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 polynuropathy
- Extravascular eosinophilic/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

- Drug or toxic reaction
- Parasitic/helminthic infection
- Nonparasitic infection (TB, Cocc)
- Myeloid neoplasms/Lymphoma

EVALUATIONS AND TESTS TO CONSIDER
- Drug and dietary supplement history
- Concentration of potential causative agents
- Travel history
- Stools for ova and parasites
- Serologies for parasitic infection (based on travel history)
- TB skin test, IGRA, M. tuberculosis cultures
- Coccidioides serologies, fungal cultures
- T cell skin test, IGRA, M. Tuberculosis cultures
- Cerebrospinal fluid, fungal cultures
- Blood immunophenotyping and molecular phenotyping
- (e.g. FIP1L1-PDGFRα)
- Bone marrow aspirate/biopsy with cytogenetics, immunophenotyping
- HIV serology
- Allergen testing (skin testing and specific IgE testing), Aspergillus specific IgE’s and precipitins
- Auto-antibodies (ANA & autoantibody testing for pertinent rheumatologic conditions), specialized clotting studies
- Anti-neutrophil cytoplasmic antibodies (ANCA), ELISA, Western blot
- Skin biopsy for histopathology
- Stool studies for parasitic and nonparasitic infection
- HIV serology
- ALLERGY TESTING:
  - Skin prick test, RAST
  - Blood immunophenotyping and molecular phenotyping
  - (e.g. FIP1L1-PDGFRα)
  - Bone marrow aspirate/biopsy with cytogenetics, immunophenotyping
- CT/MR scan
- c-KIT mutation analysis, serum tryptase level
- Myeloid neoplasms/Lymphoma

STEP 3 Exclude other diseases associated with eosinophilia

LUNG DISEASES
- Asthma/eosinophilic bronchitis
- Allergic bronchopulmonary aspergillosis
- Bronchocentric granulomatosis
- Cryptogenic organizing pneumonia
- Hyperreactivity pneumonitis
- Idiopathic pulmonary fibrosis
- Pulmonary Langerhans cell histiocytosis
- Postinfection pneumonitis
- Chronic eosinophilic pneumonia

SYSTEMIC DISEASES
- Rheumatoid arthritis
- Sarcoidosis
- Sjögren syndrome
- Hypereosinophilic Syndrome

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Breathing Science is Life.
Distinguish between the primary pulmonary eosinophilic disorders

**Step 4**

**CHOICE EOSINOPHILIC PNEUMONIA**
- Acute febrile illness; hypoxemic respiratory failure; diffuse pulmonary infiltrates; BAL, eosinophils > 25% previously healthy person
- Indicate dense eosinophils in lung tissue and blood; isolated pulmonary infiltrates may be peripheral in location
- Marked peripheral eosinophilia, marked eosinophilic vasculitis of small and intermediate vessels

**CHRONIC EOSINOPHILIC PNEUMONIA**
- Indolent illness; eosinophils in lung tissue and blood; bilateral pulmonary infiltrates
- Sustained eosinophilia may occur; doesn’t always cause disease

**HYPEREOSINOPHILIC SYNDROMES**
- Sustained eosinophilia of small to medium-sized blood vessels; eosinophilic vasculitis of vessels, end-organ damage may include myocardial fibrosis, lymphadenopathy, and idiopathic variants

**EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS**
- Necrotizing vasculitis of small to medium-sized blood vessels; asthma, eosinophil-rich granulomatous inflammation of respiratory tract; involves multiple organs

**Treatment**

**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:**

**Step 5**

**Comparison of ANCA-associated vasculitides**

<table>
<thead>
<tr>
<th>Vasculitides</th>
<th>GPA</th>
<th>EGPA</th>
<th>MPA</th>
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</thead>
<tbody>
<tr>
<td>Clinical features</td>
<td>Almost Always ANCA positive</td>
<td>Sometimes ANCA positive</td>
<td>Almost always ANCA positive</td>
</tr>
<tr>
<td>C-ANCA and PR3 specificity</td>
<td>Unlikely to exhibit asthma</td>
<td>p-ANCA and MPO specificity</td>
<td>p-ANCA and MPO specificity</td>
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<tr>
<td>Unlikely to exhibit blood eosinophilia</td>
<td>Glomerulonephritis common</td>
<td>Asthma common</td>
<td>Unlikely to exhibit blood eosinophilia</td>
</tr>
</tbody>
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**Step 6**

**Treatment**

**Acute:**
- Corticosteroids, 1-2 mg/kg
- CNS
- Cardiac
- 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
  - Methotrexate (MXT)
  - Azathioprine (AZA)
  - Mycophenolate mofetil (MMF)

**Clinical benefit:**
- Remission (BVAS 0 and ≤ 4 mg/day GC)
- ≥50% reduction in OCS dose
- Relapse-free (78% Mepolizumab vs 32% Placebo) AND/OR

**Eosinophilic granulomatosis with polyangiitis (EGPA) was previously called Churg-Strauss syndrome.**

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

<table>
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<tbody>
<tr>
<td>Pulmonary infiltrates</td>
<td>Diffuse</td>
<td>Peripheral</td>
<td>Patchy</td>
</tr>
<tr>
<td>Subsequent respiratory failure</td>
<td>Frequently Occurs</td>
<td>Rarely Occurs</td>
<td>Rarely Occurs</td>
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<tr>
<td>Asthma history</td>
<td>Rarely Occurs</td>
<td>Commonly Occurs</td>
<td>Rarely Occurs</td>
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<tr>
<td>Smoking history</td>
<td>Commonly Occurs</td>
<td>Rarely Occurs</td>
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<tr>
<td>Vasculitis</td>
<td>Rarely Occurs</td>
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<tr>
<td>ANCA</td>
<td>Rarely Occurs</td>
<td>Rarely Occurs</td>
<td>Commonly Occurs</td>
</tr>
<tr>
<td>Cardiac involvement</td>
<td>Rarely Occurs</td>
<td>Occasionally Occurs</td>
<td>Frequently Occurs</td>
</tr>
<tr>
<td>Neurologic involvement</td>
<td>Rarely Occurs</td>
<td>Occasionally Occurs</td>
<td>Frequently Occurs</td>
</tr>
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**Comparison Table:**

- **Onset Acute**
  - GPA: Indolent (weeks/months)
  - EGPA: Indolent (months/years)
  - MPA: Indolent (months/years)

- **Pulmonary infiltrates**
  - GPA: Diffuse
  - EGPA: Peripheral
  - MPA: Patchy

- **Fulminant respiratory failure**
  - GPA: Frequently Occurs
  - EGPA: Rarely Occurs
  - MPA: Rarely Occurs

- **Asthma/allergy history**
  - GPA: Rarely Occurs
  - EGPA: Commonly Occurs
  - MPA: Rarely Occurs

- **Smoking history**
  - GPA: Commonly Occurs
  - EGPA: Rarely Occurs
  - MPA: Rarely Occurs

**Abbreviations:**
- GPA, granulomatosis with polyangiitis (Churg-Strauss syndrome); EGPA, eosinophilic granulomatosis with polyangiitis; MPA, microscopic polyangiitis

**References:**