Vasculitis and the Lung: 2024

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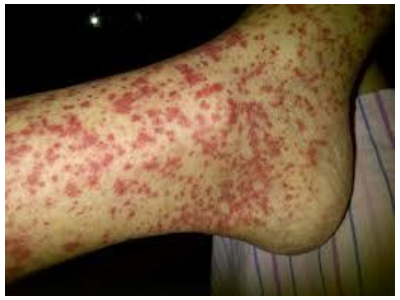
Disclosures

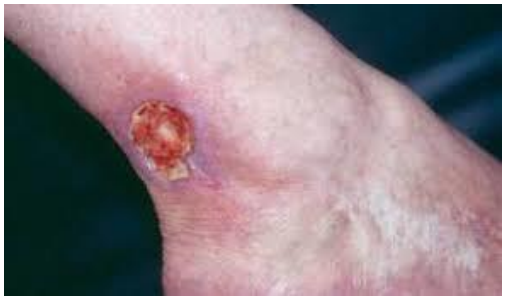
- Up to Date
- FDA Advisory board

Vasculitis: Summary

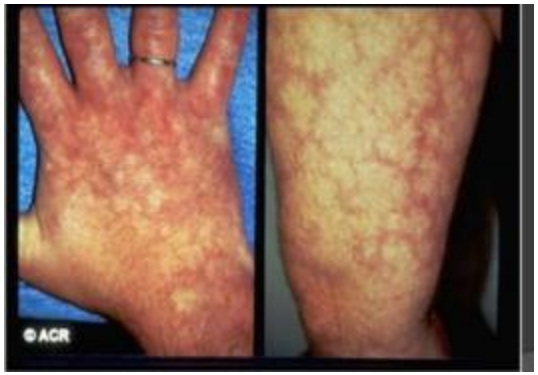
- A heterogeneous group of disorders characterized by vascular inflammation leading to vessel occlusion, local thrombi and tissue ischemia and necrosis.
- Pattern recognition is key to early diagnosis and early therapeutic intervention.
- Vasculitis of the lung is typically associated with ANCA and can present as part of the **pulmonary renal syndrome** such as in GPA and MPA , but other protean manifestations may obscure and delay the diagnosis.
- EGPA is characterized as a ANCA related vasculitis but ANCA is + in only about 40% of cases.
- ANCA + and ILD can exist as a UIP like phenotype with or without evidence of active or pre existing vasculitis
- Other diseases such as Bechet's , cryoglobulinemia and SLE can result in vasculitis of the lung but are rare.

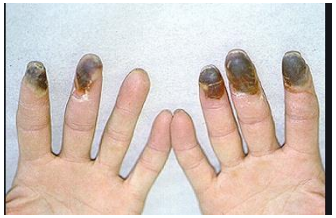
When to suspect vasculitis: clinical features



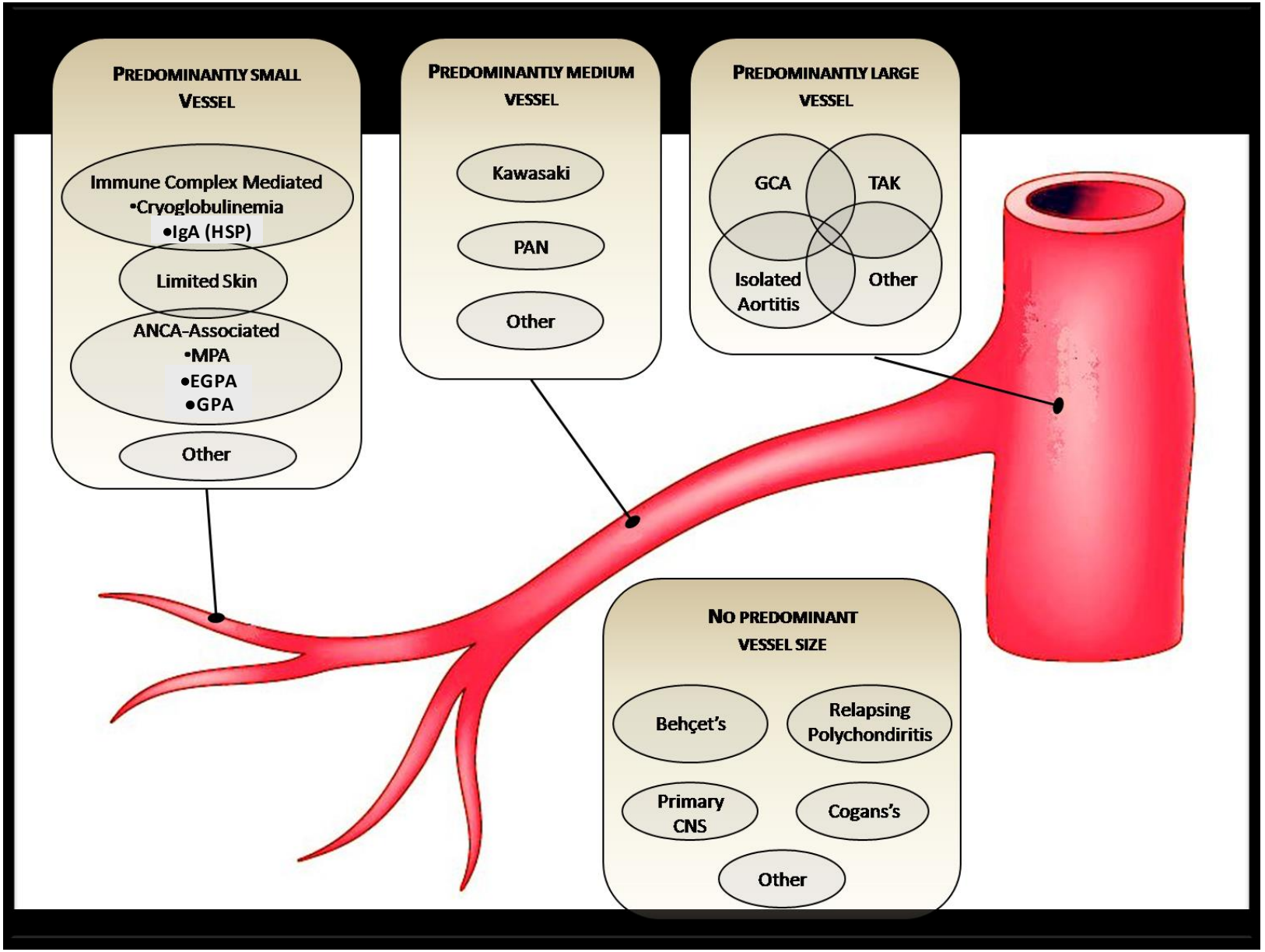


- Multisystem disease
- Unexplained constitutional signs and symptoms
- Skin lesions (palpable purpura or necrotic skin lesions, livedo, urticaria)
- Ischemic vascular changes (gangrene, claudication, Raynaud's
- phenomenon, livedo)
- Glomerulonephritis
- Mononeuritis multiplex
- Myalgia, arthralgia/arthritis
- Diffuse alveolar Hemorrhage/Lung nodules
- Abdominal (intestinal angina) or testicular pain





Classification of Vasculitis



Watts et al. Rheumatology 2011

Vasculitis: common clinical patterns

- **Polyarteritis nodosa**: abdominal pain, skin ulcers, neuropathy
- **Microscopic polyangiitis:pulm/renal syndrome, MPO ANCA**
- **Granulomatosis with polyangiitis (Wegeners granulomatosis): upper and lower respiratory tract, pulm/renal syndrome, PR3 ANCA predominate DAH being the classic but not only presentation**
- **Eosinophilic Granulomatosis with Polyangiitis (Churg Strauss):asthma, eosinophilia, pulmonary infiltrates ANCA + 40%**
- Cryoglobulinemic vasculitis:cutaneous vasculitis, nerve, rarely lung
- **IgA vasculitis**:cutaneous, abdominal pain, glomerulonephritis **rare DAH**
- **Behcets**:oral and/or genital ulcers, rash, uveitis, CNS and **pulmonary aneurysm**
- **Takayasu's arteritis**: pulseless syndrome affecting younger females.
- **Giant Cell Arteritis**;headache, jaw claudication, visual loss, PMR
- **Hypersensitivity vasculitis**: usually due to drugs.

Causes of DAH (KK Brown 2006 Proc ATS)

CAUSES OF DIFFUSE ALVEOLAR HEMORRHAGE

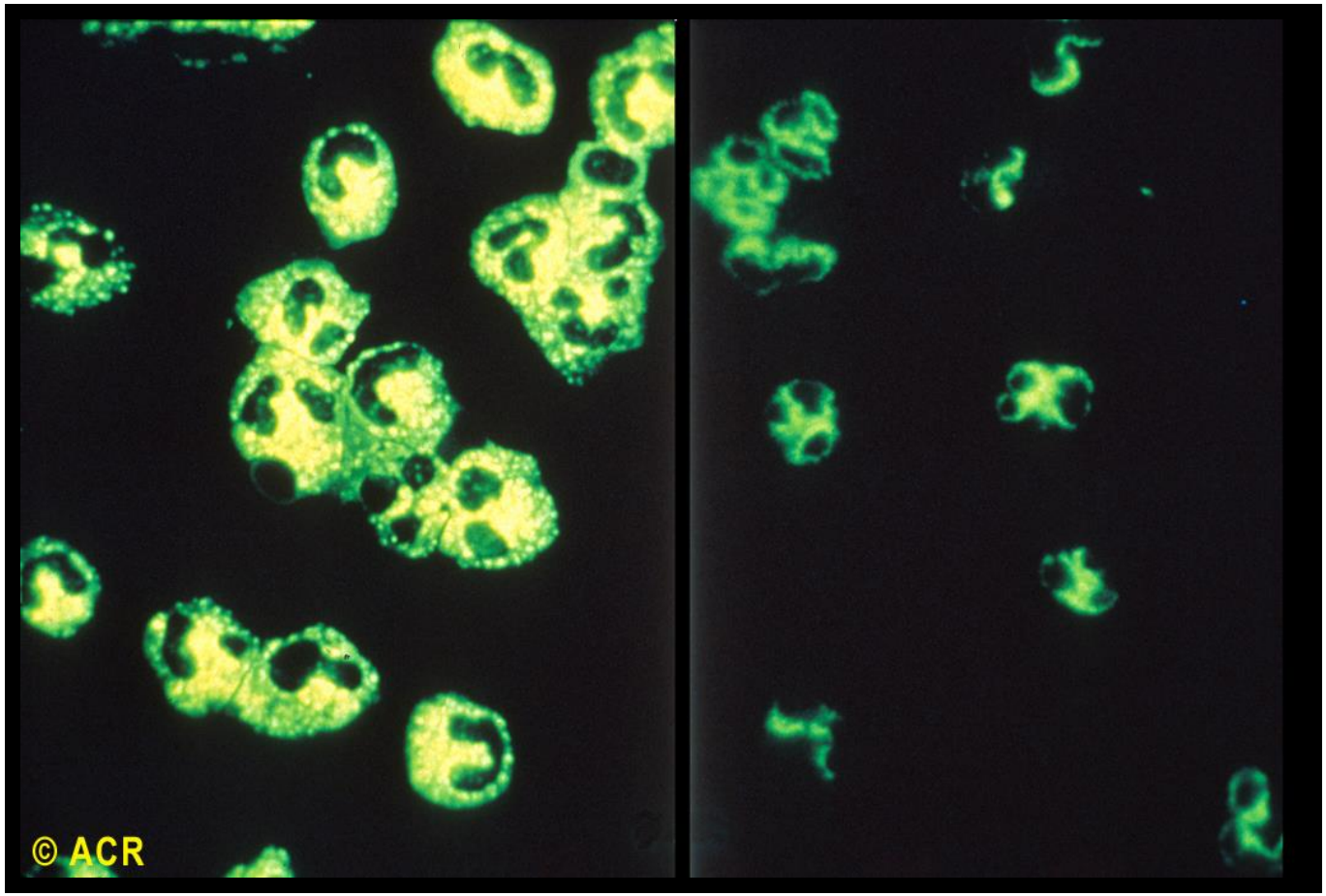
- With pathologic capillaritis
  - Primary idiopathic small vessel vasculitis
    - Wegener's granulomatosis
    - Churg-Strauss syndrome
    - Microscopic polyangiitis
    - Isolated pauci-immune pulmonary capillaritis
  - Primary immune complex–mediated vasculitis
    - Goodpastures syndrome
    - Henoch-Schönlein purpura
  - Secondary vasculitis
    - Classic autoimmune disease
      - Systemic lupus erythematosus
      - Rheumatoid arthritis
      - Antiphospholipid antibody syndrome
      - Mixed connective tissue disease
      - Polymyositis/dermatomyositis
    - Essential cryoglobulinemia
    - Behçet's disease

Op

Conditions that mimic systemic vasculitis

- Atheroembolic disease
- Cardiac myxoma
- Thrombotic disorders
  - Anti-phospholipid antibody syndrome
  - Thrombotic thrombocytopenic purpura
- Drug-induced vascular damage
  - Ergot derivatives
  - Cocaine
  - Amphetamines
- Infective endocarditis

ANCA: pattern noted on immunofluorescence is cytoplasmic or perinuclear: Clinically relevant antigens are PR-3 and MPO.



ANCA Associated Vasculitis

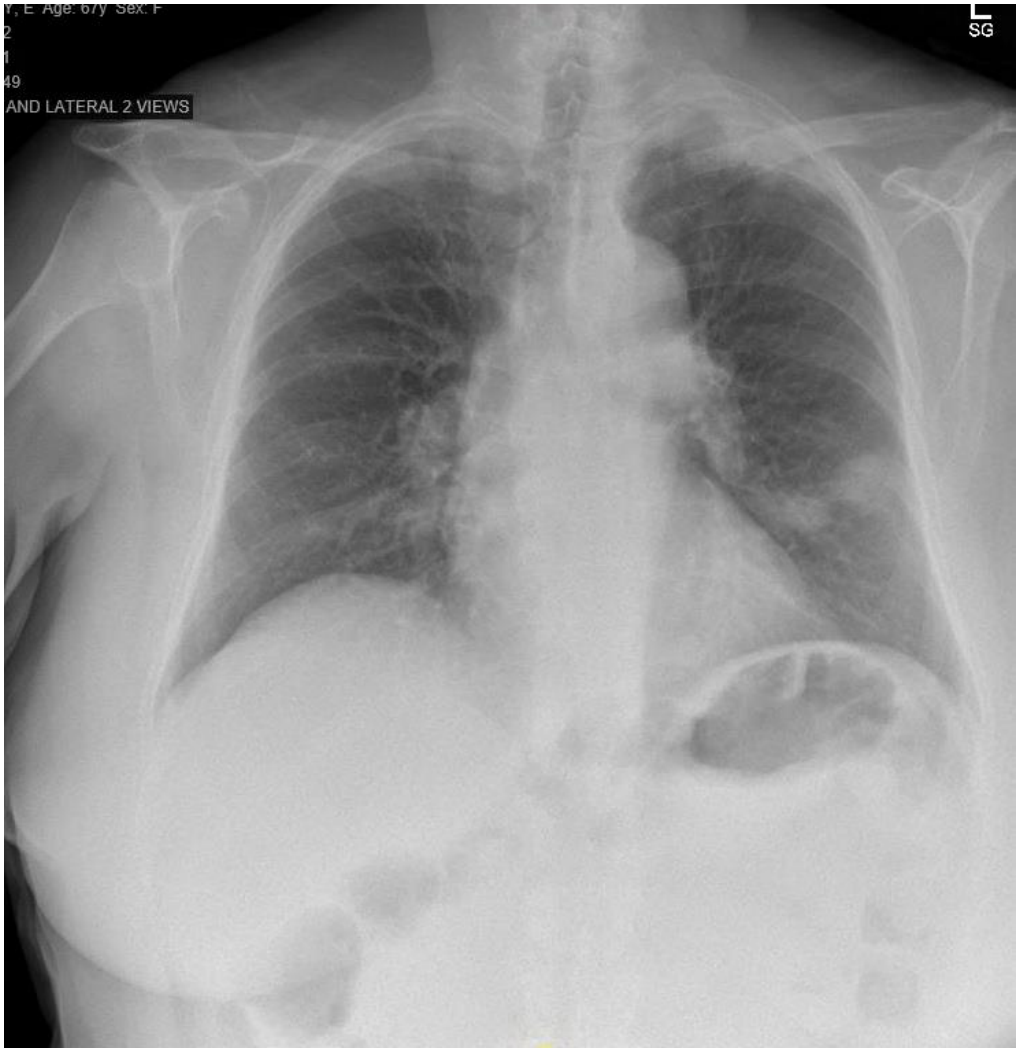
- C-ANCA with PR3 reactivity most commonly found in GPA though p-ANCA-MPO has been noted in 10% of cases of WG
- P-ANCA-MPO most often seen in microscopic polyangitiis. Occasionally ANCA and anti-GBM can be concurrent
- EGPA: ANCA + in 40% (MPO)
- Some pts can have both types of ANCA
- In initial treatment, the ANCA type is irrelevant, though mortality is **higher** with PR3 ANCA
- Concomitant ANCA and GBM can occur

ANCA and ANCA Associated vasculitis: pulmonary renal syndrome

- Very high titer ANCA (esp MPO) raises possibility of drug induced vasculitis (including cocaine also allopurinol, PTU, others)
- Prozone phenomenon described (ANCA thought to be “negative”
- ANCA is useful diagnostically but does not necessarily predict relapse
- Think of ordering an ANCA when you see a patient with nephritis or nephritis with nephrotic syndrome, DAH, or the pulmonary renal syndrome, recurrent sinusitis with epistaxis or recurrent otitis in a adult.
- The differential diagnosis of the pulmonary renal syndrome is ANCA vasculitis, SLE, Antiphospholipid syndrome and cryoglobulinemia

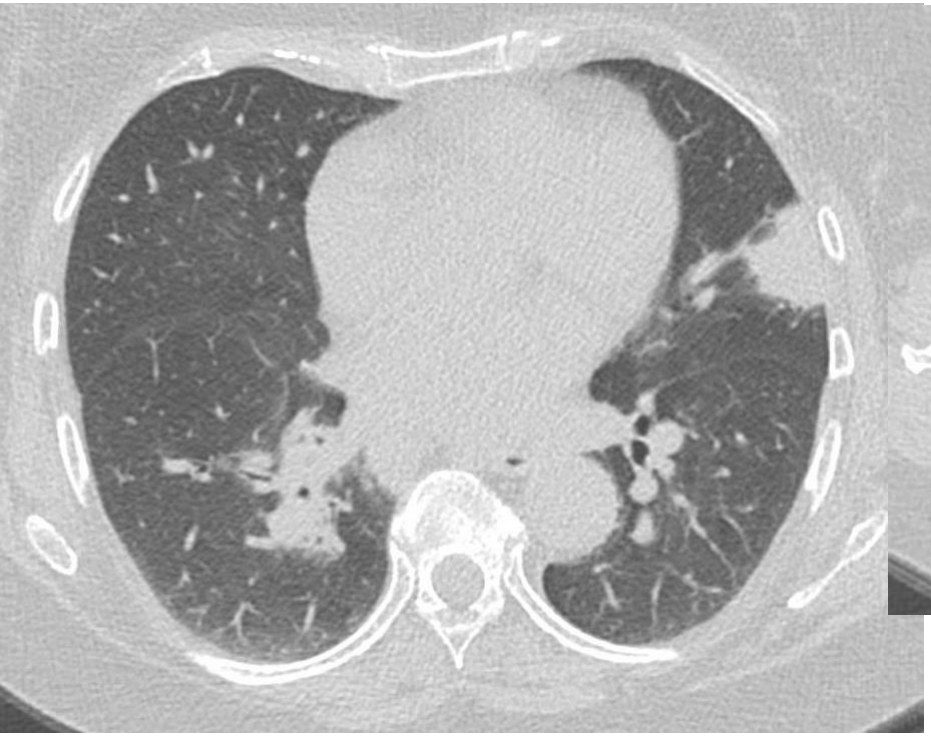
Case 1: 65 yo female with ear pain

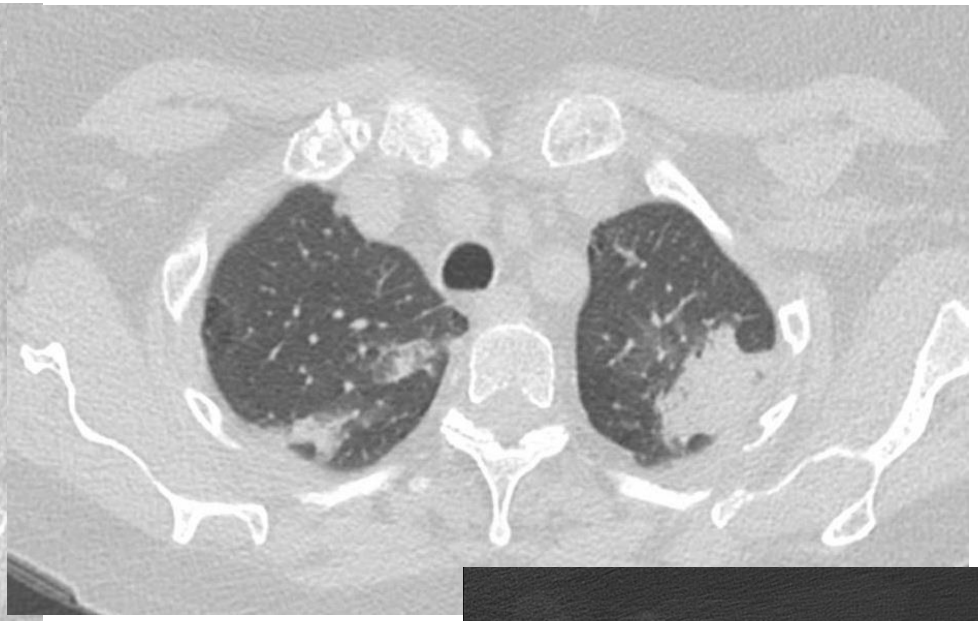
- April 2016 **left otitis media**: left vent tube placed by ENT and patient did well
- Erythema nodosum lower extremities July 2016 responded to colchicine
- Pt did well **until joint pain and arthritis May 2017**, NSAID no effect, responded to low dose steroids (7.5-15 mg) in June 2017
- Low + RF but CCP negative (labelled as possible RA at this point)
- Early **Aug 2017 dry cough, sinusitis**, Rx with Amoxicillin/Clav, no better: CXR done 8/15.

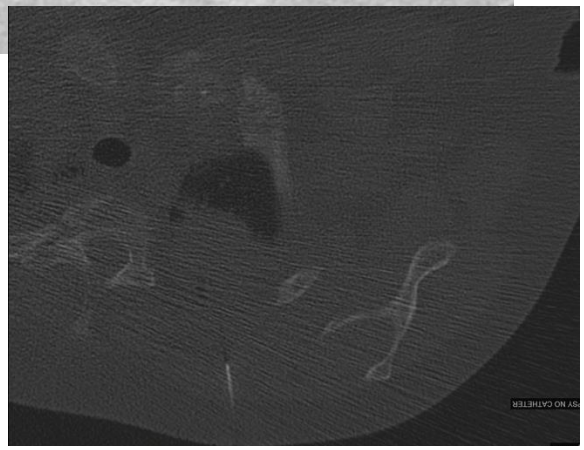


multiple new nodular opacities in the upper lobes and left lower lobe or lingual

The differential for this finding would include pulmonary rheumatoid nodules, vasculitis, tuberculosis, or other atypical infection.

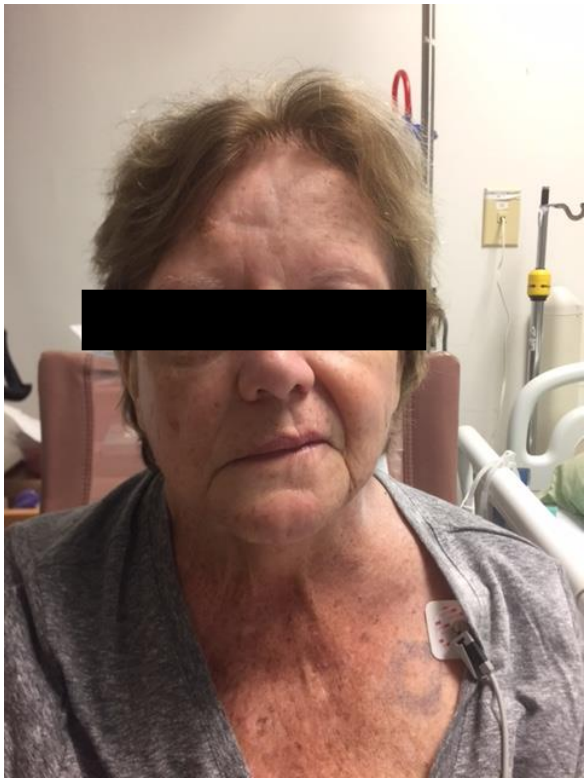


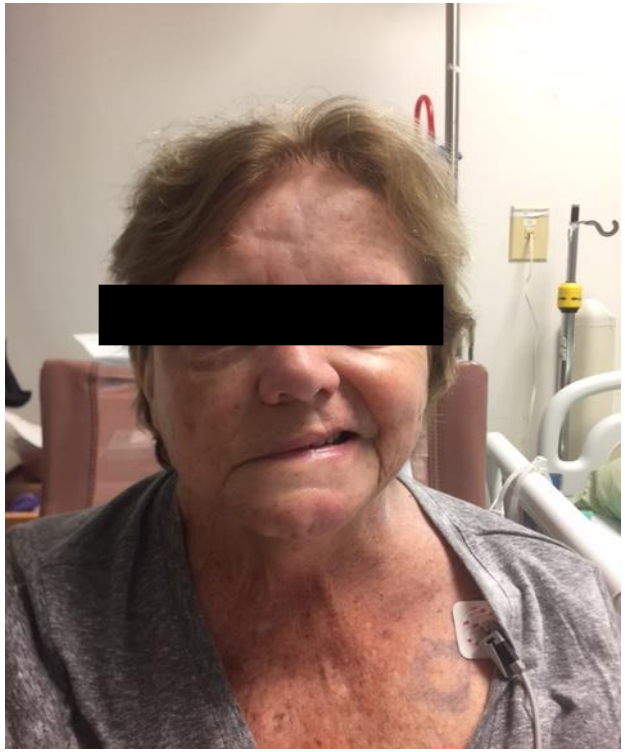


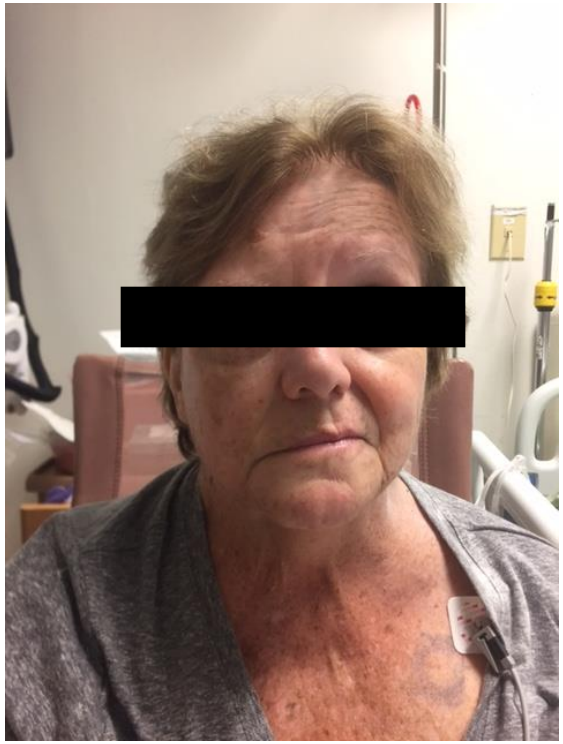


- Multifocal peripheral consolidation with associated bronchial wall thickening, most consistent with cryptogenic organizing pneumonia.
- Differential considerations include necrobiotic rheumatoid nodules, vasculitis and chronic eosinophilic pneumonia.

few days later…..plus 1 AV block on EKG



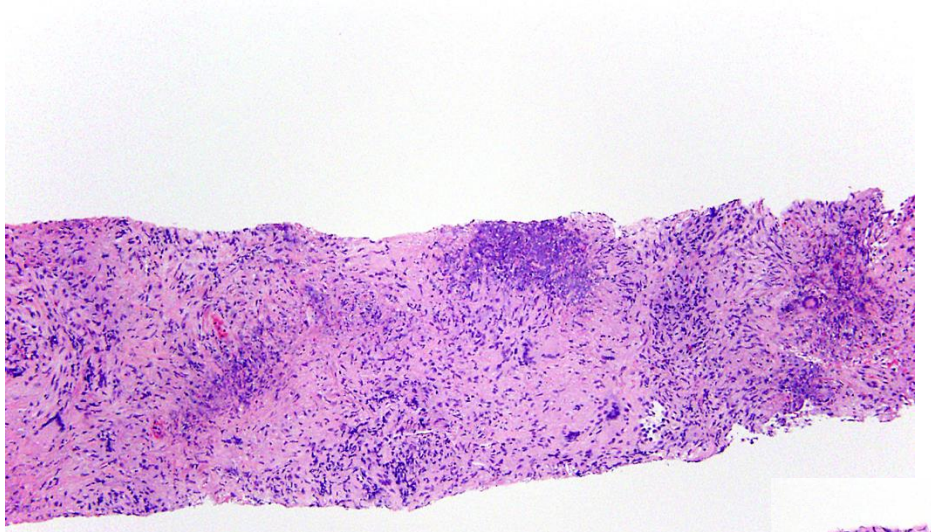


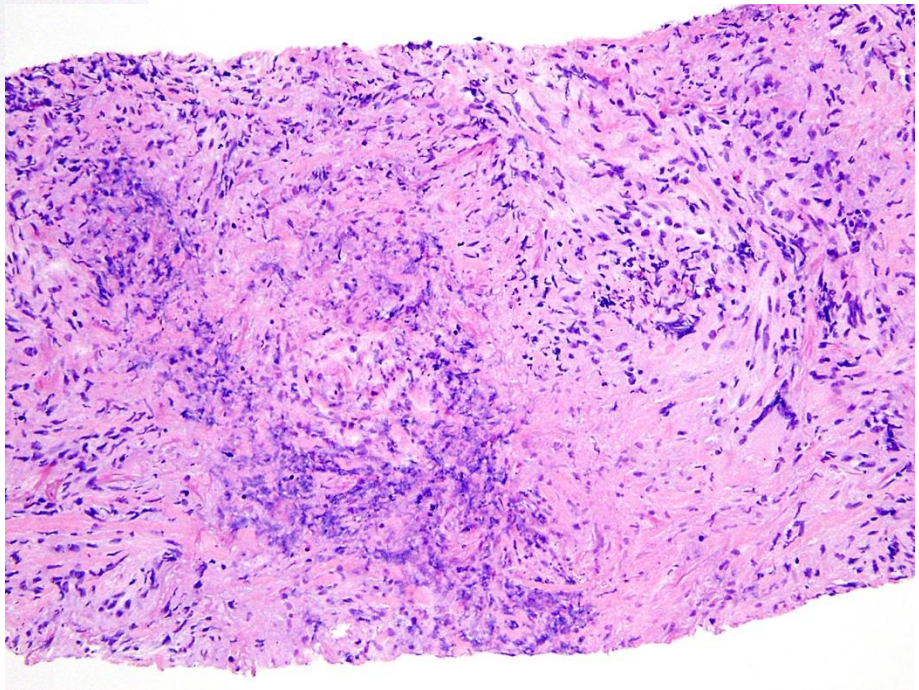


Labs

- RF 94
- UA trace blood 1 RBC
- CCP negative
- ANCA: **indirect immunofluorescence negative**
- ELISA : Pending

- What does this patient have?
- What to do? (?treat ?biopsy tissue ?send ANCA again)





Follow-up

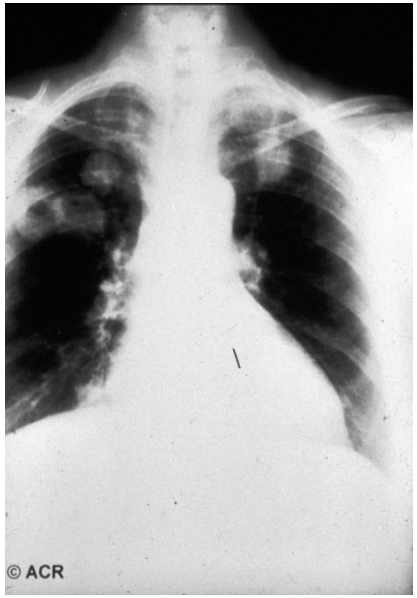
- ANCA immunofluorescence “re-read” at BWH and diluted out and also send out to MGH: + (Prozone effect) **ELISA PR3 + 113**
- **Biopsy of the lung showed necrotizing granuloma and vessel wall inflammation**
- Patient treated for GPA with high dose steroids and RTX (RAVE trial NEJM 2010)

Key points of this case

- Classic upper respiratory symptoms are a tip off to the disease
- Unusual manifestations like cranial neuropathy or CNS vasculitis are rare but can occur in GPA
- Remember the rare but important **prozone phenomenon** in ANCA testing

Granulomatosis with Polyangiitis (GPA)

- Classic patterns include upper respiratory symptoms, sinusitis, epistaxis, hearing loss, otitis media (***remember, adults otherwise rarely get otitis media)***
- **Upper airway obstruction**
- Lower respiratory symptoms (bronchitis, hemoptysis due to capillaritis)
- Glomerulonephritis
- Mononeuritis multiplex, cranial neuropathy, orbital pseudotumor, arthritis
- Constitutional symptoms (fever, weight loss,fatique)
- Pattern recognition helps but doesn't all tell the tale……..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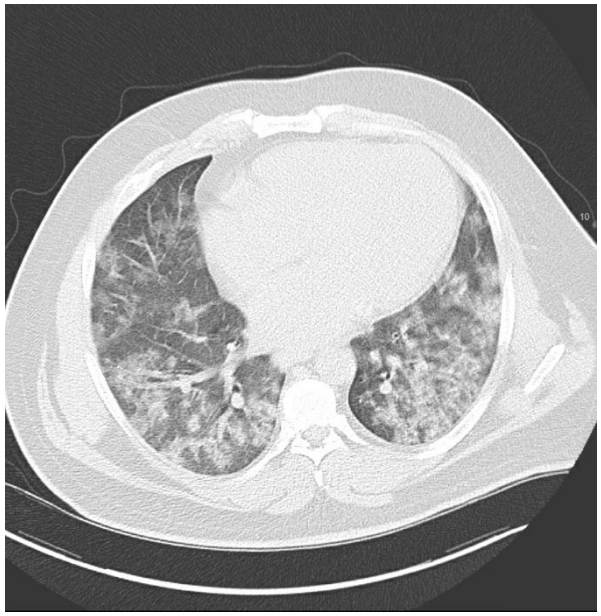

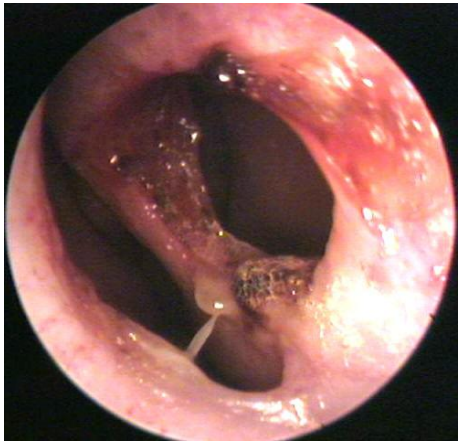

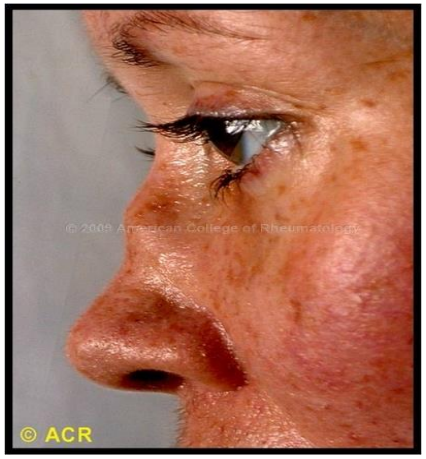
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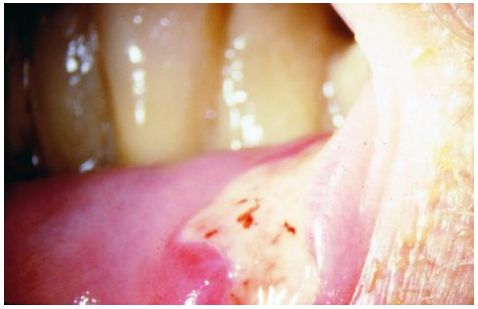
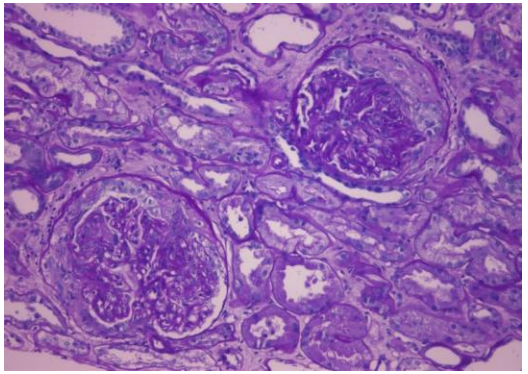
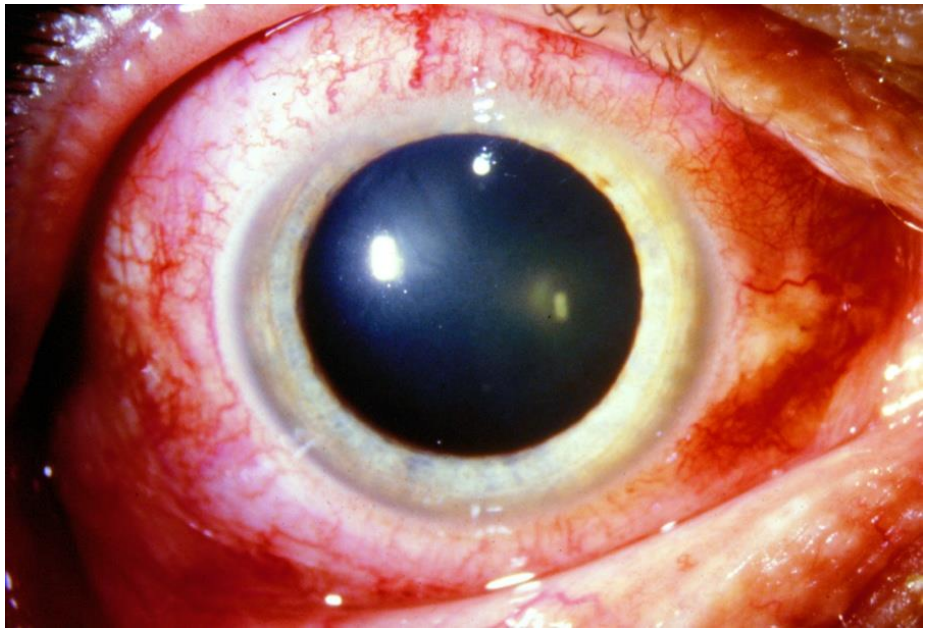
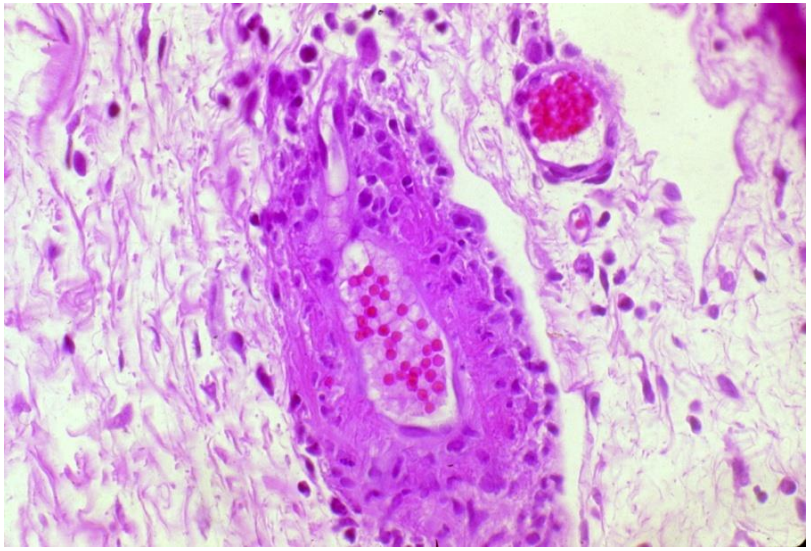
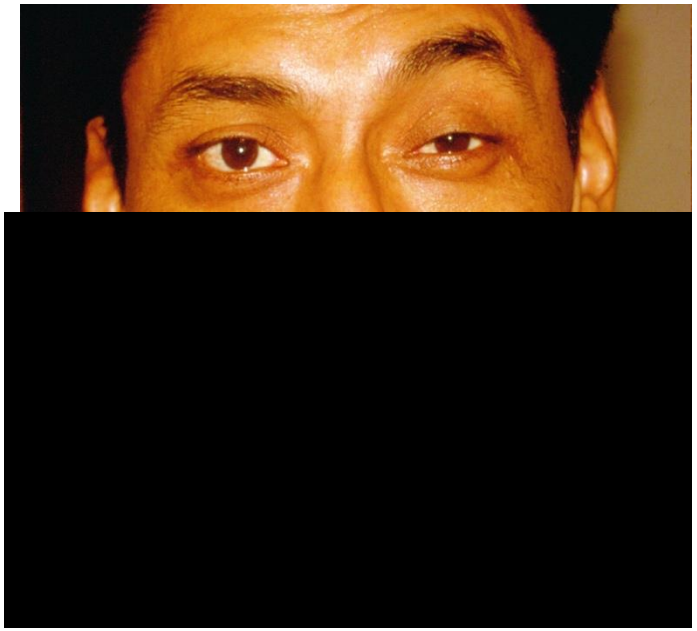


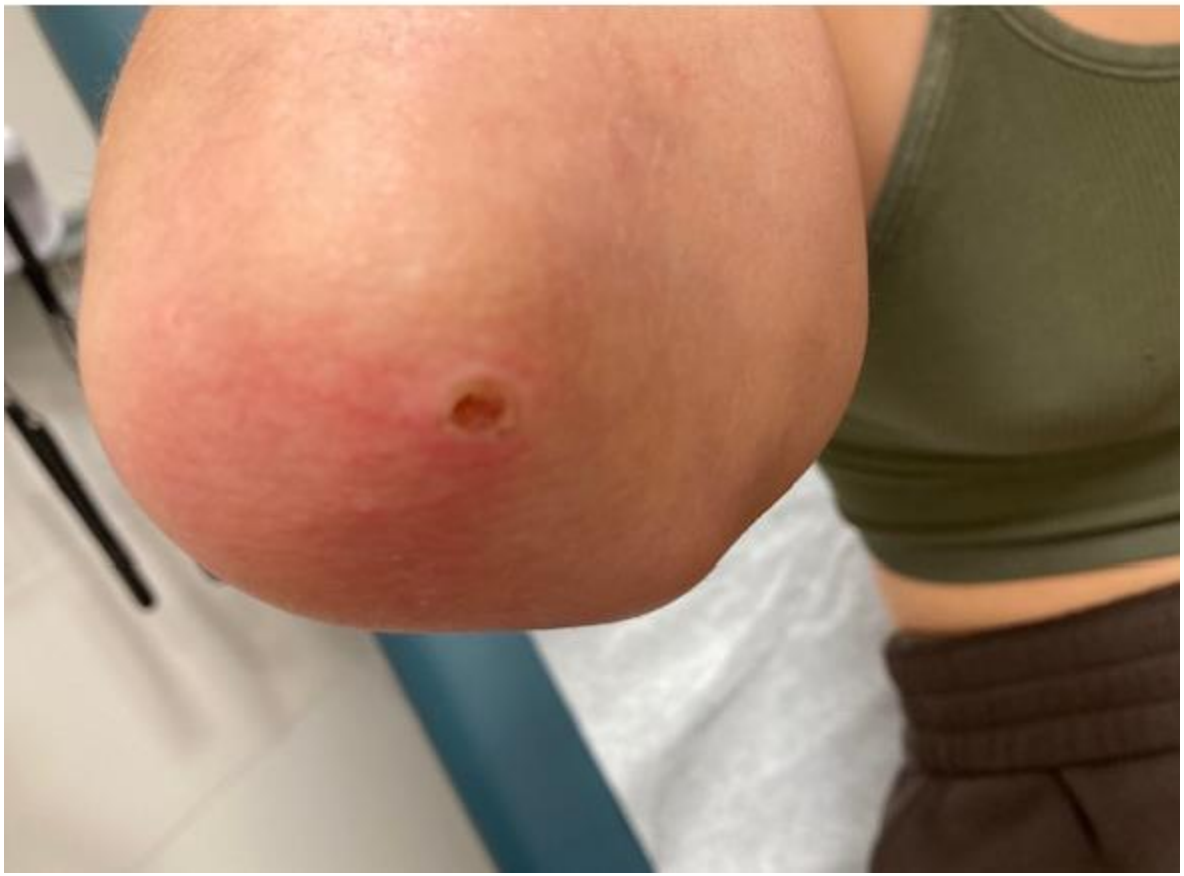








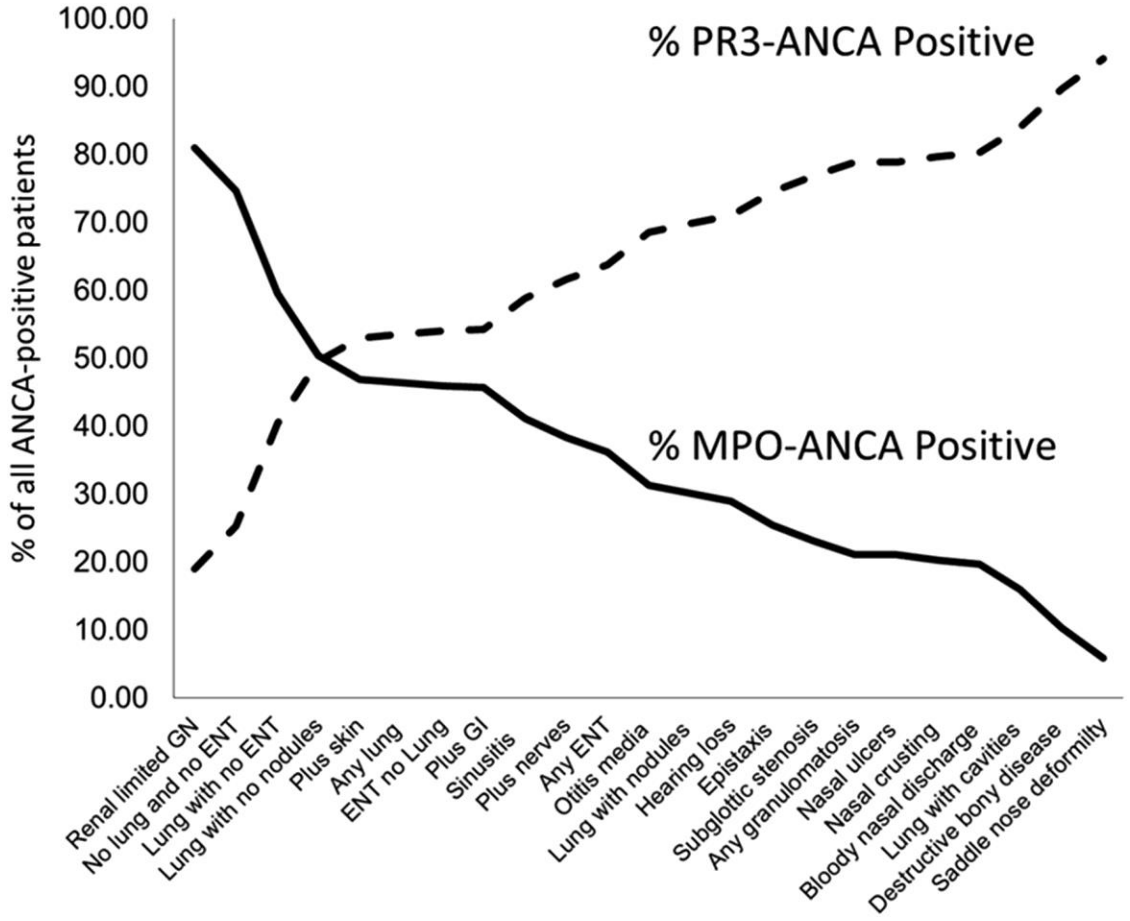
Granulomatous elbow lesions in ANCA



Microscopic polyangiitis

- Present with GN as major clinical finding
- Mononeuritis multiplex
- Alveolar hemorrhage
- Sometimes difficult to distinguish from GPA(WG)
- ANCA is pANCA pattern (**MPO ab**)
- Treatment algorithm similar

Clinical phenotypes and ANCA subtype (Jeanette C CJASN 2017)



Case II: Less “Typical” ANCA case

- 60 y.o. female presented in Feb 2016
- She was well until she returned from a trip from Aruba Nov 2014 and the day after in Nov 2014 she noted **sudden achiness head to toe**, couldn't move, no fevers, no rash, no cough, no abd pain, just achy, no joint swelling.
- She was given a short taper of steroids 20 mg per day , did well but then the achiness in her calves and upper arms leading to resumption of low dose steroids

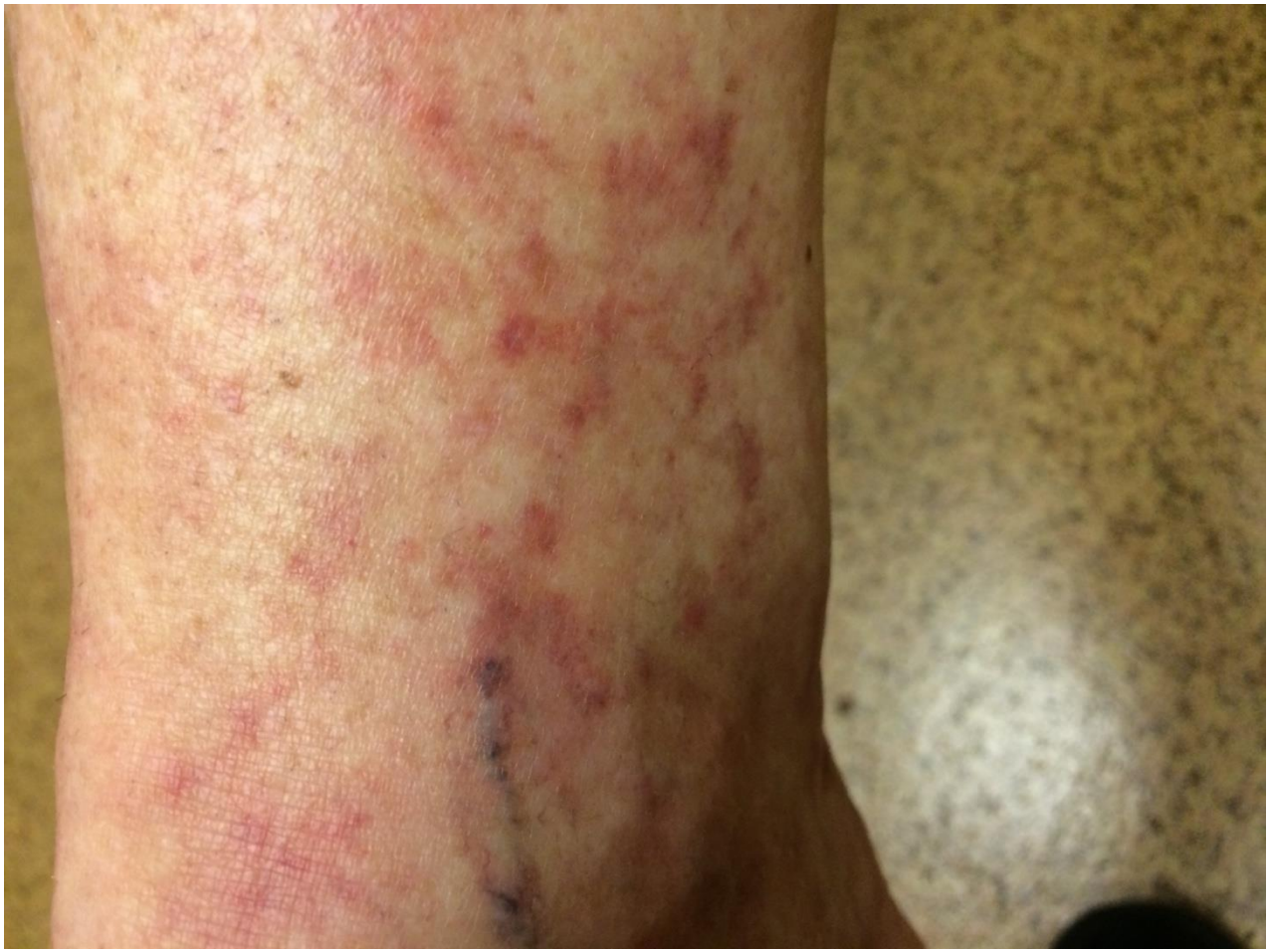
- **Current Outpatient Medications:**
- **lisinopril 5 daily**
- **prednisone mg 5 mg bid,**
- **Atorvastatin, on hold since sept 2015**

Laboratory evaluation

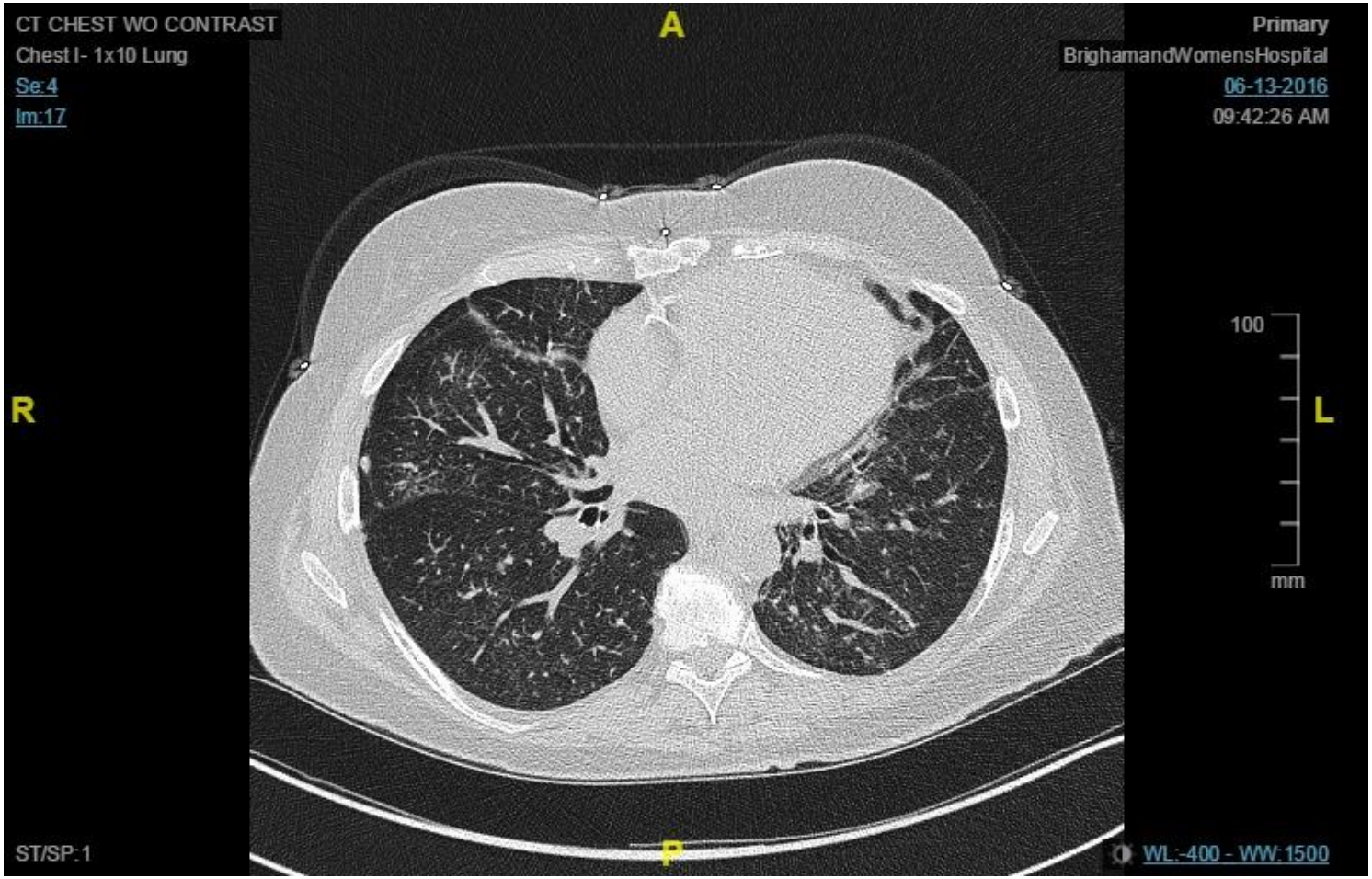
- **RF 336**
- **CCP 8 (borderline)**
- CRP 32
- ESR 51
- ANA 1:40 ENA negative
- **Based on this and her inability to get below 10mg, Rx with hydroxychloroquine for her joint pain**

- She was started on hydroxychlorquine in March 2016 200 mg bid and
- She was able to taper her steroids to 2 mg of prednisone.
- **Then she developed a new rash lower legs, more fatique , thighs/calves ache and *new dry cough*. No fever, no chest pain, no DOE.**

PT KE developed skin lesions on legs



Pt KE


CT CHEST WO CONTRAST
Chest I- 1x10 Lung
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CT scan chest

- IMPRESSION:
- Constellation of findings including diffuse septal thickening
- with **beaded appearance, perilymphatic nodularity** and subtle groundglass.
- superimposed scattered nodules,
- mildly enlarged mediastinal lymph nodes.
- **Radiologist: This may represent sarcoidosis, lymphangitic spread of cancer less likely.**

Labs

- CRP 132 ESR 104
- UA trace protein, no RBCs
- Cryoglobulins negative
- Hep B and C negative
- **pANCA + MPO 136**
- **Drug screen negative**

Derm: biopsy done

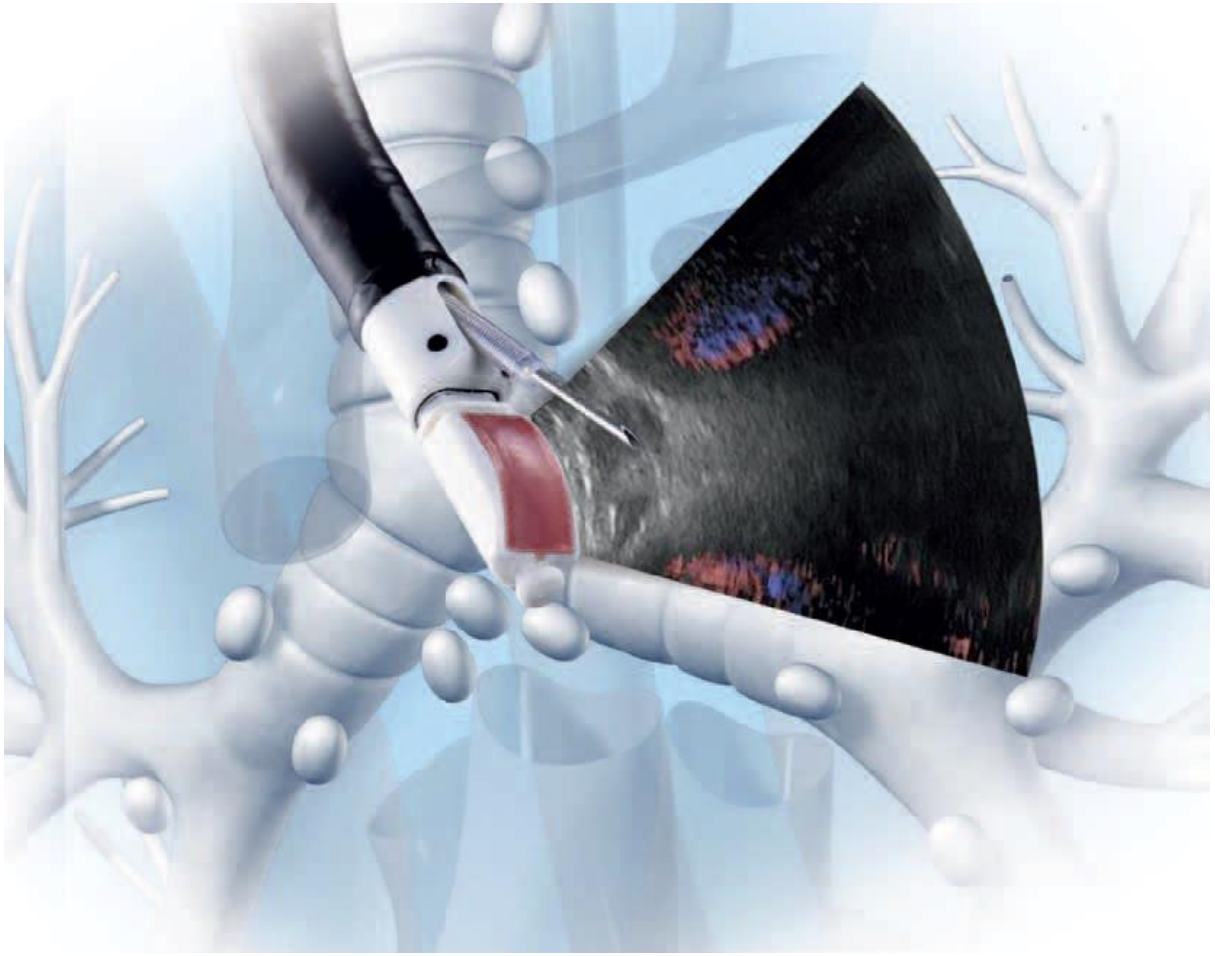
- PATHOLOGIC DIAGNOSIS:

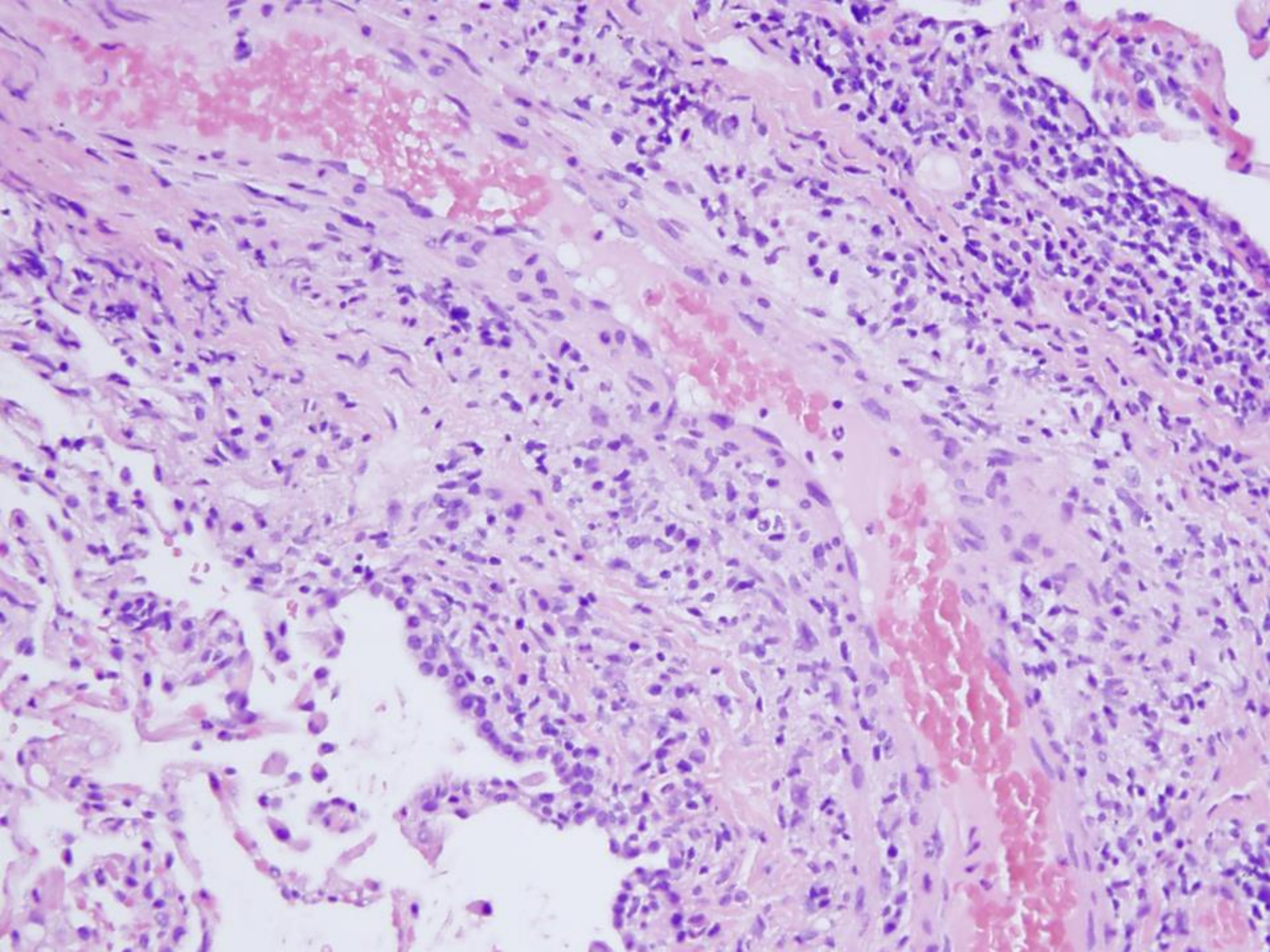
  C. SKIN, RIGHT CALF, PUNCH BIOPSY:
  Acute necrotizing vasculitis (leukocytoclastic vasculitis) involving superficial to mid-dermal vessels.

  D. SKIN, LEFT DISTAL MEDIAL SHIN, PUNCH BIOPSY:
  Acute necrotizing vasculitis (leukocytoclastic vasculitis) involving superficial to mid-dermal vessels.

- AFB and fungal stains and culture negative

EBUS





Path diagnosis

- A. LUNG, RIGHT MIDDLE LOBE, TRANSBRONCHIAL BIOPSIES:
  Active and healing vasculitis involving both arterioles and venules, see NOTE.

  NOTE: The sections show multiple vessel profiles with mural infiltration by
  mixed, predominantly lymphohistiocytic inflammation with occasional giant
  cells/granulomas and eosinophils. The differential diagnosis includes Granulomatosis with Polyangiitis (Wegener's), Churg-Strauss Syndrome, and
  microscopic polyangiitis. Clinical and serologic correlation is needed.
- **Treatment: Pt treated with steroids/RTX.**

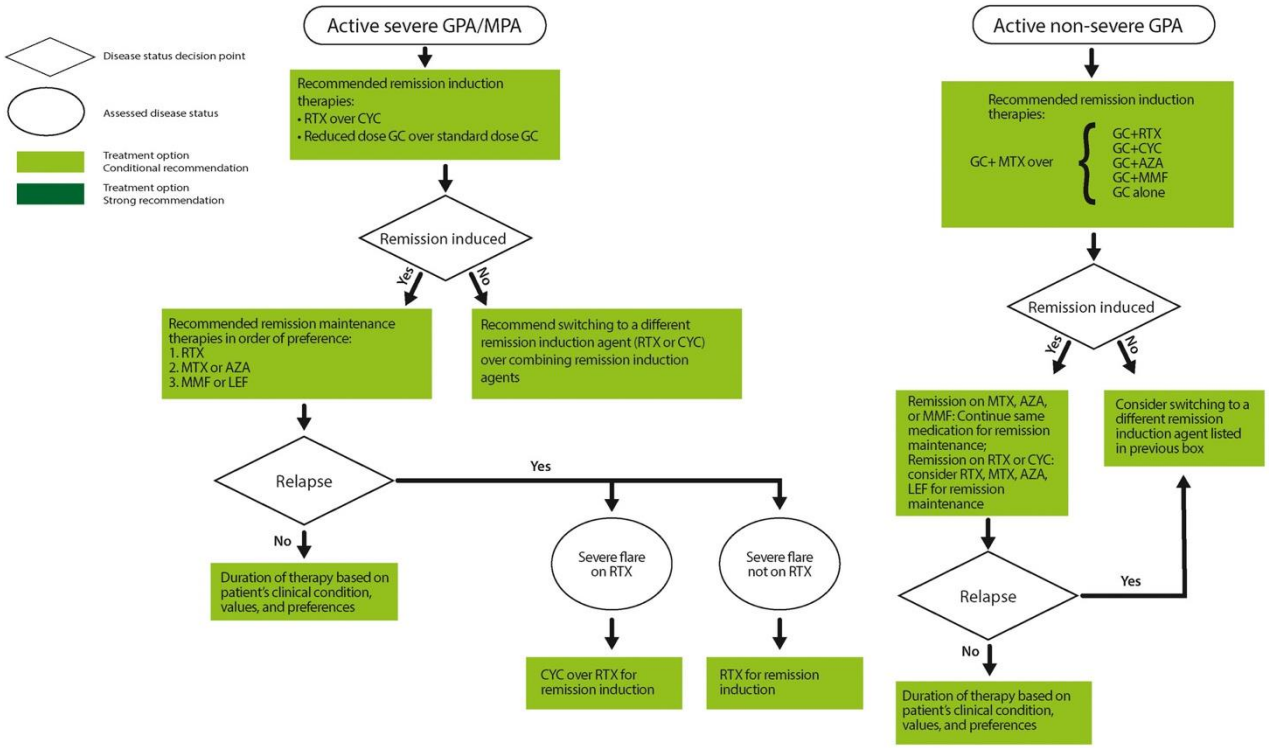
Key points of this case

- Initial presentation of ANCA associated vasculitis can be protean, especially with initial presentations, RA like presentations, PMR fatigue, pleurisy, pericarditis, valvular disease, amongst others
- Review of CT findings in 51 MPA patients with pulmonary involvement. Ground-glass attenuation in 94% of patients, consolidation in 78%, **thickening of bronchovascular bundles in 51%, honeycombing in 37%,** nodules larger than 1 cm in 29%, bronchiectasis in 27%, pleural effusion in 27% and enlarged mediastinal lymph nodes in 18%. (Ando et al J Comput Assist Tomogr, 28 (2004) p. 710–6
- **The yield of a TBBX is low in vasculitis*. We got lucky this time.***

Modern treatment of ANCA vasculitis

- Induction: Rituxan over cyclophosphamide for induction
- Remission: Rituxan or DMARD (MTX, AZA > MMF)
- Consideration for adding avocopan which is a C5a receptor antagonist (steroid sparing ? renal protection)
- Role for plasmapheresis (PLEX) is diminished in GN and DAH related to ANCA vasculitis (PEXIVAS trial)

Key recommendations for the treatment of granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA)



AZA = azathioprine, CYC = cyclophosphamide, GC = glucocorticoids, LEF = leflunomide, MMF = mycophenolate mofetil, MTX = methotrexate, RTX = rituximab

Chron Respir Dis 2021; **18**: 147997312199456.

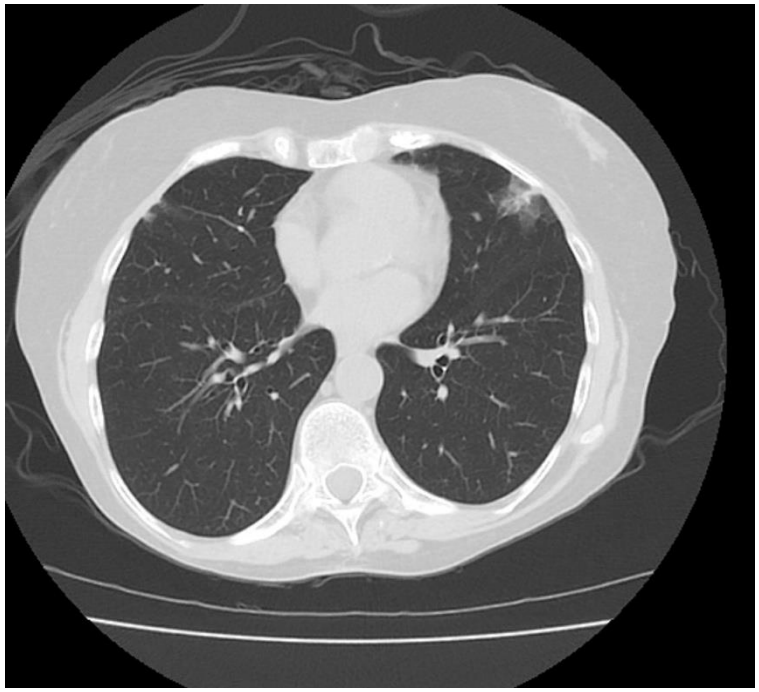
ANCA and ILD

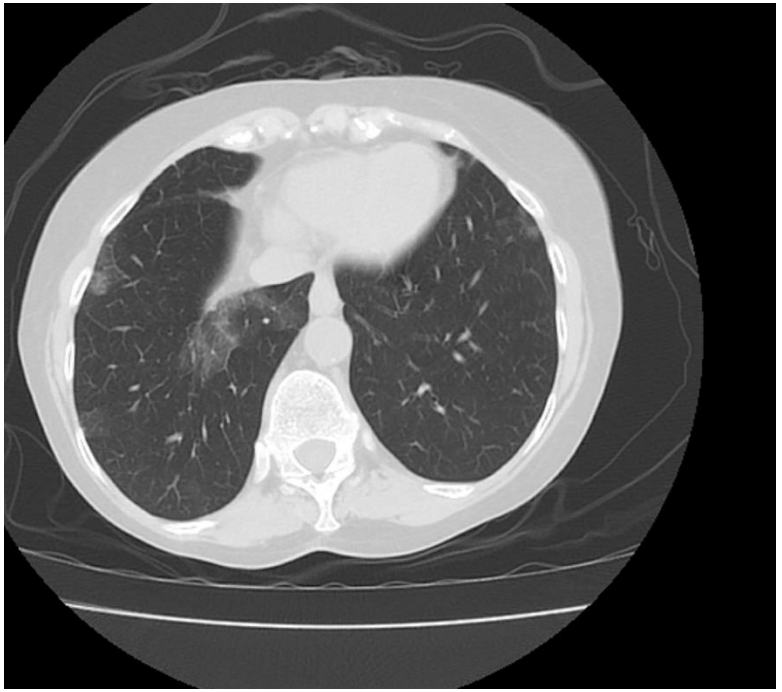
- Some pts with UIP pattern are ANCA + typically MPO but sometimes PR3
- ILD patterns can co exist with active vasculitis or may be present without evidence of vasculitis (only IIP) ,which is what we typically see
- We have mostly been treating these patients for UIP as opposed to offering immunosuppression.
- Meta-analysis 2.9-fold increased risk of death in patients with AAV-ILD when compared with the control group of AAV patients without ILD higher in the UIP group (Zhou P Chr Resp Dis 2021)
- In surgical lung biopsy (SLB) findings in 18 patients with IIP and MPO-positivity showed UIP pattern in 56%, with 40% of the patients with a UIP pattern found to have additional inflammatory changes not typical of the UIP pattern in patients with IPF (Baquir M et al *Sarcoidosis Vasc Diffuse Lung Dis* 2019

Not all lung vasculitis is related to ANCA!

- 72 y.o. female was well until 3 years ago when she noted feeling mild dyspnea with her exercise
- The dyspnea worsened about a year ago, with some chest pain noted with exertion. She underwent a ETT and cardiac cath and there was no evidence of CAD.
- She has been moderately fatigued, + mild dry eyes and mouth, no fevers, no nite sweats no swollen parotids, no hair loss, no cough no hemoptysis. + occ canker sores, no skin lesions, no hair loss no facial rash.
- She has had occ epistaxis right nostril only no ear pain no eye pain no hearing loss.
- She has had multiple sinus surgeries for infections in the past and had been on IVIG For >10 years but was stopped 6 months ago.
- No cocaine use
- Lifelong non smoker, no inhalants, dust mold, pets birds.

CT chest showed fleeting GGOs



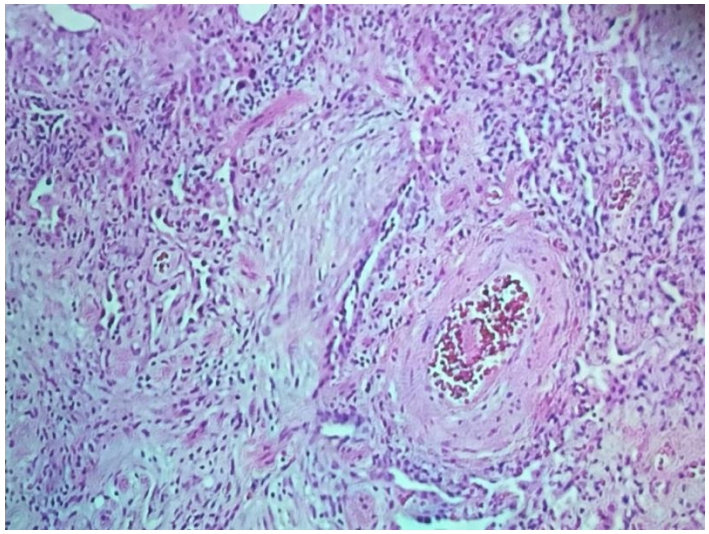


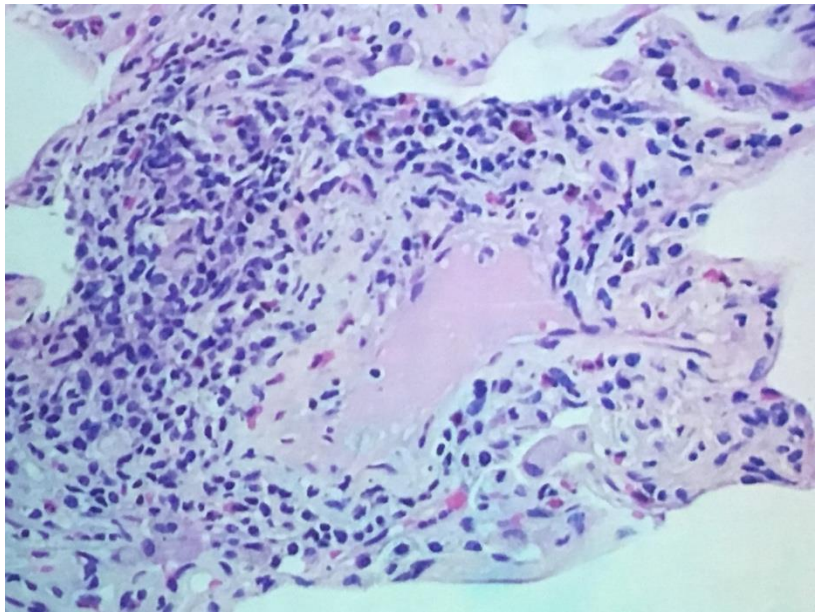
Labs

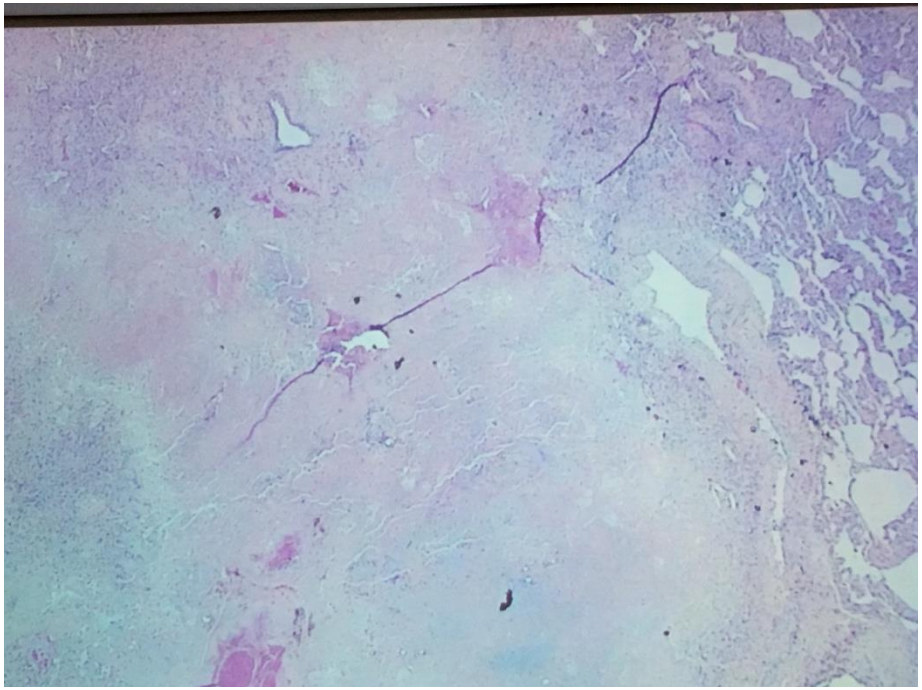
- ANA, ENA, ANCA, ACA, UA negative CBC diff and met profile negative
- **ESR >118 CRP 8**
- **Pulmonary Function Tests**
- 4/1/19 (BIDMC): FEV1 67%, FVC 69%, FEV1/FVC 73%
- 9/17/18 (BIDMC): FEV1 70%, FVC 77%, FEV1/FVC 69%, DLCO 79%
- 7/10/18 (BIDMC): FEV1 67%--> FVC 63%, FEV1/FVC 81%
-
- **Cardiology Testing**
- 4/16/19 TTE (BIDMC): Normal biV cavity sizes and systolic function (LVEF 61%). Mild PA systolic hypertension (est PASP 29 mmHg). Mild MR with normal valve morphology.

-

Lung biopsy





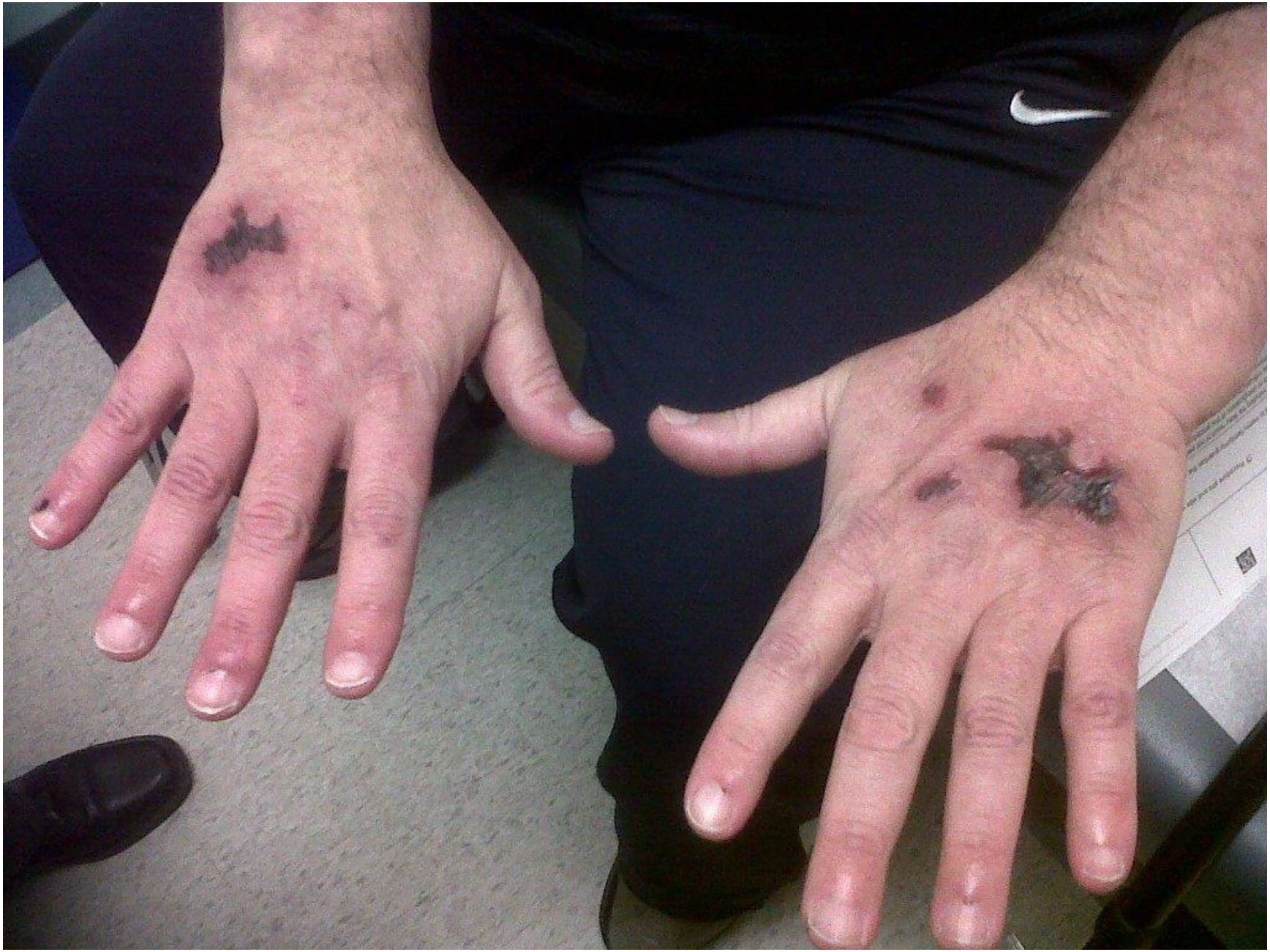


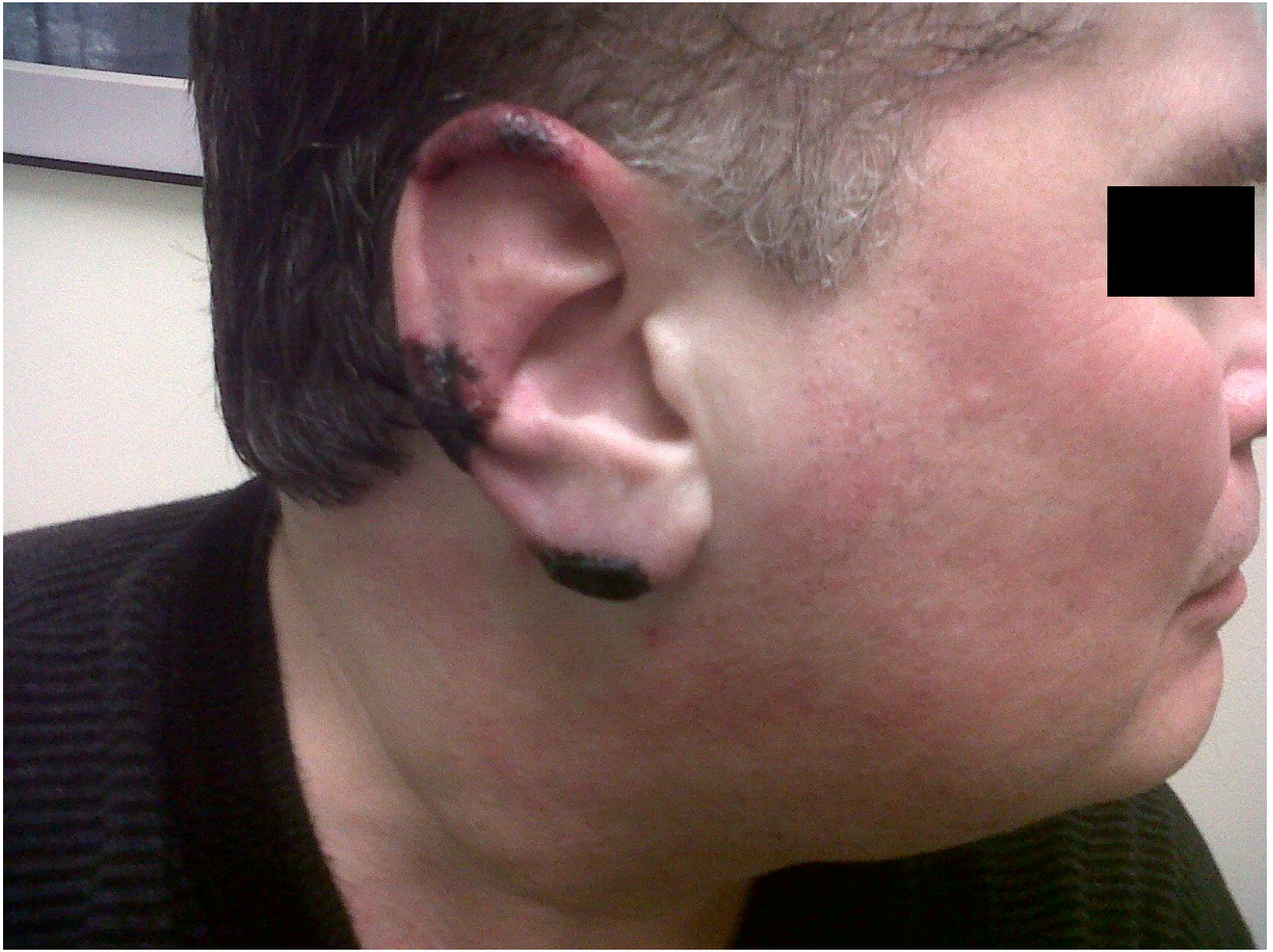
- A-C.) LUNG, RIGHT UPPER LOBE, RIGHT MIDDLE LOBE, AND RIGHT LOWER LOBE, WEDGE
  RESECTIONS:
  ACTIVE VASCULITIS, predominantly affecting small vessels with occasional large vessel involvement and multifocal organizing/organized intravascular ***thrombi***, see NOTE.
  Multifocal remote and recent infarcts.
  Patchy mild chronic interstitial inflammation, including rare poorly formed ***non-necrotizing granulomas.***
  Focal lymphocytic bronchiolitis and focal pleuritis.
  Emphysematous changes and minimal interstitial fibrosis.
  AFB, Fite, and GMS performed at an outside institution and reviewed at BWH are negative for organisms.
  There is no evidence of malignancy.
- ***Of note V/Q scan was +***

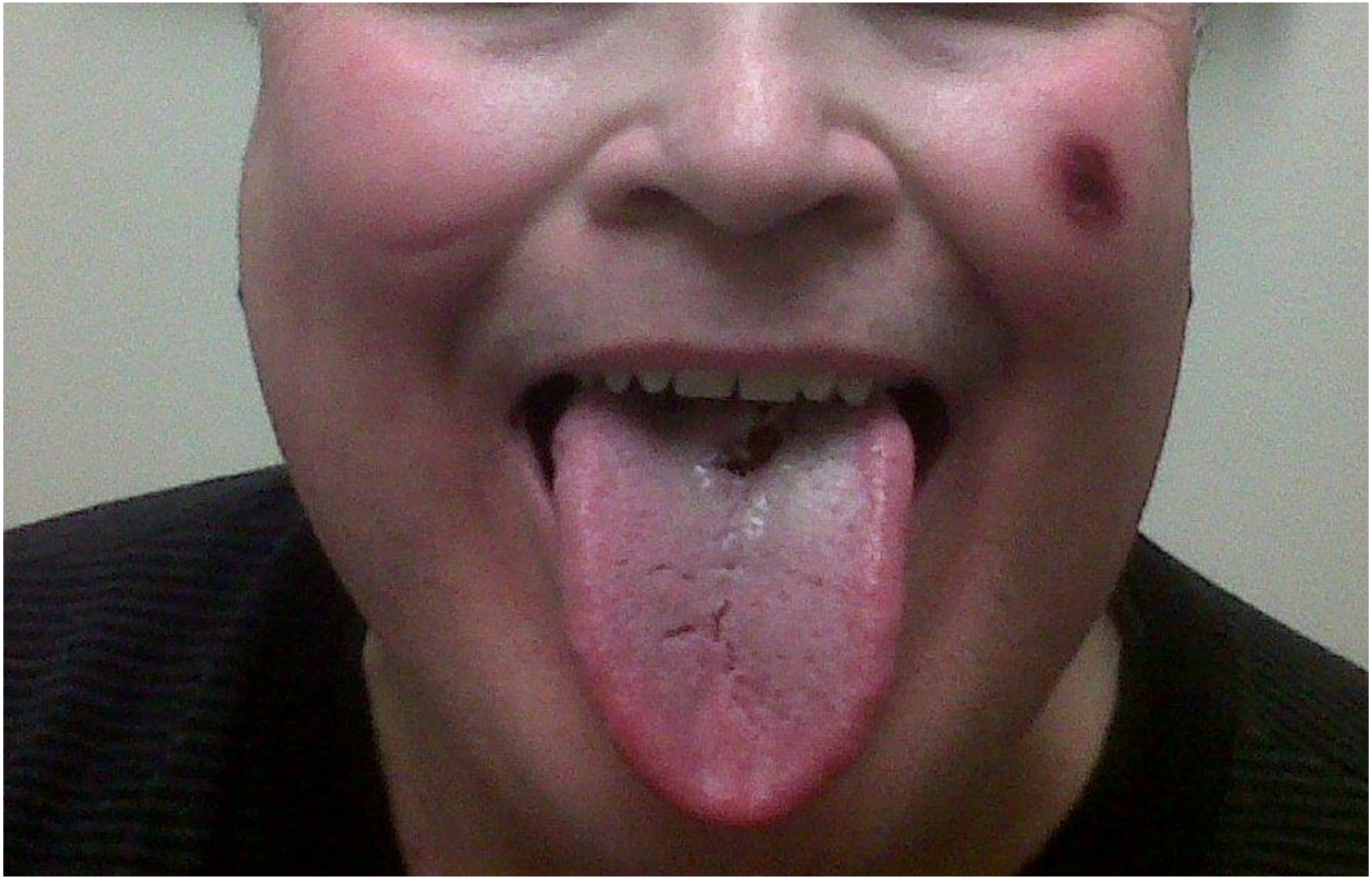
Is this Primary Vasculitis of the Lung ?

- What to do for this patient?
- Is this ANCA negative vasculitis?
- When serologies are negative, can immunopathology help us on a biopsy?
- Treated with steroids, anticoagulation and Rituxan with stabilization of lung function and persistent but not progressive GGOs

Bonus Question: What is this?







What could this be?

- PAN (necrotic lesions, often nodular)
- Cryoglobulinemia (maybe but pretty dramatic)
- **Drug induced ANCA vasculitis** (typically skin disease) (cocaine, PTU, Allopurinol, minocycline, others)

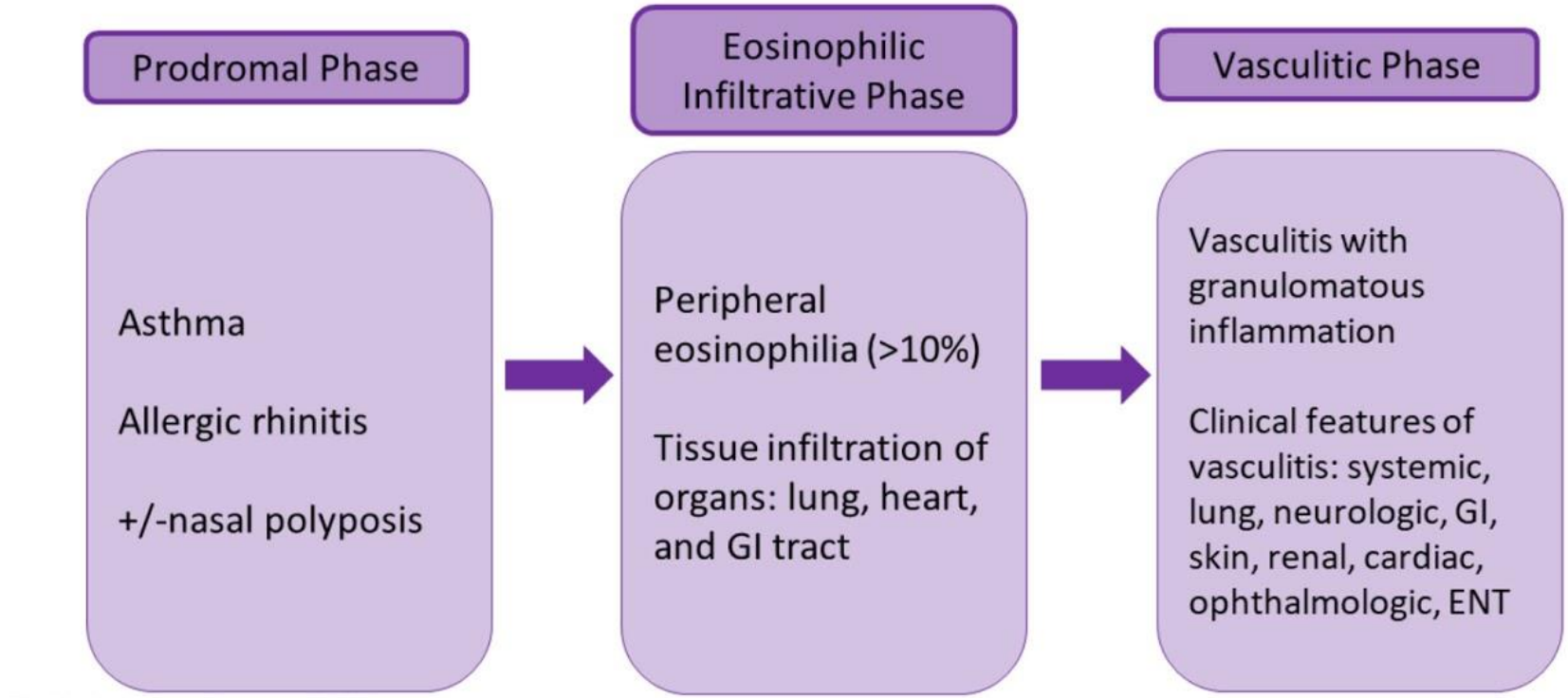
- AN**SWER : pt used cocaine, this is due to levamisole contamination causing a drug induced ANCA syndrome which can cause a systemic vasculitis**

Eosinphilic Granulomoatosis with polyangiitis (EGPA)

When to consider EGPA: sometimes its straightforward but often it is challenging

- Longstanding asthma with persistent eosinophilia , accelerating sinus features or requirement of higher dose of steroids for difficult to control asthma .
- Longstanding asthma and then systemic features that including skin nodules, abdominal pain or heart failure or neurologic deficit (mononeuritis)
- Recall classification criteria are NOT diagnostic criteria

Stages of EGPA



Gioffredi A, *Front Immunol* 2014

Emmi, G., Bettiol, A., Gelain, E. *et al.* Evidence-Based Guideline for the diagnosis and management of eosinophilic granulomatosis with polyangiitis. *Nat Rev Rheumatol* **19**, 378–393 (2023). https://doi.org/10.1038/s41584-023-00958-w

- ***There are no diagnostic criteria for EGPA***. Classification criteria (including the 1990 ACR criteria and 2022 ACR–EULAR criteria) have established sensitivity and specificity, but should not be used as diagnostic criteria, as they were not developed for this purpose.
- Additional criteria (such as those used in the MIRRA trial) are based on expert opinion and require validation.
- A diagnosis of EGPA should be based on highly suggestive clinical features, objective evidence of vasculitis (for example, from histology) and ANCA. (L: 2b; G: B)

EGPA Diagnosis

Preferably via tissue showing eosinophilic infiltration with vasculitis.

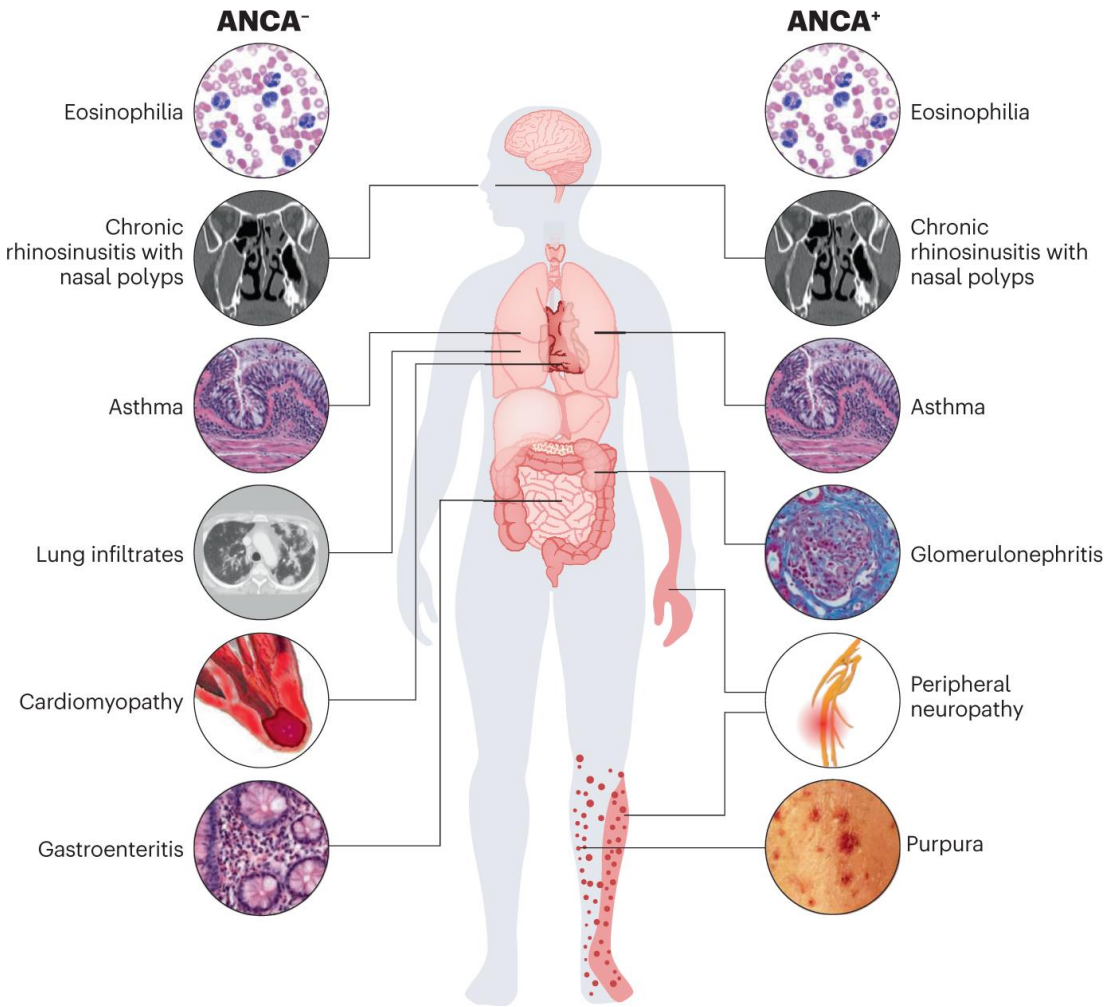
In 2022, the American College of Rheumatology and European Alliance of Associations for Rheumatologic (EULAR) revised the classification system to identify EGPA among patients with small- or medium-sized vessel vasculitis. In this revised system a score of 6 or more had a sensitivity of 85 percent and a specificity of 99 percent for EGPA compared with expert consensus.

Considerations when applying these criteria	
▪ These classification criteria should be applied to classify a patient as having eosinophilic granulomatosis with polyangiitis when a diagnosis of small- or medium-vessel vasculitis has been made ▪ Alternate diagnoses mimicking vasculitis should be excluded prior to applying the criteria	
Clinical criteria	
Obstructive airway disease	**+3**
Nasal polyps	**+3**
Mononeuritis multiplex	**+1**
Laboratory and biopsy criteria	
Blood eosinophil count ≥1 × 10^9/liter	**+5**
Extravascular eosinophilic-predominant inflammation on biopsy	**+2**
Positive test for cytoplasmic antineutrophil cytoplasmic antibodies (cANCA) or antiproteinase 3 (anti-PR3) antibodies	**−3**
Hematuria	**−1**
Sum the scores for 7 items, if present. A score of ≥6 is needed for classification of eosinophilic granulomatosis with polyangiitis.	

2022 American College of Rheumatology (ACR)/European Alliance of Associations (EULAR) for Rheumatology Classification Criteria for Eosinophilic Granulomatosis with Polyangiitis (EGPA). This classification scheme is used to distinguish EGPA from other vasculitides in patients with known small or medium-vessel vasculitis.

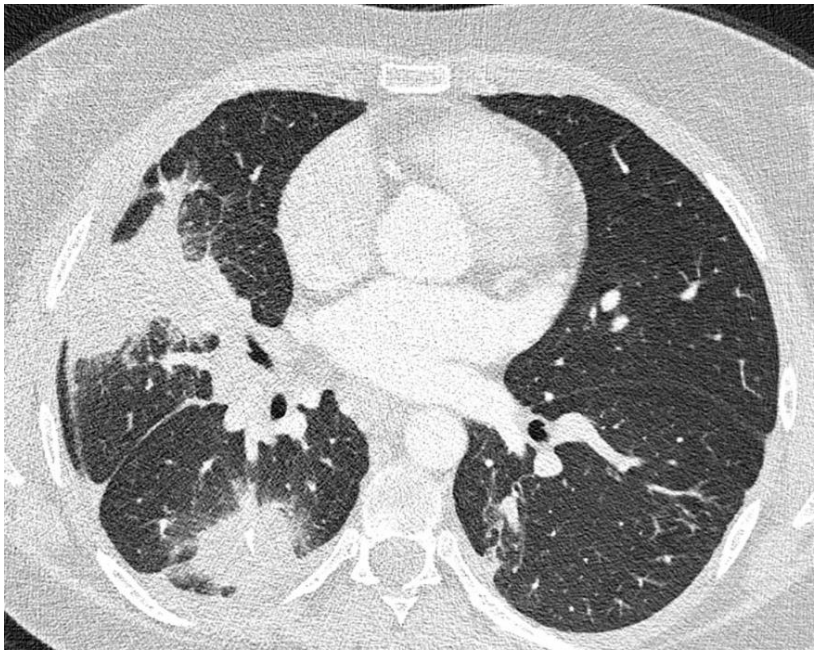
Making a diagnosis of EGPA: Challenges.

- Eosinophilia (> 1000 cells/microL)
- ANCA testing
- IGE levels
- Biopsy of tissue (skin, lung nerve) showing eosinophilic infiltration in vessel walls ,vasculitis or necrotizing granulomatous disease
- Overlap with other vasculitis syndromes (like GPA or MPA) can be challenging and consideration for other disease processes (eosinophilic leukemia, parasites etc)
- What about patients with systemic disease but no biopsy findings? Is that EGPA or otherwise termed hypereosinophilic asthma with systemic features.

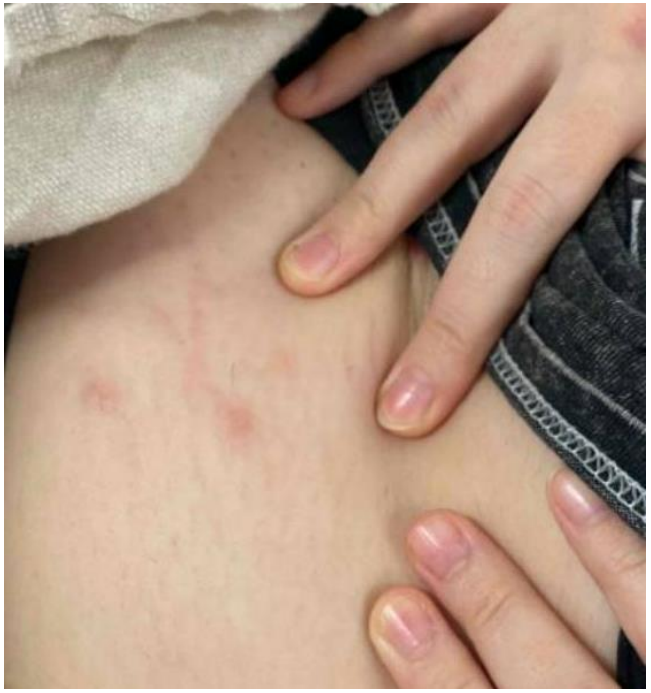


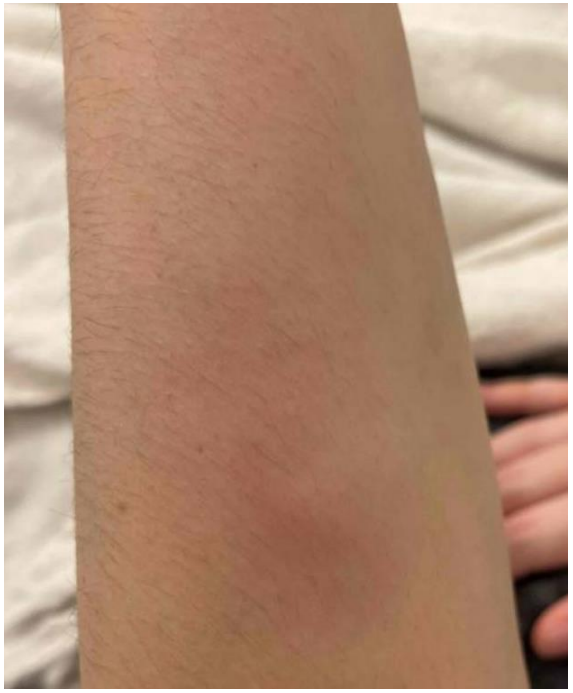
Nature reviews rheumatology. 2023.

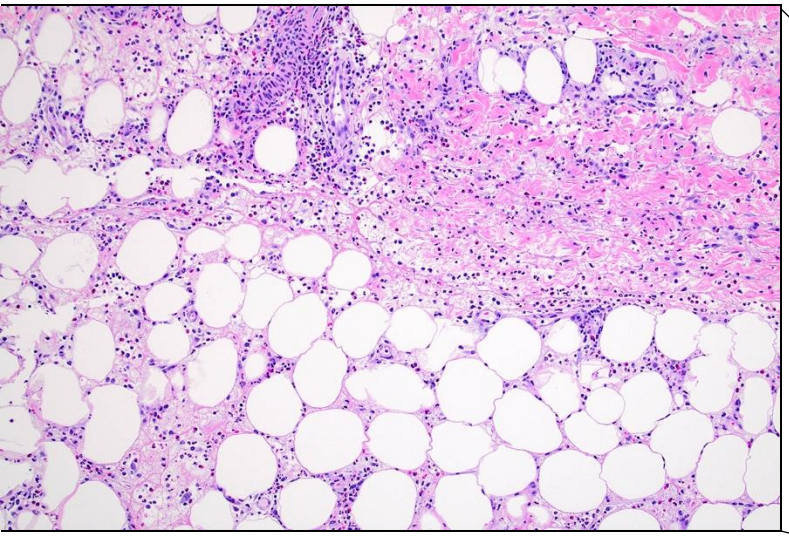
CM: 27 yp with longstanding asthma and persistent eosinophilia presented in Aug 2024 with cough chest pain and hypereosinophilia

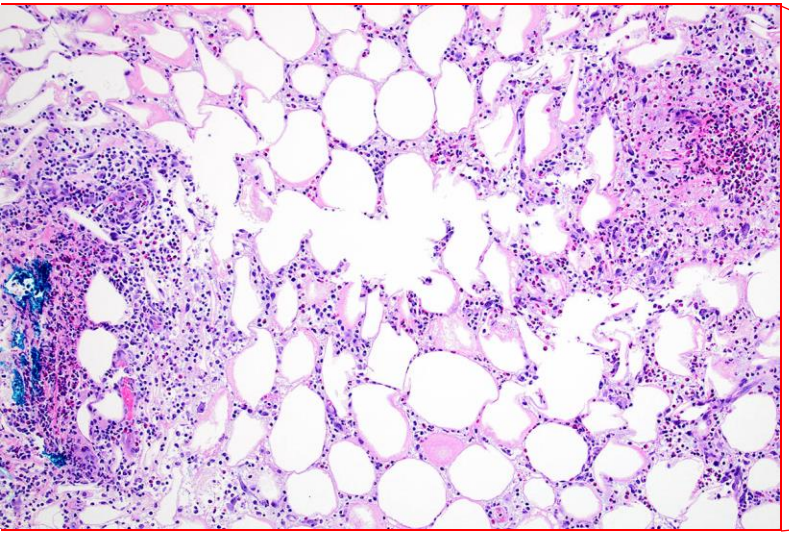


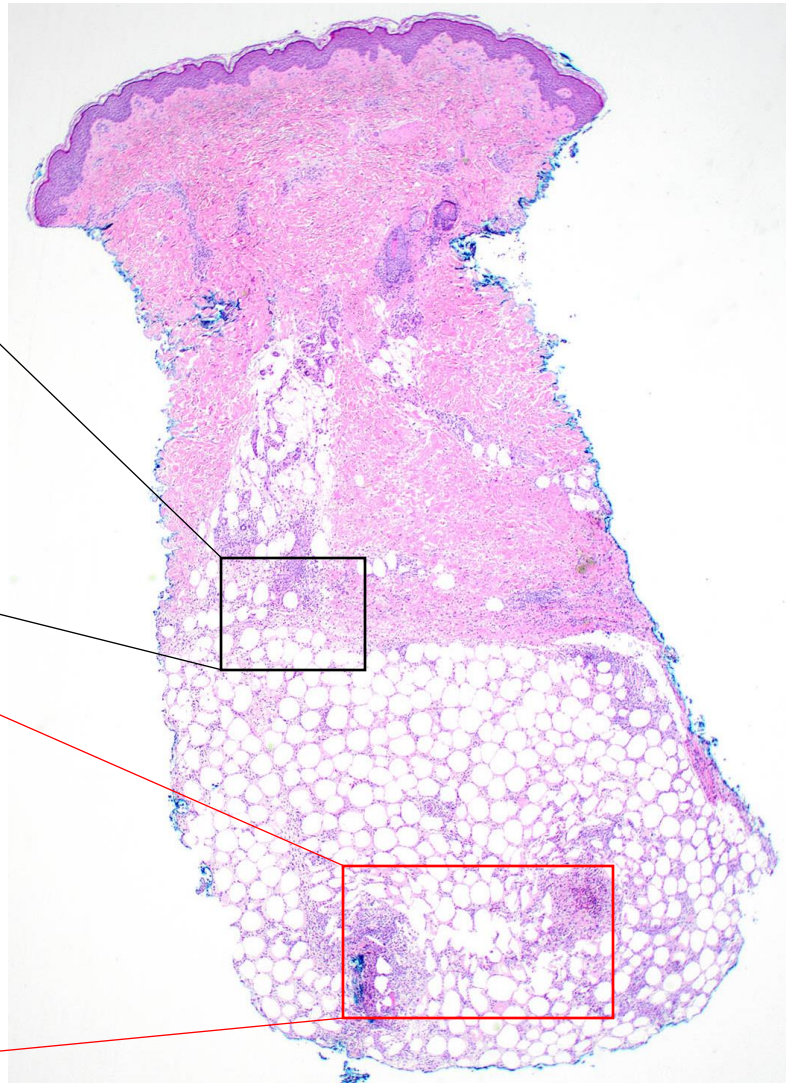
New painful skin nodules

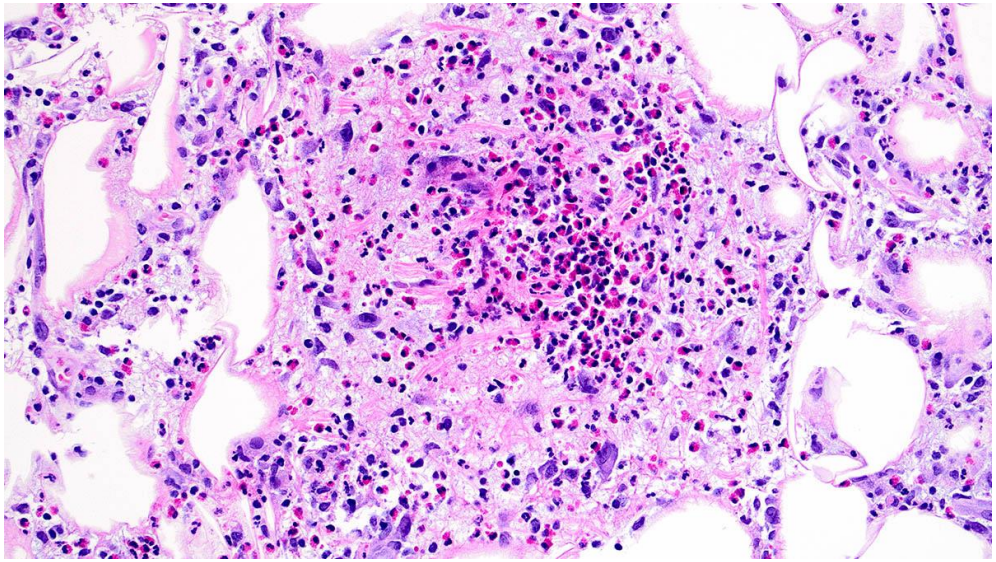












Path : Deep dermal and subcutaneous mixed inflammatory infiltrate, including numerous eosinophils, neutrophils, and histiocytes, with granuloma formation and
vasculitis involving vessels in the deep dermis and subcutis

Treatment strategies: severe vs non severe disease (revised FFS Five factor score) Guilleven L et al *Medicine* **90**, 19–27 (2011).

- Age> 65 years
- Cardiac failure (CHF, arrythmia, valvular disease, pericarditis)
- Renal failure (plasma creatinine concentration >1.7 mg/dL)
- Gastrointestinal disease (enteritis, vasculitis with ischemia)
- Absence of ENT involvement. (presence indicates better prognosis)
- Other considerations for severe disease (DAH, mononeuritis multiplex)
- **Highest risk attached to older age, and the presence of cardiac and GI disease**
- * FFS greater than or =1

Cardiac manifestations of EGPA (Dennert R et la Arthritis Rheum 2010, Donogue Auto Rev 2015)

- In the absence of symptoms and major EKG abnormalities, cardiac involvement could still be detected in nearly 40% of the patients, indicating that the absence of symptoms or the presence of a normal EKG does not exclude cardiac involvement.
- We therefore recommend that the evaluation for cardiac involvement in patients with CSS should include not only detailed history of cardiac symptoms and EKG, but also imaging with echocardiography or cardiac MRI.

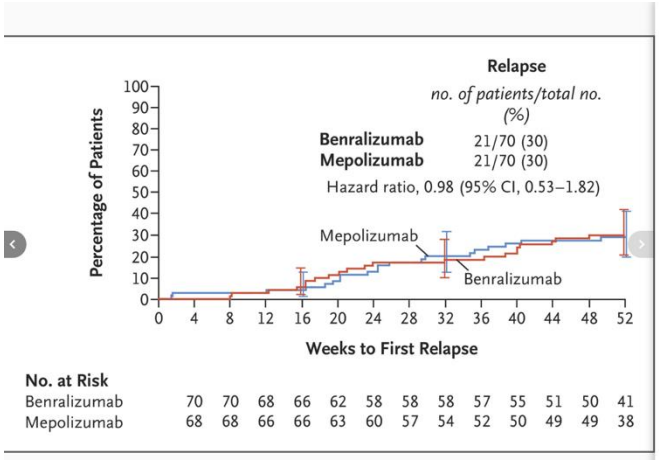
Baseline CMRI results according to cardiomyopathy status.

	All (n = 42)	Cardiomyopathy (n = 17)	No cardiomyopathy (n = 25)	P
Age at CMRI (years)	50.38 [16.75; 74.69]	49.38 [16.75; 66.69]	53.12 [17.42; 74.69]	0.63
Delay diagnosis-CMRI (years)	0.42 [− 0.02; 12.54]	0.08 [− 0.02; 9.81]	0.79 [0; 12.54]	0.037
Delay last flare-CMRI (years)	0.5 [0.01; 9.55]	0.17 [0.01; 9.17]	0.75 [0.05; 9.55]	*< 0.01*
Circumstances of CMRI				
First flare	23/41	12/17	11/24	0.10
Remission	16/41	3/17	13/24	0.025
Relapse	3/41	2/17	1/24	1
CMRI results				
Myocardial LGE	25 (59.52%)	14 (82.35%)	11 (44%)	0.024
Myocardial LGE when CMRI at diagnosis	14/23 (60.87%)	10/12 (83.33%)	4/7 (36.36%)	0.036
Myocardial T2-weighted signal	6 (14.29%)	3 (17.65%)	3 (12%)	0.67
Early myocardial gadolinium enhancement	8 (19.05%)	5 (29.41%)	3 (12%)	0.23
Hypokinesia	9 (21.43%)	7 (41.18%)	2 (8%)	0.019
Myocardial perfusion defect	13 (30.95%)	5 (29.41%)	8 (32%)	1
Pericardial inflammation	14 (33.33%)	7 (41.08%)	7 (28%)	0.51
Pericardial effusion	16 (38.1%)	6 (35.29%)	10 (40%)	0.73
Intraventricular thrombus	1 (2.38%)	1 (5.88%)	0 (0%)	0.40

Treatment options:

- Corticosteroids: unfortunately, still the mainstay of treatment.
- DMARDs: Azathioprine, Methotrexate, Mycophenolate.
- IL-5 and Anti IL 5 R blockade (mepolizumab, Benralizumab)
- B cell depletion (Rituximab and obinutuzimab)
- Cyclophosphamide

Benralizumab versus Mepolizumab for Eosinophilic Granulomatosis with Polyangiitis (Weschler M et al N Engl J Med 2024;390:911-921)



End Point	Benralizumab (N=70)	Mepolizumab (N=70)	Difference or Odds Ratio (95% CI)
Primary end point: remission at weeks 36 and 48 — adjusted % of patients	59	56	3 (–13 to 18)†‡
Secondary end points*			
Accrued duration of remission — no. (%)			1.36 (0.75 to 2.48)§
0 wk	9 (13)	15 (21)	
0 to <12 wk	12 (17)	10 (14)	
12 to <24 wk	8 (11)	8 (11)	
24 to <36 wk	21 (30)	19 (27)	
≥36 wk	20 (29)	18 (26)	
Mean daily dose of oral glucocorticoid during weeks 48 through 52 — no. (%)¶			1.42 (0.77 to 2.62)§
0 mg	29 (41)	19 (27)	
>0 to ≤4 mg	20 (29)	30 (43)	
>4 to ≤7.5 mg	14 (20)	13 (19)	
>7.5 mg	7 (10)	8 (11)	
Reduction in oral glucocorticoid dose — adjusted % of patients¶			
≥50% reduction	86	74	12 (–1 to 25)‡
100% reduction	41	26	16 (1 to 31)‡

Treatment of EGPA comparing approaches

	Active severe EGPA With life- or organ-threatening manifestations (e.g., alveolar hemorrhage, **renal involvement**, nervous system involvement, cardiac involvement, gastrointestinal involvement)		
	2021 ACR/VF guidelines	**2022 EULAR recommendations**	**2023 evidence-based guidelines**
Remission Induction	Pulse IV or high-dose daily oral GCs + CYC or RTX	High-dose daily oral GCs + CYC (or RTX)	(Pulse IV followed by) high-dose daily oral GCs + CYC or RTX
Remission Maintenance	*Remission with CYC* Switch CYC to MTX, AZA or MMF *Remission with RTX* Consider RTX prosecution	Switch CYC to AZA, MTX, MEPO or RTX	GCs + RTX and/or MEPO and/or DMARDs
Relapse Treatment	*Severe disease relapse after remission with CYC or RTX* Pulse IV or high-dose daily oral GCs + RTX	*Severe disease relapse* High-dose daily oral GCs + RTX	*Severe disease relapse* (Pulse IV followed by) high-dose daily oral GCs + CYC or RTX

Reggiani, (2023). Renal involvement in eosinophilic granulomatosis with polyangiitis. Frontiers in Medicine. 10. 10.3389/fmed.2023.1244651.

EGPA summary

- The Diagnosis of EGPA requires an index of suspicion in patients with pre-existing asthma who develop difficult to control asthma , sinusitis, and systemic features that suggest vasculitis
- Ideally a diagnosis will incorporate histological evidence supporting the diagnosis of EGPA
- Treatment options are guided by severity of disease
- Concern for underlying cardiac manifestations should always be considered, screening guidelines need to be clarified.
- Working with a multidisciplinary team is important in optimizing patient care.

Summary: Vasculitis and the Lung

- A heterogeneous group of disorders characterized by vascular inflammation leading to vessel occlusion, local thrombi and tissue ischemia and necrosis.
- Pattern recognition is key to early diagnosis and early therapeutic intervention.
- Vasculitis of the lung is typically associated with ANCA and can present as part of the pulmonary renal syndrome such as in GPA and MPA , but other protean manifestations may obscure and delay the diagnosis.
- EGPA is characterized as a ANCA related vasculitis but ANCA is + in only about 40% of cases.
- ANCA + and ILD can exist as a UIP like phenotype with or without evidence of active or pre existing vasculitis
- Other diseases such as Behcets , cryoglobulinemia and SLE can result in vasculitis of the lung but are rare.

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