Spectrum of Eosinophilic End-Organ Manifestations

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KEYWORDS

• Eosinophils pathology • Eosinophils immunology • Humans
• Pulmonary eosinophilia • Eosinophilic esophagitis • Hypereosinophilic syndrome
• Churg-Strauss syndrome • Eosinophilic granulomatous vasculitis

KEY POINTS

- Eosinophilia may affect any organ and cause end-organ damage.
- Mechanisms by which eosinophilia promotes tissue damage include infiltration, fibrosis, thrombosis, and allergic inflammation.
- Patterns of eosinophil-mediated end-organ dysfunction are particularly well characterized for the lungs, heart, and gastrointestinal tract.

INTRODUCTION

The purpose and function of eosinophils in health and disease are complex and cannot be readily crystallized into a single summary statement. This has become increasingly true as myriad potential immunoregulatory behaviors of eosinophils have been uncovered in recent years.[1,2] However, the traditional characterization of eosinophils as end-organ effector cells, causing tissue damage through release of cationic granule proteins, is borne of the observation of a spectrum of eosinophil-associated disorders encompassing practically all organ systems of the body. These disorders may affect one organ alone, such as the eosinophilic pneumonias or eosinophilic esophagitis, or affect multiple organ systems simultaneously, such as the hypereosinophilic

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syndromes or eosinophilic granulomatosis with polyangiitis (EGPA, formerly known as Churg-Strauss syndrome).[3–6] This article provides an overview of eosinophilic end-organ manifestations, setting the stage for the organ-specific articles discussed elsewhere in this issue. **Table 1** provides a partial tabulation of organs and organ-systems that may be affected by eosinophilia and potential diagnostic tests and assays that can reflect end-organ dysfunction.

MECHANISMS OF END-ORGAN MANIFESTATIONS

Although the specific mechanisms by which tissue eosinophilia results in end-organ dysfunction require further investigation, some general themes can be constructed based on current knowledge. These themes may be overlapping in specific disease processes but can be useful in parsing the pathologic effects of eosinophils in disease.[7]

The first is that the infiltration of eosinophils in tissue can, in and of itself, be pathologic if it is extensive enough. For example, in the eosinophilic pneumonias, the main finding observed on lung biopsy is often simply extensive infiltration of eosinophils into the lung parenchyma.[3,8,9]

Second, eosinophils may also cause organ damage mediated through associated fibrosis.[10] Several in vitro studies have demonstrated the potential of eosinophils to promote fibroblast activation, proliferation, and extracellular matrix production, likely through their secretion of transforming growth factor (TGF)-β and interleukin (IL)-1β.[11–15] Eosinophil cationic protein, one of the granule-stored proteins of eosinophils, has been observed in vitro to promote fibroblast migration and TGF-β release, potentially implicating granule protein deposition as a mechanism for eosinophil-mediated tissue fibrosis.[16,17] Eosinophil-associated tissue fibrosis is observed in the heart, specifically the endocardium; in hypereosinophilic syndromes; and in the subepithelial fibrosis that is characteristic of eosinophilic esophagitis and asthma.[18–20]

Table 1
Detection of eosinophilic end-organ dysfunction

Organ System Affected by Eosinophilia	Selected Studies
Cardiac	Serum troponin Electrocardiogram Echocardiogram Cardiac MRI
Gastrointestinal	Endoscopy with tissue biopsy Serum liver function testing Serum amylase, lipase
Pulmonary	Chest radiograph Chest computed tomography Pulmonary function testing Bronchoscopy with bronchoalveolar lavage Lung biopsy
Neurologic	Head MRI Head computed tomography Nerve conduction studies Nerve biopsy
Skin	Skin biopsy
Renal	Serum creatinine Urine eosinophils Kidney biopsy