Eosinophils are one of the many types of white blood cells involved in pathophysiology of different lung diseases. Eosinophils have a role in a wide variety of disorders including allergy, asthma, helminthic or parasitic infections, and rare hyper eosinophilic disorders, and can induce tissue damage through release of toxic substances including eosinophil derived neurotoxin, major basic protein, eosinophilic cationic protein and myeloperoxidase. While asthma has long been recognized as an eosinophilic disorder, as many as 1/3 of COPD patients may also have evidence of eosinophilic inflammation. Other hyper eosinophilic syndromes (HES), including idiopathic hyper eosinophilic syndrome (IHES), platelet-derived growth factor receptor-a (PDGFRA)-associated HES, lymphocytic variant HES (L-HES), familial hyper eosinophilia, and eosinophilic granulomatosis with polyangiitis (EGPA, previously known as Churg-Strauss Syndrome), are a heterogeneous group of uncommon disorders that are characterized by marked eosinophilia in the peripheral blood and/or tissues often without an identifiable cause. Other causes of pulmonary eosinophilia include cryptogenic organizing pneumonia, hypersensitivity pneumonitis, and pulmonary Langerhans Cell granulomatosis, but other systemic disorders that affect the lungs may also present with eosinophilia including different malignancies, sarcoidosis, and Sjogren’s Syndrome.

In the past, many of these conditions were lumped together as idiopathic hyper eosinophilic syndrome (IHES), defined by: 1) the presence of eosinophilia (>1500 eosinophils/mm³ for at least 6 months) that remains unexplained despite a comprehensive evaluation for known causes of eosinophilia (including parasitic helminth infections, HIV, drug hypersensitivity, non-hematologic malignancies, lymphomas, and primary allergic disorders) and 2) evidence of organ dysfunction directly attributable to the eosinophilia or otherwise unexplained in the clinical setting. IHES was distinguished from other idiopathic eosinophilic disorders that involved limited organs, such as the eosinophilic pneumonias, EGID, and eosinophilic cystitis. More recently, the heterogeneous group of disorders have begun to be reclassified as clinical subtypes have been recognized and new molecular and immunologic markers are described. Currently recognized subtypes include PDGFRA-associated HES, L-HES, chronic eosinophilic leukemia (CEL), and familial eosinophilia. EGPA is associated with significant peripheral eosinophilia, constitutional symptoms and eosinophilic tissue infiltration, but is different from HES in that it is a complex disease characterized by the presence of eosinophilic vasculitis that may involve multiple organ systems. The hallmark diagnostic criteria of EGPA include eosinophilic vasculitis in addition to one or more of the following: asthmatic airway obstruction, pulmonary infiltrates, sinusitis, neuropathy and positive anti-neutrophil cytoplasmic antibody (ANCA). HES and EGPA need to be distinguished from acute eosinophilic pneumonia (an acute febrile illness associated with eosinophilic lung infiltration, diffuse pulmonary infiltrates and often acute respiratory failure that is often self-limited) and chronic eosinophilic pneumonia (that presents sub-acute in association with asthma, sinusitis and presence of lung eosinophilia and constitutional symptoms).

Extensive workup including Complete blood count with differential, sedimentation rate, C-Reactive Protein, ANCA, B12, serum immunoglobulins and tryptase staining should be performed in all patients but one must also consider bone marrow biopsy, flow cytometry and imaging as indicated. Although corticosteroids are the first line treatment for many of these disorders, they are associated with significant morbidity, and some patients require more cytotoxic therapies. Recent advances in our understanding of the etiologies of eosinophilic disorders coupled with the availability of new agents targeting specific components of the immune response have already changed our approach to therapy in some cases. The successful use of imatinib in PDGFRA-associated HES or anti Interleukin-5 (the cytokine associated with eosinophil maturation and proliferation) therapy with mepolizumab in EGPA or eosinophilic asthma highlight the need for a rational therapeutic approach in the management of these challenging disorders. Eosinophilic lung diseases have significant morbidity so one must work hard to formulate a definitive diagnosis and one needs to treat these diseases aggressively. While corticosteroids and cytotoxic therapies have historically been utilized for the management of these disorders, newly approved monoclonal antibodies targeting interleukin-5 offer promise.
References


