Rheumatology Case Presentation
October 2024, Santa Fe, NM

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History of Present Illness (October 2011)

- Initial Presentation to ED:

34-year-old F with history of idiopathic bilateral scleritis, asthma, anxiety, prediabetes, GERD, remote cocaine use, chronic cough and congestion, woke up in the morning in acute respiratory distress.

Spouse called 911, transported to ED

In ED she was found to be hypoxic to 90%, had signs and symptoms of upper airway obstruction, became cyanotic and coughed up a large mucous plug, which was dark in color and appeared to be blood, O2 saturation improved subsequently.

Patient was admitted to medicine floor for further evaluation.

History of Present Illness and PMHx (continued)

- Years of cough with thick sputum, recently secretions are darker in color and coughing more frequently.
- Seen in past by UNM rheumatology for co-management of idiopathic bilateral sclerokeratitis.
  - Negative vasculitis workup
  - Tried and Failed: Methotrexate, Azathioprine and Mycophenolate. All with GI intolerance

Review of System remarkable for:

- ❑ Chronic cough with thick secretion, recently dark color sputum, sometimes feels like choking
- ❑ 100-pound weight loss
- ❑ Heat intolerance

Vital Signs:

- Temperature: 36.7
- HR on monitor: 104
- SBP: 112
- DBP: 53
- Respiratory rate: 26
- SpO2: 98% on 6 LPM NC

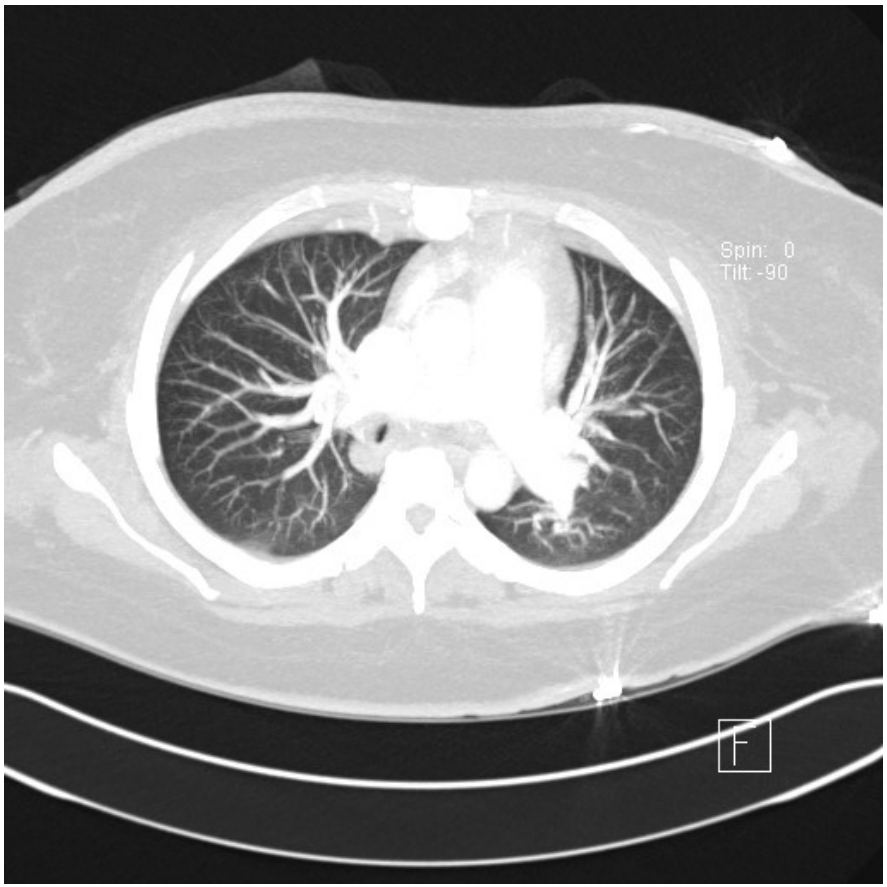
Physical Exam:

- General: Patient appears anxious and mildly obese
- Cardiovascular: Tachycardic with irregular rhythm
- Lungs: Coarse breath sounds bilaterally
- Abdomen: Normoactive bowel sounds, no organomegaly
- Extremities: No lower extremity edema, no cyanosis, capillary refill <2 seconds
- Skin: No rashes

Initial Laboratory in ED

- WBC: 6.4
- H&H: 9.9/29
- Platelets: 167
- Creatinine: 0.3
- HIV: non-reactive

CT Chest:



Pulmonology Consultation:

- Patient is high risk for OSA and pulmonary hypertension:
  - Recommend:
    - Rule out TB
    - Sleep study
    - PFTs
    - TTE
    - Bronchoscopy if hemoptysis worsens/recurs
- AFB/PPD: Negative
- PFT: Normal
- TTE: Moderate pulmonary hypertension, PA systolic pressure: 40-45 mmHg

Endocrinology Consultation:

Methimazole started for new diagnosis of hyperthyroidism (TSH: 0.07)

Rheumatology Consultation:

	10/16/2011	06/06/2008
Antinuclear Antibody Screen:	Negative	Equivocal
Antinuclear Antibody Titer		1:40
Anti-DNA:	2	
Antineutrophil Cytoplasm AB:	Negative	
Antiproteinaase-3 (PR-3) Antibody:	13	
Antimyeloperoxidase (MPO) Antibody:	77	
Anti-Scleroderma Antibody:	25	
SS-A (RO) Precipitin:	75	(H) 114
SS-B (LA) Precipitin:	17	13
Immunoglobulin A:	223	
Immunoglobulin G:	1160	
Immunoglobulin M:	78	
Immunoglobulin E:	38.6	
Complement 3:	108	
Complement 4:	20	
Cyclic Citrullinated Peptide:	2.1	
Rheumatoid Factor:	<10	

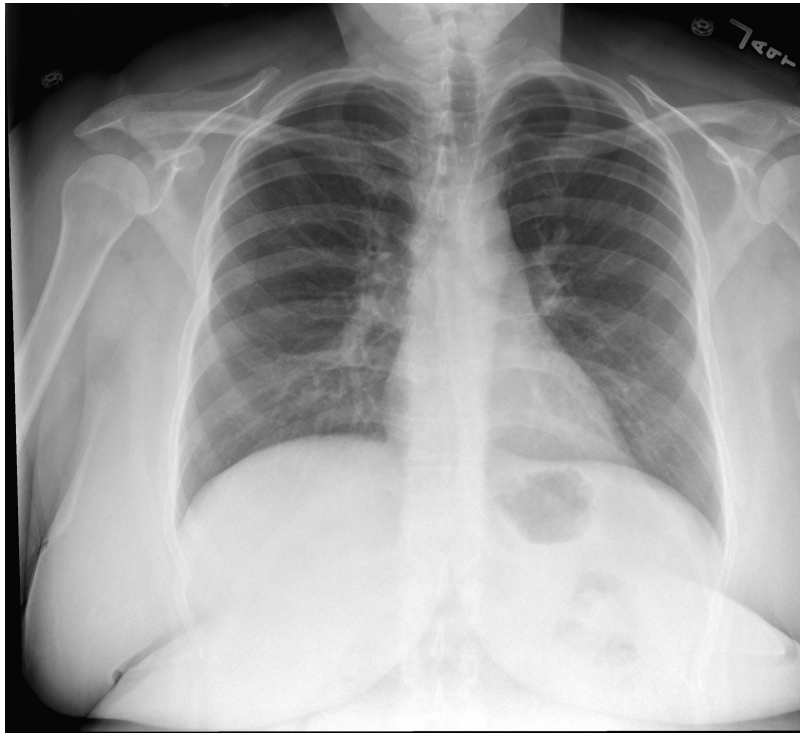
Rheumatology Consultation:

- No evidence of ANCA vasculitis at the skin level, sclerokeratitis believed to be idiopathic.
- Patient was noted to have intolerance to multiple steroid sparing agents, she was returned to her ophthalmologist for treatment of sclerokerititis as prior.

Patient was medically optimized and discharged.

Interval History:

Pulmonary Clinic Visit in 2012 for cough with sputum production, no hemoptysis



- The patient continues to have this cough over the last year; by history appears to be drainage from nasal sores.
- CT scan did not show evidence of bronchiectasis.
- ENT evaluation was requested for evaluation of hoarse voice and concern that cough was sinus origin.
  ENT recommended nasal steroids

Re-admission in September 2023

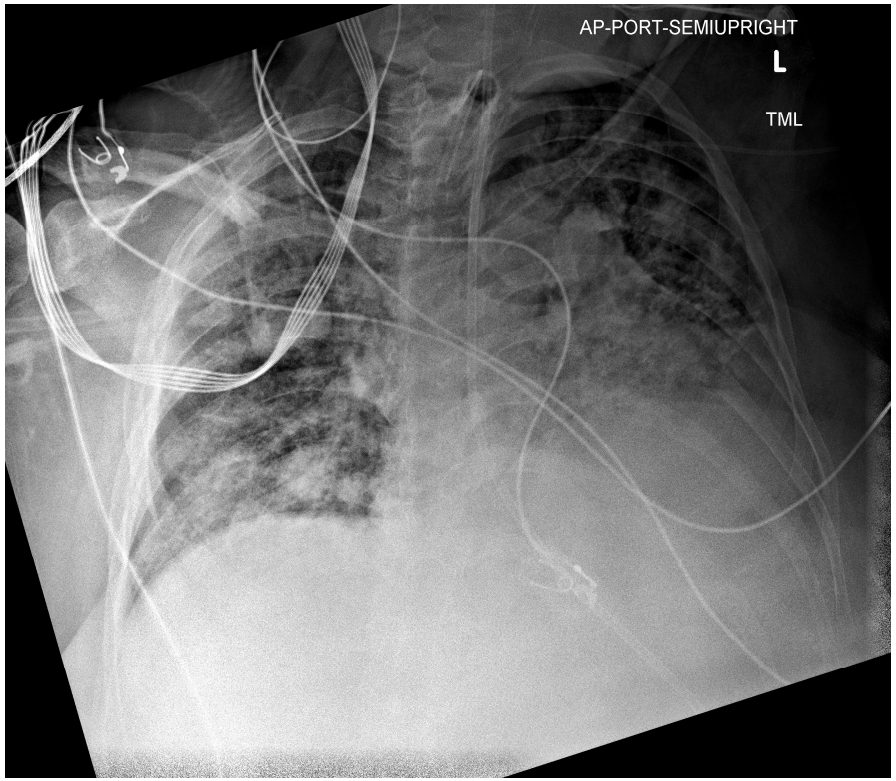
- Admitted for acute respiratory failure
- Found to have diffuse alveolar hemorrhage
- Rapidly deteriorated on the day of her admission, requiring transfer from MICU to CTV ICU with right IJ cannulation for V-V ECMO.
- Just prior to admission, patient had recently been found to have bilateral pulmonary nodules and been scheduled for outside biopsy.

Vital Signs and Physical Exam:

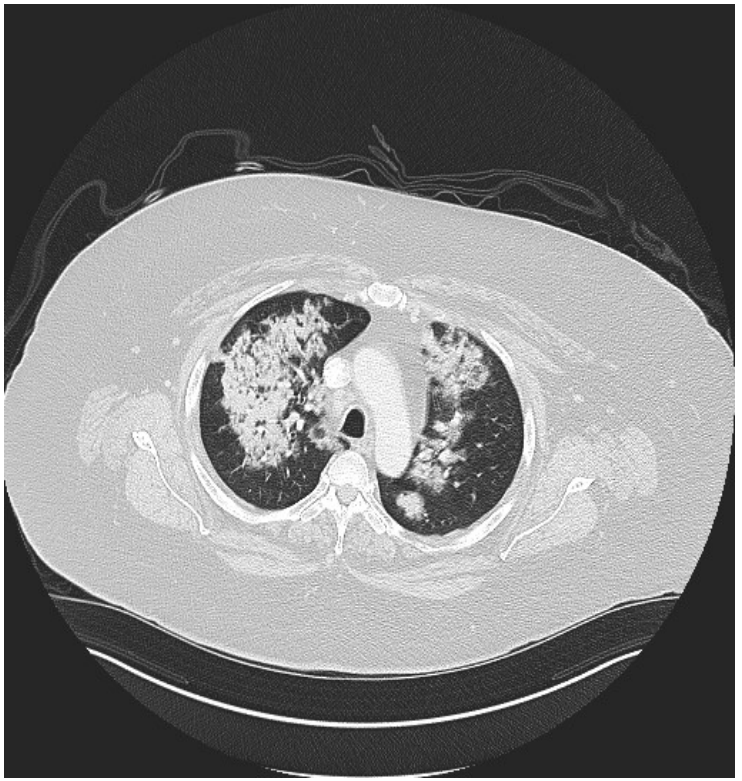
- Temperature: 36.8
- Heart rate: 85
- SBP: 116
- DBP: 67
- RR:10
- SpO2: 98%
  - FiO2: 100%
  - O2 flow rate 40

- PERRL: EOMI, normal conjunctiva
- HEENT: ETT in place
- Neck: No obvious JVD coarse breath sounds bilaterally
- Heart: Normal rate, regular rate no murmur
- Abdomen: Soft, nontender, nondistended, normal bowel sounds
- Musculoskeletal: No significant lower extremity edema, unable to assess muscle strength secondary to intubated and sedated, ECMO cannulas in place
- Skin: Warm, dry, pink, no rashes or lesions
- Genitourinary: No hematuria
- Neurologic: Intubated and sedated

CXR



CT Chest



Rheumatology Consultation:

September 2023	
Antinuclear Antibody Screen:	Positive
Antinuclear Antibody Titer	1:640
Anti-DNA:	1
Antineutrophil Cytoplasm AB:	Duplicate
Antiproteinaase-3 (PR-3) Antibody:	0.2
Antimyeloperoxidase (MPO) Antibody:	1.2
Anti-Scleroderma Antibody	
SS-A (RO) Precipitin	
SS-B (LA) Precipitin	
Immunoglobulin A	
Immunoglobulin G	
Immunoglobulin M	
Immunoglobulin E	
Complement 3:	(L) 59
Complement 4:	(L) 7
Cyclic Citrullinated Peptide:	< 0.5
Rheumatoid Factor	

Rheumatology Consultation:

- Alveolar hemorrhage on bronchoscopy
- Reported sinus issues in the past
- Pulmonary nodules - can be associated with GPA
- MPO low positive: 1.2

→ High suspicions for ANCA associated vasculitis, continued on IV methylprednisolone

- Sputum was positive for Serratia, lack of tissue diagnosis
  - no immediate benefit for cyclophosphamide or Rituxan but can reconsider after Plex course, pending infection rule out.
- Continued decline in C3 and C4: C3: 39, C4: 7
- Developed decreased urinary output, concern for progression to intrarenal nephrotic versus nephritic syndrome possibly secondary to GPA versus EGPA versus Goodpasture
  - Nephrology consulted
  - Planning kidney biopsy once patient has become medically stable

Rheumatology Recommendations:

- ANCA Associated Vasculitis ? – previous work up negative in 2006 and 2011.
- Other rheumatology causes such as Goodpasture's, antiphospholipid, scleroderma, SLE as well as malignancy or infection are among differential diagnoses

Recommended work up:

- ANA, ANCA, ESR, CRP, HIV, hep C, and TB
- Recommended to obtain CCP, DNA, C3, C4, CH 50, CK, anti-GBM, antiphospholipid panel, UA, urine protein creatinine, urine drug screen (remote history of cocaine use)
- Cocci, Aspergillus galactomannan, histoplasma to rule out fungal infection
- Empiric methylprednisolone 1 g daily 3 to 5 days pending further workup

Progression:

- Continues to be on ECMO 2 days later
- Deterioration in clinical status despite steroids and PLEX
- DC PLEX and transition to IVIG 1 g/kg for 2 days after obtaining immunoglobulin panel
- WBC and CRP trended down
- Rituximab 1000 mg IV recommended; methylprednisolone 125 mg daily was continued.

- *If kidney function or DAH worsens can reassess for IV cyclophosphamide versus anti-CD-5 Eculizumab or Avacopan presuming no infectious concerns exist.*

Labs Summary, Impression and Management:

- ANA + 1: 640, DNA negative, decreased C3/C4
- Smith, RNP negative, cryoglobulin negative, hep/TB negative, GBM IgG negative, ANCA negative, MPO low positive 1.2, PR-3 negative
- SLE related vasculitis could not be ruled out since patient has been ANA positive with low complement on admission, but as per family without other obvious clinical manifestation of SLE

→ Atypical vasculitis versus SLE associated vasculitis

Management:

- 7 days of plasma exchange
- 2 days of IVIG total 2 g/kg
- Rituximab 1000 mg IV
- 3 days of pulse dose methylprednisolone 1000 mg; subsequently titrated down to 1 mg/kg 125 mg IV daily, tapered down further to 80 mg daily.

Summary of Serologies Progress/Changes Over Years:

Rheumatology lab work 2002
ANCA screen high normal, PR-3 negative, MPO: 1

Rheumatology lab work 2008
ANCA negative, ANA titer 1:140 speckled pattern, SSA 114, SSB 13

Rheumatology lab work in 2011
ANCA negative, PR-3 negative, MPO negative, ANA negative, SSA/SSB negative, ACE: 98

Rheumatology lab work in 2023:
ANCA negative, PR-3 negative, MPO low positive 1.2, ANA + 1: 640, DNA negative, decreased C3/C4

Lab work in follow-up rheumatology clinic:
HLA-B 51: positive

Clinical Settings in Which It Is Appropriate to Check ANCA and in Which Positive Testing for Anti-proteinase 3 or Anti-myeloperoxidase Antibodies Could Be Considered Diagnostic of GPA or MPA [a]

Disease	Manifestation	Examination Technique	Laboratory and Other Testing	Imaging	Problems With Biopsy
GPA > MPA	Scleritis	Ophthalmologic examination			
GPA	Orbital pseudotumor	Routine inspection, or with measurement tool		CT or MRI	
GPA > MPA	Sensorineural hearing loss		Audiography		Impossible
GPA	Sinonasal inflammation	Otoscope or fiberoptic examination		CT of sinuses	All 3 characteristic features [b] seen in only 10% of GPA
GPA	Subglottic inflammation	Laryngoscopy		CT of neck	Correlates poorly with examination or outcome
GPA	Pulmonary nodule(s)			CT of chest	1. Transbronchial: all 3 diagnostic features [b] are seldom seen 2. Surgical biopsy: invasive
GPA/MPA	Alveolar hemorrhage	Inspection (witnessed hemoptysis) or bronchoscopy with BAL		CT of chest	Invasive, and patient is often critically ill
GPA/MPA	Digit ischemia	Routine inspection		Angiography	Impossible
GPA/MPA	Peripheral neuropathy	Neurologic examination: sensory and motor	Nerve conduction studies/electromyography		Likely to result in an area of permanent sensory deficit; small chance of chronic pain
GPA/MPA	Nephritis		Urine sediment: RBC casts		

Firestein & Kelley's Textbook of Rheumatology

Discussion:

- p-ANCA and “atypical ANCA” (the term for ANCA patterns that are not clearly c-ANCA or p-ANCA) may be due to a variety of different antibodies and can be present in a wide range of diseases.
- **Specific antibodies that may result in positive p-ANCA or atypical ANCA patterns include antibodies directed against MPO**, elastase, cathepsin G, lactoferrin, and β-glucuronidase.

Rheumatology Secrets 4th edition

Discussion:

Methimazole induced vasculitis with diffuse alveolar hemorrhage?

Arai N, Nemoto K, Oh-Ishi S, Nonaka M, Hayashihara K, Saito T. ***Methimazole-induced ANCA-associated vasculitis with diffuse alveolar haemorrhage. Respirol Case Rep.*** *2018 May 8;6(5):e00315. doi: 10.1002/rcr2.315. PMID: 29760925; PMCID: PMC5939900.*

Discussion:

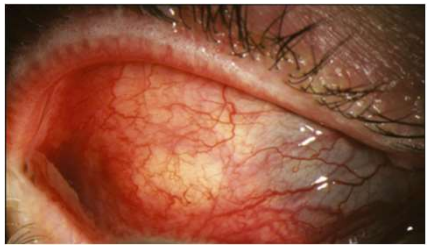
Sclerokeratitis refers to the simultaneous inflammation of the sclera and the cornea, rare but serious condition often associated with systemic inflammatory diseases, including vasculitis.

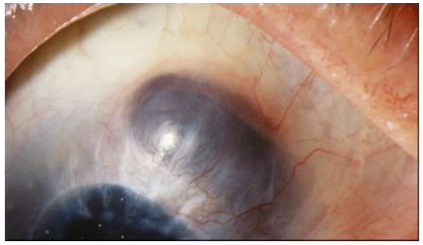
Common Types of Vasculitis Associated with Sclerokeratitis:

- ❑ Granulomatosis with Polyangiitis (GPA)
- ❑ Rheumatoid Vasculitis
- ❑ Polyarteritis Nodosa (PAN)
- ❑ SLE vasculitis
- ❑ Behcet's Disease:
- ❑ Relapsing Polychondritis

Discussion:

- ❑ Ocular manifestations of GPA may be the first symptom of a previously not manifested or undiagnosed systemic disease.
- ❑ After rheumatoid arthritis, GPA is stated as the second most common connected systemic pathology with scleritis.
- ❑ Scleritis is stated in 12% as the first symptom indicating GPA.
- ❑ Scleritis is the most frequent ocular manifestation of GPA.
- ❑ Scleritis is mostly bilateral, manifested more often as anterior than posterior inflammation of the sclera, more frequently nodular than diffuse and in men in up to 67% in the necrotizing form of scleritis in GPA.





CZECH AND SLOVAK OPHTHALMOLOGY 5/2018
Images: Firestein & Kelley's Textbook of Rheumatology

Discussion:

- **Recurrences of ocular manifestations of GPA may be the first sign of relapse of inflammations** of other organs affected by this disease.
- For determination of a correct and timely diagnosis and the application of targeted treatment of GPA it is essential to ensure good interdisciplinary co-operation with a nephrologist, immunologist, rheumatologist, otorhinolaryngologist, dermatologist, gastroenterologist, radiologist and histopathologist.

CZECH AND SLOVAK OPHTHALMOLOGY 5/2018

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Thank You