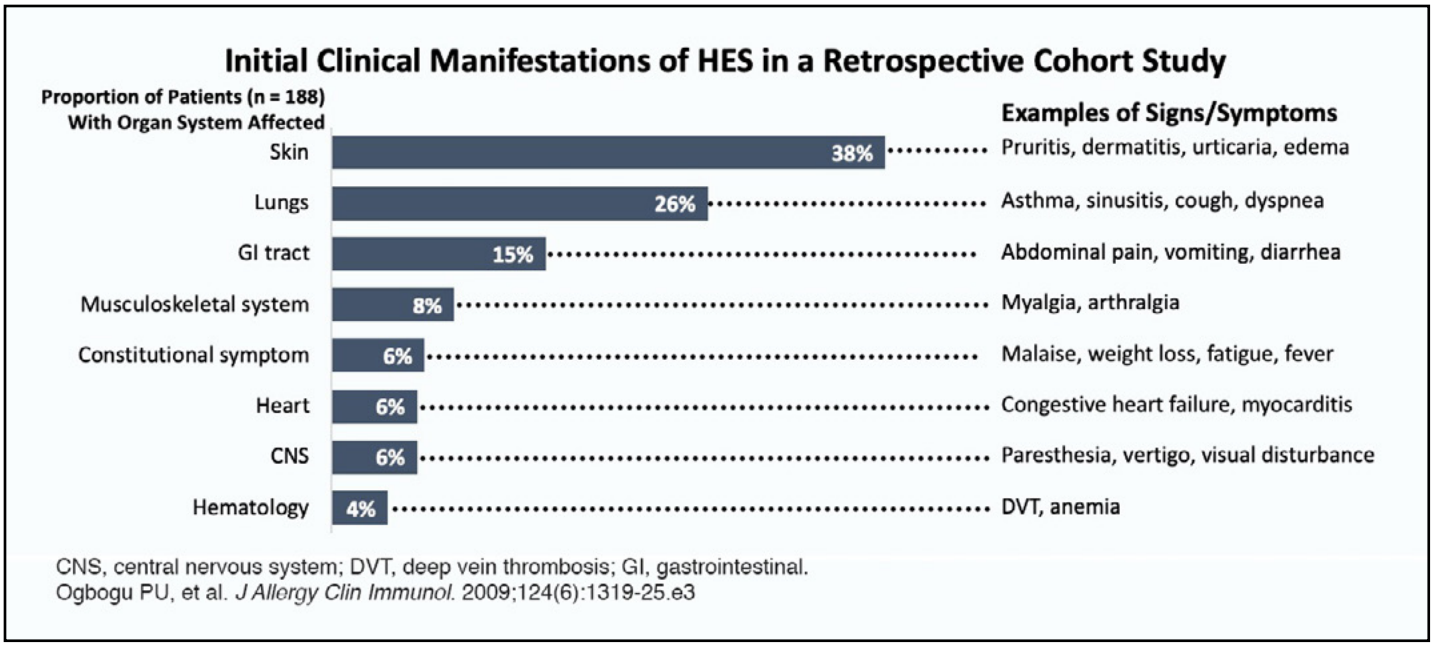
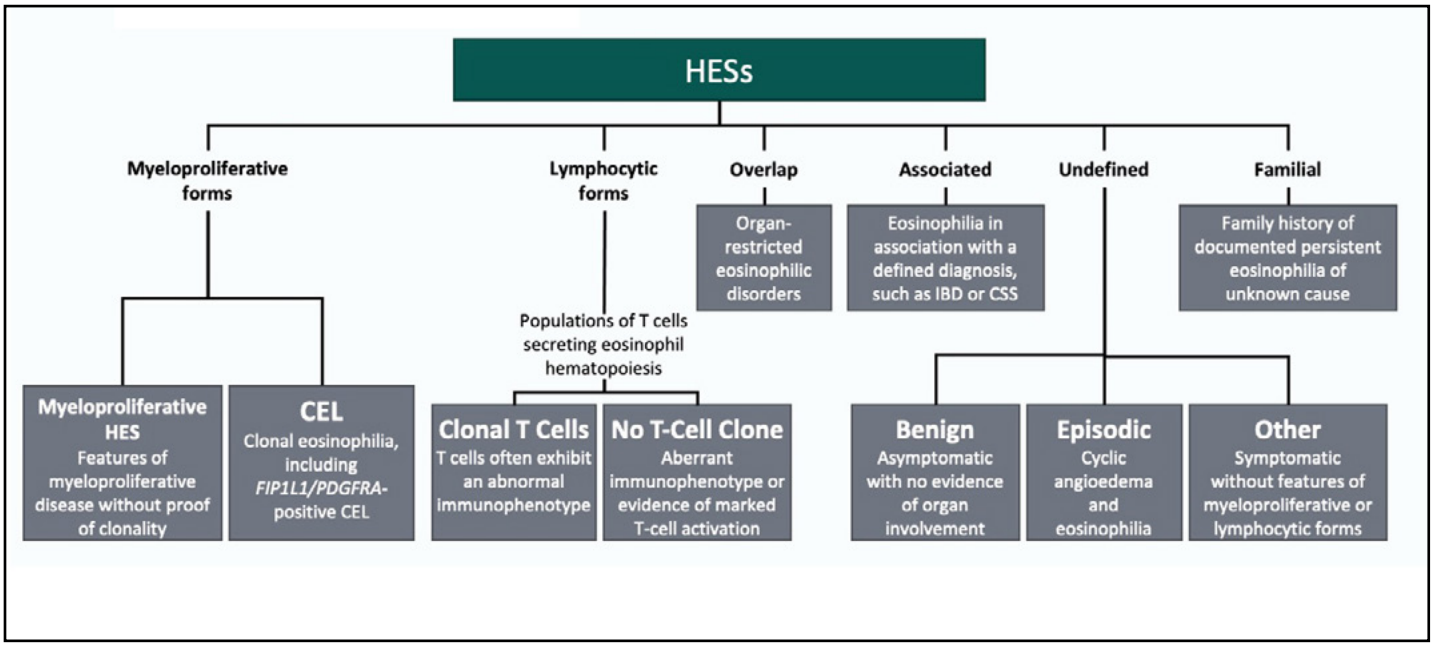
2. Hypereosinophilic Syndrome Overview

Hypereosinophilic syndromes (HESs) encompass a broad range of disorders, which can be defined according to the following 3 criteria: (1) blood hypereosinophilia (absolute eosinophil count [AEC] ≥1500/mm3) or marked tissue eosinophilia according to an experienced pathologist, (2) evidence of end-organ involvement with clinical manifestations, and (3) the lack of an alternative diagnosis (ie, no infection, no malignancy, and no drug reactions). The most common presenting symptoms of HES are dermatologic, pulmonary, or gastrointestinal. With disease progression, an estimated 20% of patients with HES will eventually experience cardiovascular disease or neurologic complications.



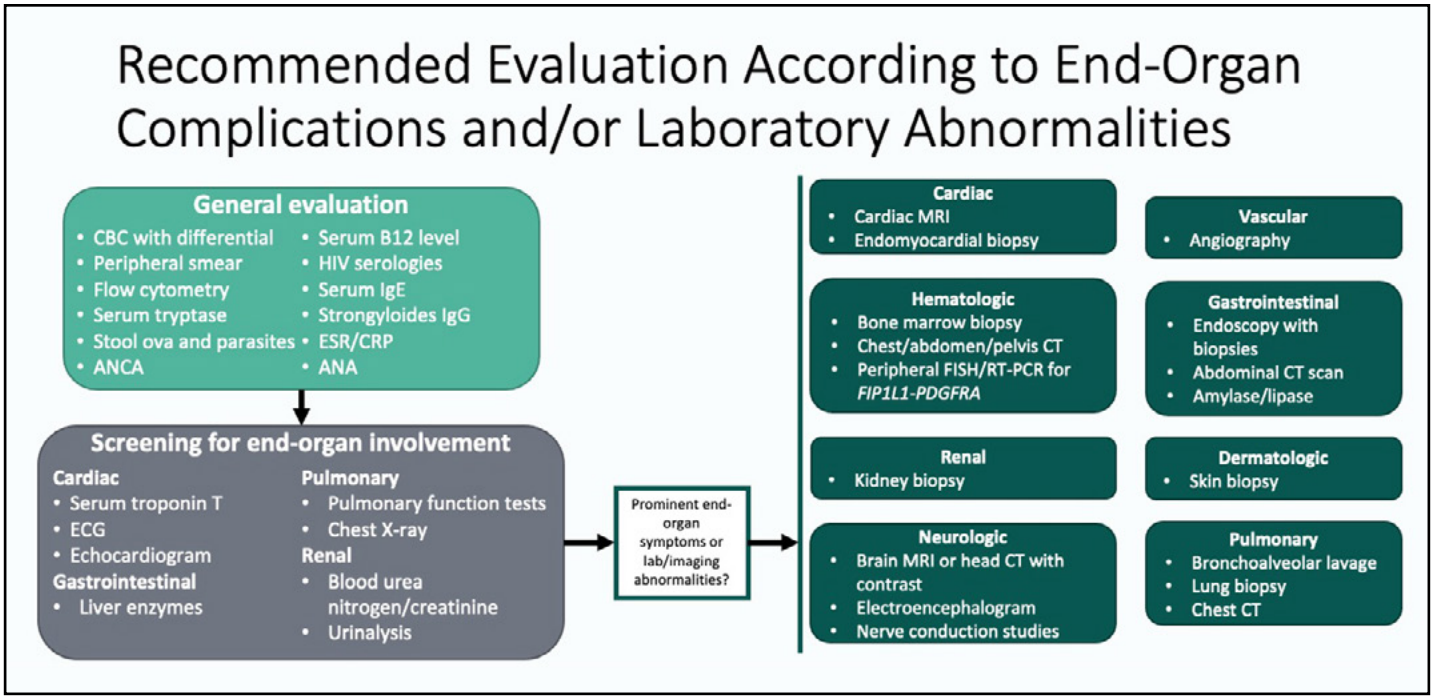
3. HES Classification

HES can be broadly classified into myeloproliferative, lymphocytic, overlap, undefined, and familial forms. To properly classify HES, clinicians must consider the presence of T-cell clonality, genetic alterations, end-organ manifestations, and family history, among other features. The most common type of HES is undefined, which is an HES of unknown cause that does not meet criteria for any of the other categories. People with undefined HES often have multisystem organ involvement.



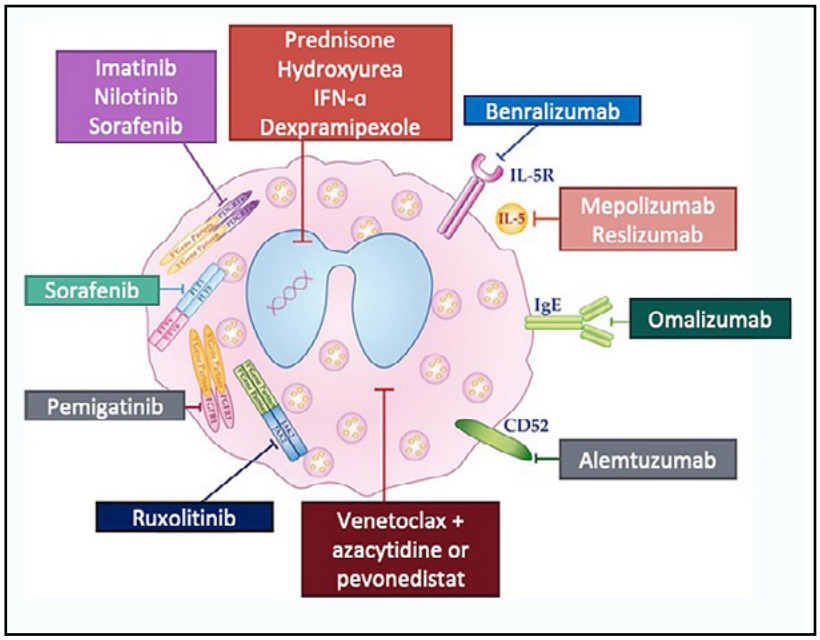
4. Evaluation of Hypereosinophilia

Evaluation of hypereosinophilia is often a multistep process. Original evaluation should include assessment for the cause of hypereosinophilia along with ruling out drug hypersensitivity, parasitic infections, and neoplasms. Patients should then receive screening for end-organ involvement, including cardiovascular, gastrointestinal, pulmonary, and renal workups.



5. Treating HES

Proper treatment of HES depends upon appropriate classification. For those patients who do not respond to corticosteroids or cannot taper off corticosteroids, targeted therapies can be considered, including imatinib for PDGFR-associated myeloid neoplasms and the anti-IL-5 monoclonal antibody mepolizumab for HES that has persisted for more than 6 months. Second-line immunomodulatory treatments to consider include prednisone, hydroxyurea, interferon-α, and imatinib (for other forms of myeloid HES).



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