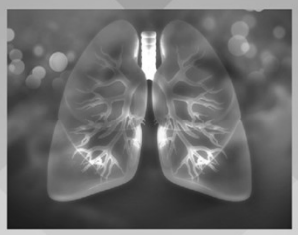
Differential Diagnosis and Treatment selection for Eosinophilic Granulomatosis with Polyangiitis (EGPA)



BEST HOSPITALS U.S.News PULMONOLOGY & LUNG SURGERY 2019-20

#1 in Respiratory Care

National Jewish Health®

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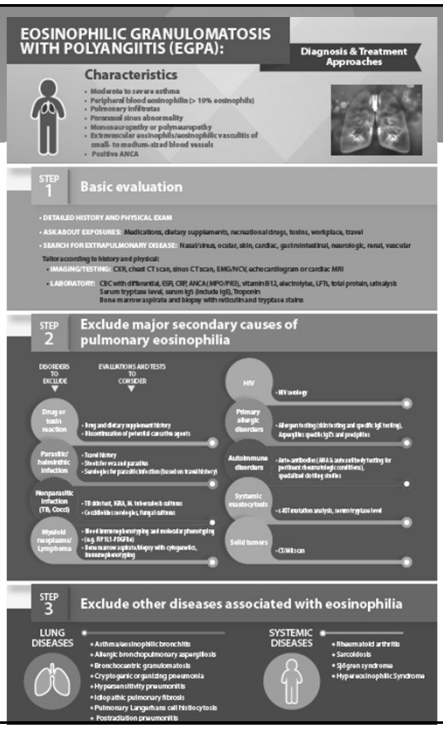
The infographic entitled *Eosinophilic Granulomatosis with Polyangiitis (EGPA): Diagnosis and Treatment Approaches* will guide the discussion for this activity.

A copy of the guide can be found in your meeting materials.



Program Learning Objectives

- Identify clinical features that distinguish EGPA from other eosinophilic lung diseases
- Review best practices for early evaluation and differential diagnosis of EGPA
- Select appropriate treatments for patients with EGPA

Differential Diagnosis and Treatment selection for Eosinophilic Granulomatosis with Polyangiitis (EGPA)

Overview of EGPA

Michael E. Wechsler, MD, MMSc

Director of The Cohen Family Asthma Institute

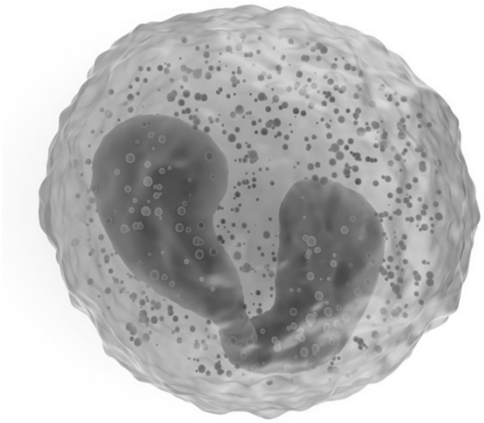
Professor of Medicine

Division of Pulmonary, Critical Care and Sleep Medicine

National Jewish Health

Denver, CO

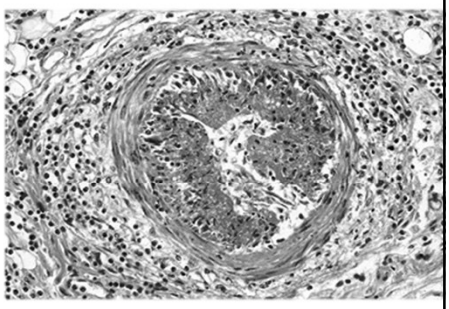
The Eosinophil



EGPA Is an Eosinophilic Vasculitis

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



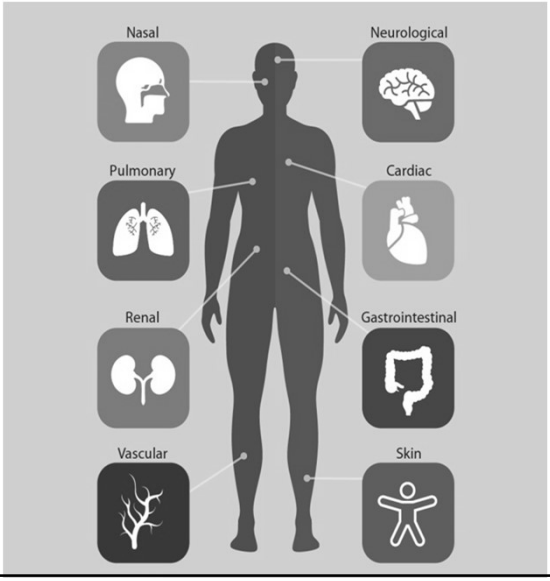
UpToDate®

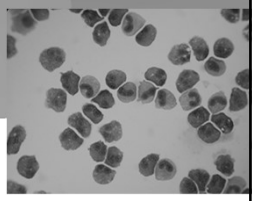
EGPA: Clinical Course

- EGPA evolves in a phasic, developmental pattern
  - **Stage I**: Initial allergic diathesis (usually allergic rhinitis), progressing into asthma
  - **Stage II**: Peripheral blood eosinophilia, eosinophilic infiltration in various organs
  - **Stage III**: Terminal vasculitic stage; necrotizing vasculitis and granuloma formation
- Usually develops over years, but can develop over months

EGPA May Affect Multiple Organ Systems

- Respiratory tract
- Nervous system
- Heart
- Kidney
- GI tract
- Vascular system
- Skin





EGPA Cases

Paneez Khoury, MD, MHSc, FAAAAI
Associate Research Physician
Allergy/Immunology
National Institutes of Health
Bethesda, Maryland

NIH
NIAID

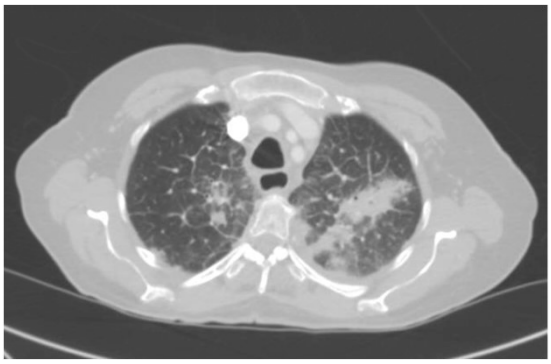
Image used with permission from Human Eosinophil Section, NIAID

Case 1

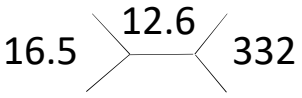
- 77 year old Indian woman with a history of asthma and allergic rhinitis
- Main complaint: chronic cough since age 64
- Allergic rhinitis , post-nasal drip, and nausea
- Symptoms
  - increased sputum production
  - Abdominal pain, nausea, poor appetite
  - fevers
  - 2-3 ER visits/yr X 3 years for asthma or bronchitis
  - Hospitalized with pneumonia 2 mo ago
- Asthma and peripheral eosinophilia up to 1400/mm3 recently
- Treated: Advair 500/50 + occ prednisone bursts 2-3X/yr

Record review

- Hospitalization records :
  - Absolute eosinophil count: 7434/mm3
  - CT scan r/o PE in ED: nodular infiltrates and GGO
  - D/C: Abx and 2 week taper of prednisone
- Review of PCP records:
  - Frequent burst doses of glucocorticoids for "bronchitis"/"asthma exacerbation"
  - One episode hypoxia 86% sats during eval.



Laboratory Workup



AEC 2200/mm^3

- ESR 72 RF 1:640. ANCA and MPO negative

Clinical Course

- On way to CT scan develops CP and goes to ER
- AEC now 7000, troponin 13.5, EGK sinus tachycardia, echo-moderate pericardial effusion
- Dx: Myocarditis and prednisone 60mg started
- CT scan shows peripheral nodular infiltrates, thickened small bowel
- Anti-filarial antibodies and strongyloides serology negative
- Discharged on prednisone with f/u PCM

Case 1 revisited

Prednisone was tapered over 4 weeks.

Cough returns, AEC 1500/mm^3 at presentation to establish visit with Pulmonary, % sat 88, diffuse wheezing and shortness of breath

Readmitted

Bronchoscopy reveals granulomas with perivascular eosinophilia

Endoscopy: sheets of eosinophils in the gastric antrum

Dx: EGPA with sinus, pulmonary and gastrointestinal involvement

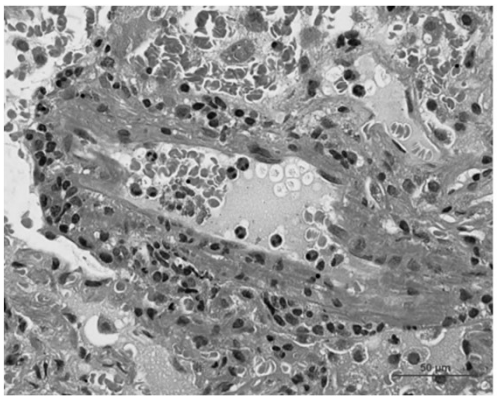


Image used with permission from NIH Pathology

Case 2

- 45 year old with no prior medical history
  - Develops cough and asthma like symptoms
  - Golf-buddies (MD's) prescribe prednisone which he self administers every 4-8 weeks "as needed"
  - Develops palpitations but schedules vacation in Montana anyways

Lucky Escape

- Drives off the road, luckily hits a bank of trees
- Taken to nearby hospital, stabilized and transferred to tertiary care center
- EF noted to be 35% attributed to trauma from accident
- Pulmonary infiltrates noted and peripheral eosinophilia
- Dx: Hypereosinophilic Syndrome

Subsequent workup

Returns to Maryland and schedules establish visit at NIH

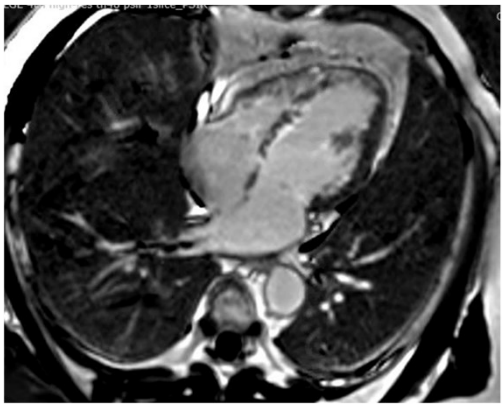
14.2 13.5 229 AEC 1900/mm^3

- ANA, ANCA negative
- ESR 20, CRP 15.1
- Troponin I mildly elevated 0.052
- PDGFRA negative, and bone marrow review reveals no dysplasia

NIH Bethesda Campus

Follow-up

- Chest MR performed reveals patchy delayed sub endomyocardial enhancement in multiple territories and mitral LGE (Late Gadolinium Enhancement)
- Elicited prior hx of asthma, sinusitis.
- Holter placed for ”palpitations” and reveals runs of VT, atrial tachycardia
- Cardiology referral
- High dose steroids restarted and referred for mepolizumab for presumed EGPA



Discussion

- Although peripheral eosinophilia, tissue eosinophilia/degranulation are hallmarks of eosinophil-associated disorders, and ANCA is seen in up to 30-50% of people with EGPA, none are sensitive or specific enough for the diagnosis of EGPA.
- A constellation of clinical features and/or confirmation with histopathology allows for making the diagnosis of EGPA

See Mast AT et al. The American College of Rheumatology 1990 criteria for the classification of Churg-Strauss syndrome (allergic granulomatosis and angiitis). Arthritis Rheum. 1990;33(8):1094.

EGPA Cases

Curry Koening, MD, MS
Associate Professor
Rheumatology
University of Utah and Salt Lake City Veterans Administration
Salt Lake City, Utah

Patient Case

52 year old male with asthma and hypereosinophilia

- Feb 2017—Cough, wheeze
- April 2017—Admit to OSH for ”pneumonia”
  - Treated with antibiotics and prednisone
  - WBC 22,000 with 11% eosinophils, cultures negative
- Improved, only to have the coughing and wheezing return
- Referred to local pulmonologist with PFTs-obstruction/asthma
  - Treated with inhaler with little improvement

Clinical Course

- Sept 2018—New bilateral lower extremity tingling
  - Gradually increased to bilateral mid shin
  - Trouble with left toes catching on stairs
  - Prednisone was increased to 60 mg/d and he was referred to rheumatology

Rheumatology visit Oct 2017

- Unable to dorsiflex left foot
- Reduced sensation
- Not better with prednisone 60 mg/d

- PMH: none
- PSH: Meniscus surgery of knee
- Allergies: none
- FH: Mother: HTN, Father HTN/DM
- Psoc: Married, no smoking/alcohol/drugs, accountant
- Meds: Prednisone 60 mg/d, albuterol INH, Steroid INH

Exam

- VS: 154/87, 101, 98.7, 92% RA
- Pertinent positives:
  - HEENT: boggy and enlarged nasal mucosa
  - Lung: Faint expiratory wheeze
  - Neuro: Left foot drop, can't walk on heels (left), reduced ankle jerks left
- Pertinent negatives:
  - Heart: normal, no rub
  - Skin: no rash

Labs

Pertinent positives

WBC 23; **23% eos**; HgB 14.1; PLT 396

CRP 2.4 mg/dl

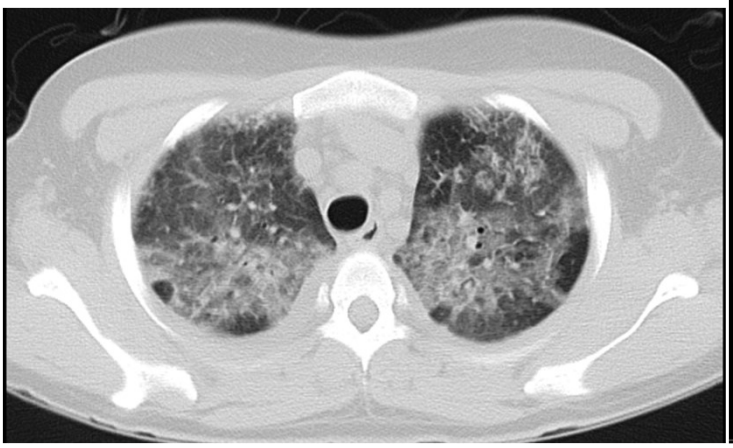
ESR 35 mm/hr

P/ANCA+, MPO 154

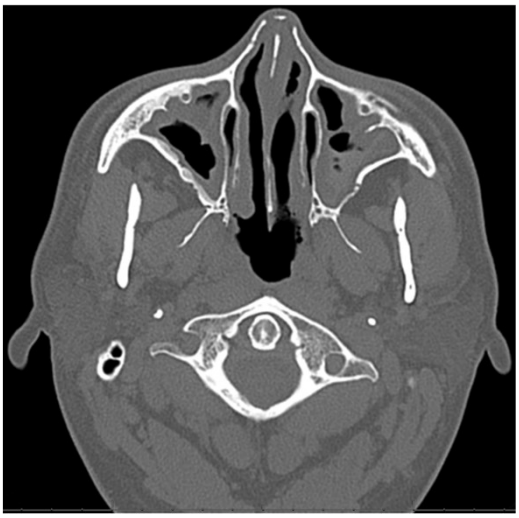
IgE 1,301 kU/L

- Pertinent negatives:
  - CMP normal
  - UA normal
  - FISH Probe with CBFB, PDGFRA, PDGFRB, FGFR1—Negative

Imaging

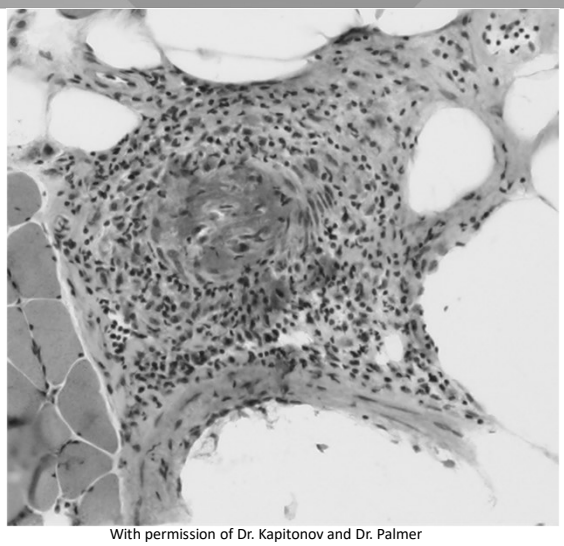


Bilateral ground glass opacities



Pansinusitis

Sural nerve biopsy



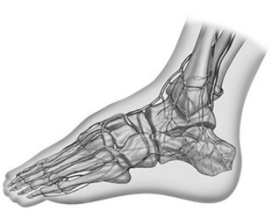
With permission of Dr. Kapitonov and Dr. Palmer

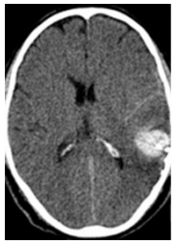
Fibrinoid and necrotizing vasculitis of artery on nerve biopsy

Diagnosis: EGPA

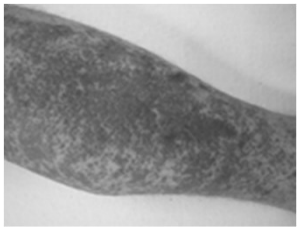
- Treatment:
  - Prednisone tapering over months
  - Oral Cyclophosphamide 2 mg/kg/d for 3 mo and then steroid sparing option
  - Sulfamethoxazole/trimethoprim DS 3 d/wk for PJP
  - Weekly alendronate for osteoporosis prevention
  - Review and update vaccines
- Other:
  - Weekly CBC and CMP for CYC toxicity
  - Yearly PFT/DLCO and echo

EGPA and vasculitis

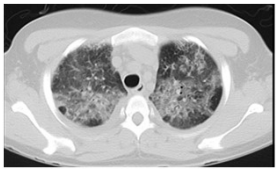




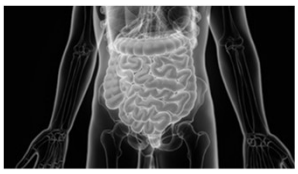
Mononeuritis multiplex/CNS vasculitis



Palpable purpura



Pulmonary hemorrhage



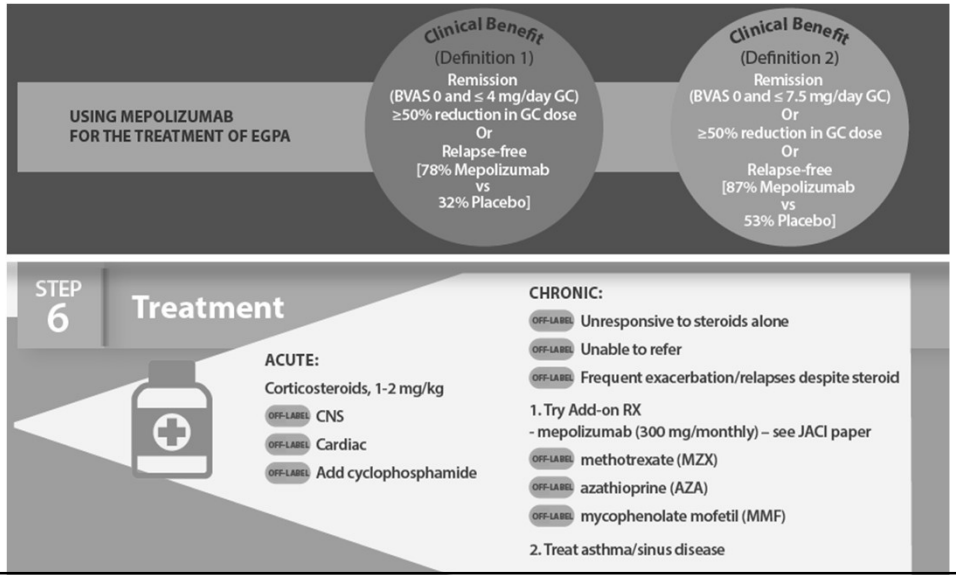
Intestinal vasculitis

EGPA and vasculitis

- Not always a late clinical finding
- +ANCA→ neuropathy, renal disease
- Vasculitis may not be seen in all patients with EGPA
- Vasculitis → morbidity and mortality
- 75% Mononeuritis
- Five Factor Score (Age, cardiac, renal, gut, absence of ENT)
- Pathology may show eosinophilic vascular infiltrate and not necrotizing/granulomatous vasculitis.

Guillevin L.Medicine.2011;90(1):19
Comarmond C.Arthritis Rheum.2013;65(1):270

Roundtable Discussion on Treatment



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Questions?

Thank you!