# EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS (EGPA):

## Diagnosis & Treatment Approaches

## Characteristics

- Moderate to severe asthma
- Peripheral blood eosinophilia (> 10% eosinophils)
- Pulmonary infiltrates
- Paranasal sinus abnormality
- Mononeuropathy or polyneuropathy
- Extravascular eosinophils/eosinophilic vasculitis of small- to medium-sized blood vessels
- Positive ANCA

## STEP 1 Basic evaluation

- **DETAILED HISTORY AND PHYSICAL EXAM**
- **ASK ABOUT EXPOSURES:** Medications, dietary supplements, recreational drugs, toxins, workplace, travel
- **SEARCH FOR EXTRAPULMONARY DISEASE:** Nasal/sinus, ocular, skin, cardiac, gastrointestinal, neurologic, renal, vascular

**Tailor according to history and physical:**

- **IMAGING/TESTING:** CXR, chest CT scan, sinus CT scan, EMG/NCV, echocardiogram or cardiac MRI
- **LABORATORY:** CBC with differential, ESR, CRP, ANCA( MPO/PR3), vitamin B12, electrolytes, LFTs, total protein, urinalysis
  Serum tryptase level, serum Ig's (include IgE), Troponin
  Bone marrow aspirate and biopsy with reticulin and tryptase stains

## STEP 2 Exclude major secondary causes of pulmonary eosinophilia

| DISORDERS TO EXCLUDE | EVALUATIONS AND TESTS TO CONSIDER |
|---|---|
| Drug or toxin reaction | • Drug and dietary supplement history<br>• Discontinuation of potential causative agents |
| Parasitic/ helminthic infection | • Travel history<br>• Stools for ova and parasites<br>• Serologies for parasitic infection (based on travel history) |
| Nonparasitic infection (TB, Cocci) | • TB skin test, IGRA, M. tuberculosis cultures<br>• Coccidioides serologies, fungal cultures |
| Myeloid neoplasms/ Lymphoma | • Blood immunophenotyping and molecular phenotyping<br>• (e.g. FIP1L1-PDGFRα)<br>• Bone marrow aspirate/biopsy with cytogenetics, immunophenotyping |
| HIV | • HIV serology |
| Primary allergic disorders | • Allergen testing (skin testing and specific IgE testing), Aspergillus specific IgE's and precipitins |
| Autoimmune disorders | • Auto-antibodies (ANA & autoantibody testing for pertinent rheumatologic conditions), specialized clotting studies |
| Systemic mastocytosis | • c-KIT mutation analysis, serum tryptase level |
| Solid tumors | • CT/MR scan |

## STEP 3 Exclude other diseases associated with eosinophilia

### LUNG DISEASES

- Asthma/eosinophilic bronchitis
- Allergic bronchopulmonary aspergillosis
- Bronchocentric granulomatosis
- Cryptogenic organizing pneumonia
- Hypersensitivity pneumonitis
- Idiopathic pulmonary fibrosis
- Pulmonary Langerhans cell histiocytosis
- Postradiation pneumonitis
- Chronic eosinophilic pneumonia

### SYSTEMIC DISEASES

- Rheumatoid arthritis
- Sarcoidosis
- Sjögren syndrome
- Hypereosinophilic Syndrome

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## STEP 4 Distinguish between the primary pulmonary eosinophilic disorders

| | ACUTE EOSINOPHILIC PNEUMONIA | CHRONIC EOSINOPHILIC PNEUMONIA | HYPEREOSINOPHILIC SYNDROME | EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS[1] |
|---|---|---|---|---|
| KEY FEATURES[1] | Acute febrile illness; hypoxemic respiratory failure; diffuse pulmonary infiltrates; BAL fluid eosinophils > 25%; previously healthy person | Subacute illness; eosinophilia in lung tissue and blood; bilateral pulmonary infiltrates may be peripheral in location | Sustained overproduction of eosinophils; marked peripheral blood eosinophilia; tissue eosinophilia; end-organ damage; includes myeloproliferative, lymphocytic, familial, and idiopathic variants | Necrotizing vasculitis of small- to medium-sized blood vessels; asthma; eosinophil-rich granulomatous inflammation of respiratory tract; involves multiple organs |
| Onset | Acute (days) | Indolent (weeks/months) | Indolent (months/years) | Indolent (months/years) |
| Pulmonary infiltrates | Diffuse | Peripheral | Patchy | Patchy |
| Fulminant respiratory failure | Frequently Occurs | Rarely Occurs | Rarely Occurs | Rarely Occurs |
| Asthma/allergy history | Rarely Occurs | Commonly Occurs | Rarely Occurs | Frequently Occurs |
| Smoking history | Commonly Occurs | Rarely Occurs | Rarely Occurs | Rarely Occurs |
| Vasculitis | Rarely Occurs | Rarely Occurs | Rarely Occurs | Frequently Occurs |
| ANCA | Rarely Occurs | Rarely Occurs | Rarely Occurs | Commonly Occurs |
| Cardiac involvement | Rarely Occurs | Occasionally Occurs | Frequently Occurs | Commonly Occurs |
| Neurologic involvement | Rarely Occurs | Occasionally Occurs | Frequently Occurs | Frequently Occurs |
| Requirement for therapies other than corticosteroids | Rarely Occurs | Rarely Occurs | Frequently Occurs | Commonly Occurs |

## STEP 5 Comparison of ANCA-associated vasculitides

### Small to medium vessel necrotizing vasculitides with differentiating features

**GPA**
- Almost Always ANCA positive
- C-ANCA and PR3 specificity
- Unlikely to exhibit asthma
- Unlikely to exhibit blood eosinophilia
- Glomerulonephritis common

**EGPA**
- Sometimes ANCA positive
- p-ANCA and MPO specificity
- Asthma common
- Always exhibits blood eosinophilia
- Glomerulonephritis less common

**MPA**
- Almost always ANCA positive
- p-ANCA and MPO specificity
- Unlikely to exhibit blood eosinophilia
- Glomerulonephritis common

## STEP 6 Treatment

**ACUTE:**

Corticosteroids, 1-2 mg/kg
- CNS
- Cardiac
- OFF-LABEL Add cyclophosphamide for severe systemic involvement

**CHRONIC:**
- Unresponsive to steroids alone
- Unable to refer
- Frequent exacerbation/relapses despite steroid

**Try Add-on RX**
- **mepolizumab** (300 mg/monthly)[2]
- OFF-LABEL methotrexate (MZX)
- OFF-LABEL azathioprine (AZA)
- OFF-LABEL mycophenolate mofetil (MMF)

**Treat asthma/sinus disease**

**USING MEPOLIZUMAB FOR THE TREATMENT OF EGPA[3]**

**CLINICAL BENEFIT**

**Remission** (BVAS 0 and ≤ 4 mg/day GC) **AND/OR**

**≥50% reduction in OCS dose** **AND/OR**

**Relapse-free [78% Mepolizumab vs 32% Placebo]**

- **Eosinophilic granulomatosis with polyangiitis (EGPA) was previously called Churg-Strauss syndrome.**
- BAL, transbronchial or open-lung biopsy may be necessary, depending on clinical and radiographic findings.
- Additional testing may be needed to evaluate for extrapulmonary disease.

**Abbreviations:**
**BAL**, bronchoalveolar lavage; **ESR**, erythrocyte sedimentation rate; **CRP**, C-reactive protein; **ANCA**, antineutrophil cytoplasmic antibody; **Ig**, immunoglobulin; **LFT**, liver function test; **TB**, tuberculosis; **IGRA**, interferon gamma release assay; **RT-PCR**, reverse transcriptase-polymerase chain reaction;

**References:** 1 Wechsler ME. Pulmonary eosinophilic syndromes. Immunol Allergy Clin N Am. 2007;27:477-492.3 2 Wechsler, ME, et al. Mepolizumab or Placebo for Eosinophilic Granulomatosis with Polyangiitis. N Engl J Med. 2017 May 18;376(20):1921-1932 3 Steinfeld J, et al. Evaluation of clinical benefit from treatment with mepolizumab for patients with eosinophilic granulomatosis with polyangiitis. J Allergy Clin Immunol 2019 Jun;143(6):2170-2177