The Art of Clinical Reasoning with Dr. Patricia Kritek

WASHINGTON STATE ACP CHAPTER MEETING

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The New York Times | https://nyti.ms/RwWmfS

HEALTH

For Second Opinion, Consult a Computer?

By KATIE HAFNER DEC. 3, 2012

SAN FRANCISCO — The man on stage had his audience of 600 mesmerized. Over the course of 45 minutes, the tension grew. Finally, the moment of truth arrived, and the room was silent with anticipation.

At last he spoke. “Lymphoma with secondary hemophagocytic syndrome,” he said. The crowd erupted in applause.

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Initial Presentation

- 54-year-old man with arthralgias and shortness of breath

day one

Initial Thoughts?

- Would you isolate this patient?

Initial Presentation

- 54-year-old man with arthralgias and shortness of breath

day one

Initial Presentation

- 54-year-old man with arthralgias and shortness of breath
- Past medical history: hypertension and glaucoma
- He takes no regular medications
- Employed as a chiropractor
- Non-smoker, non-drug user, denies significant alcohol use

day one

Initial Thoughts?

- How does this information inform your approach?
- Does this change “pre-test” probabilities in your mind?

Audience Thoughts?

- Comparative Accuracy of Diagnosis by Collective Intelligence of Multiple Physicians vs Individual Physicians

	Diagnostic Accuracy
One physician	62.5% (95% CI 60.1-64.9%)
Nine physicians	85.6% (95% CI 83.9%-87.4%)
One specialist	66.3% (95% CI 59.1-73.5%)
Two physicians	77.7% (95% CI 70.1%-84.6%)

- Barnett ML et al, JAMA Netw Open 2019 Mar 1;2(3)e190096

Audience Thoughts?

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The Human Diagnosis Project

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Initial Presentation

- History
  - Two months ago: strained back and fell injuring right leg
  - Migratory arthralgias with subjective fevers ever since
  - Conjunctivitis (resolved) during the first month
  - Two weeks ago: developed painful oral ulcer on hard palate
  - Five days ago: dyspnea and weakness upon return home from road trip

Initial Presentation

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- Examination
  - Vitals: **P-152**; **BP-93/63**; T-36.1; **RR-26**; oximetry-93% (air); **BMI-37**
  - Gen: **weak appearing; leaning forward on exam table**
  - Pulm: **breathing hard**; **cannot speak full sentences**; clear sounds
  - Cor: **tachycardiac** without murmurs
  - MSK: **1+ bilateral leg edema**
  - Skin: **rash** noted (next slide)

Initial Presentation

day one

Updated Thoughts?

- What are you thinking now?
- What are your next steps?

Diagnostic Power of H&P

- Percent of diagnoses made by Hospitalist physicians

	Correct Diagnosis
History alone	19.3%
History and Physical exam	38.6%
History and basic testing	14.7%
H&P and basic testing	18.5%

- Paley L et al, Arch Intern Med. 2011;171(15):1393-1400

Diagnostic Power of H&P

- Percent of diagnoses made by Hospitalist physicians

	Correct Diagnosis
History alone	19.3%
History and Physical exam	38.6% → ~60%
History and basic testing	14.7%
H&P and basic testing	18.5%

- Paley L et al, Arch Intern Med. 2011;171(15):1393-1400

Place Your Bets!

- What are your initial top three diagnoses?

Updated Thoughts?

- What are you thinking now?
- What are your next steps?

Initial Presentation

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  - Skin: **rash** noted (next slide)

Go directly to emergency; do not pass go

day one

Emergency Department

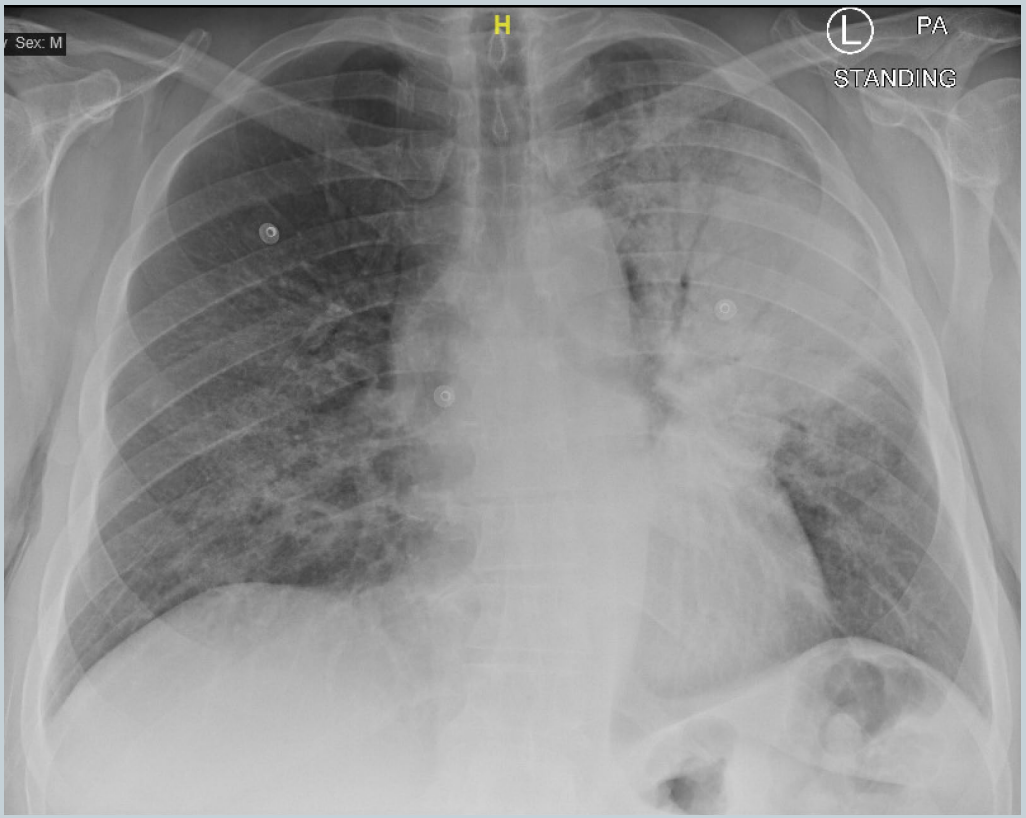
- Additional history
  - Dyspnea has been gradual (acutely worse last 5 days)
  - Has continued to work (no known COVID-19 exposures)
  - Family history: father had CLL, died of unknown other cancer

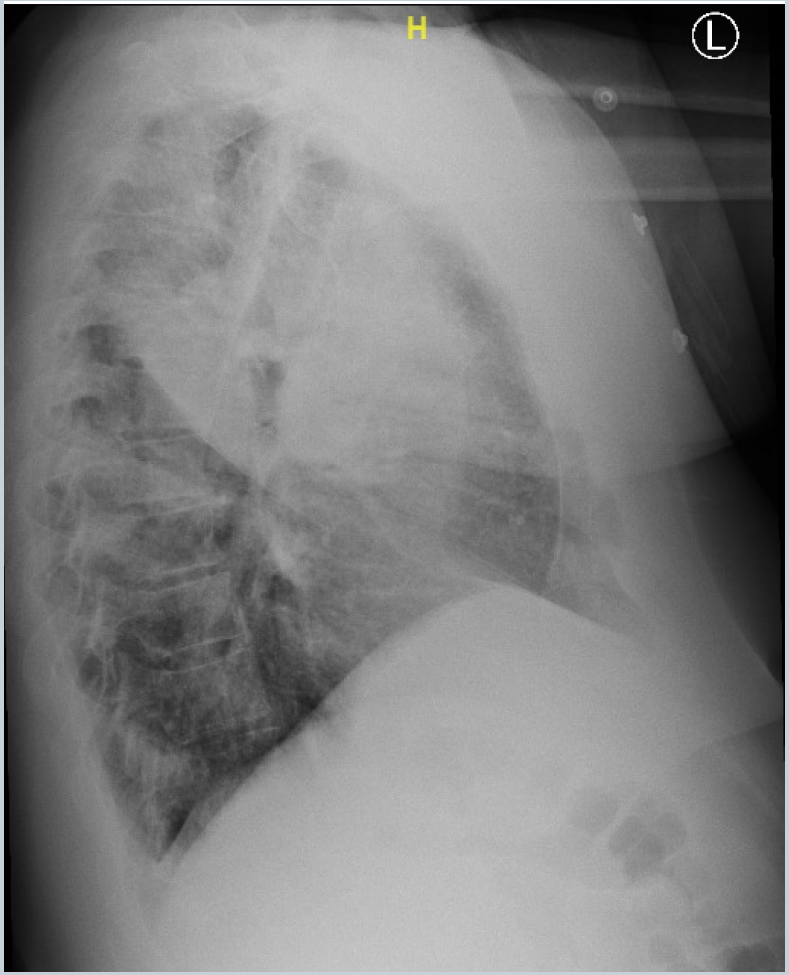
- Emergency examination
  - Vitals: **P-119**; BP-140/76; T-37; RR-20; **oximetry-90% (air**)
  - Gen: well appearing; non-toxic
  - Pulm: no increased work; normal sounds
  - Cor: **tachycardiac** without murmurs; strong equal pulses
  - MSK: trace bilateral leg edema

Emergency Room Studies

- 12-lead EKG
  - **Sinus tachycardia** (rate of 110) otherwise normal
- Chest radiograph; PA & lateral
  - (next slide)

Emergency Room Studies





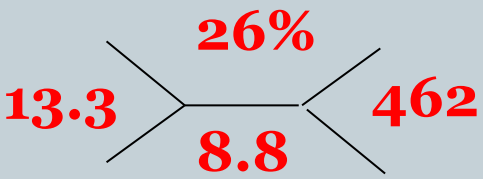
day one

Emergency Room Studies

- 12-lead EKG
  - **Sinus tachycardia** (rate of 110) otherwise normal

- Chest radiograph; PA & lateral
  - "**Opacity** occupying much of the **left upper lobe**, consistent with **infiltrate** and **pneumonia** given the proper clinical setting. There is also coarsening of the lung markings about both the hilar regions which may suggest **developing interstitial infiltrate**."

Emergency Room Labs

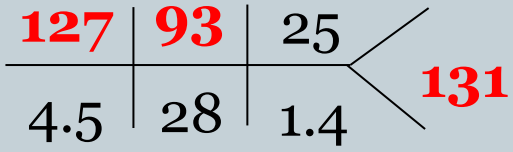


Sed rate - **99** (0-10)

MCV	82 fL (80-100)
MCH	27.4 pg (27-34)
MCHC	33.3 g/dL (32-36)
RDWCV	15% (11-15.5%)

Neutrophils	**10.4** (thou/uL)
Lymphocytes	1.6 (thou/uL)
Monocytes	0.5 (thou/uL)
Basophils	0.1 (thou/uL)
Immature granulocytes	**0.67** (thou/uL)

Emergency Room Labs



CRP – **256 mg/L**

Lactate – 1.9 mmol/L
Calcium – **8.4 mg/dL**
Protime/INR – **1.2**
Troponin-I – 0.06
BNP – 88 pg/mL

Total Protein	6.5 g/dL
Albumin	**2.6 g/dL**
Total bilirubin	**1.8 mg/dL**
AST/SGOT	34 U/L
ALT/SGPT	17 U/L
Alkaline phosphatase	85 U/L

Emergency Room Labs

- Urinalysis
  - Pending
- COVID-19 PCR
  - Pending

Initial Summary

- Initial presentation
  - 54-year-old man with two months of migratory arthralgias
  - Rash with subjective fevers
  - Progressive dyspnea, accelerating in the last 5 days
  - Hemodynamically tenuous in urgent care clinic
  - Takes no regular medications, does not drink, smoke, or use drugs

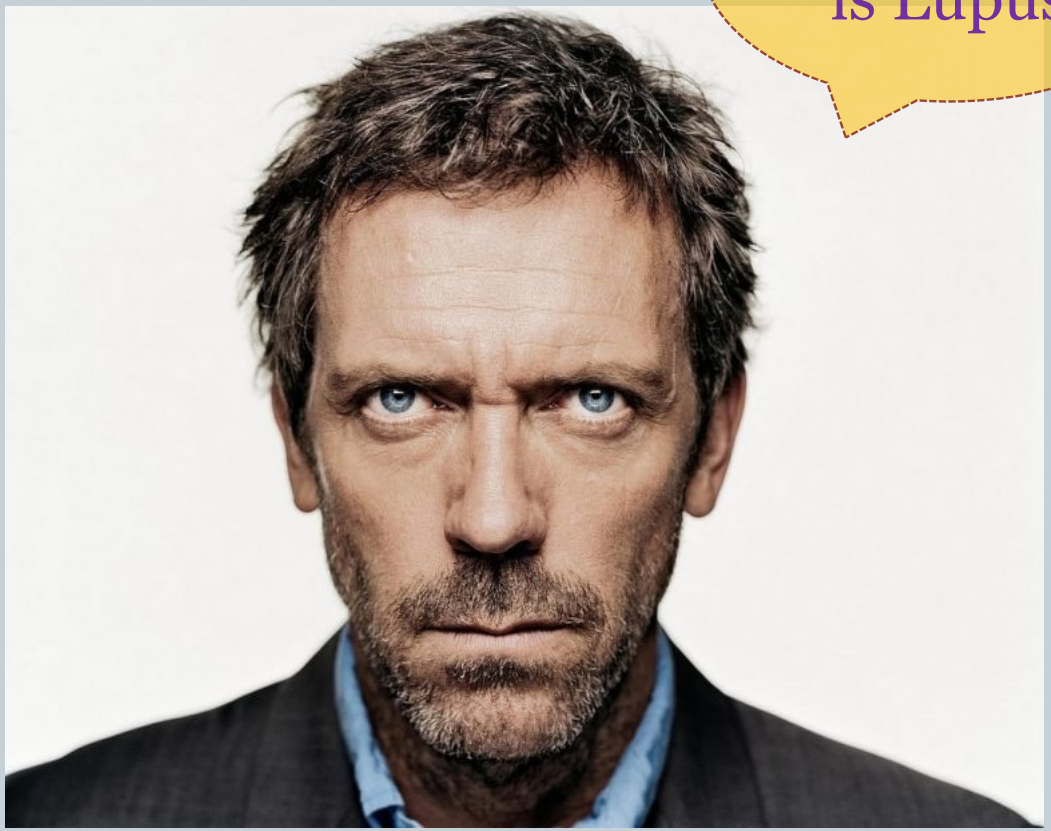
- Findings
  - Very weak, tachycardic, initial hypotension, borderline hypoxia, rash
  - Mild leukocytosis with left shift
  - Hyponatremia and borderline acute kidney injury
  - Hypoalbuminemia
  - Elevated inflammatory markers
  - Diffuse multifocal infiltrates most prominent in left upper lobe

Interpretation of Data

- How do you incorporate this new information?
- Do you recommend anything else?
- What is your initial plan?

Audience Thoughts?

Audience Thoughts?

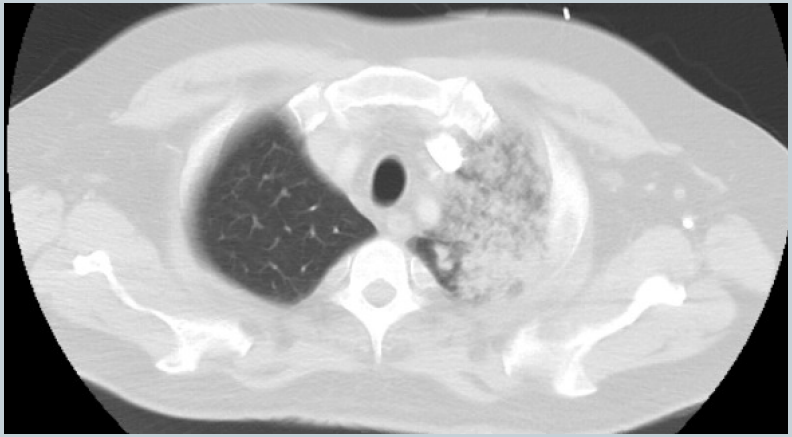


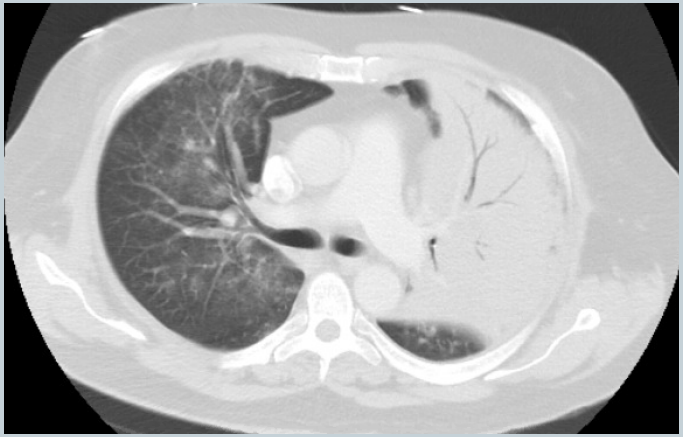
Initial Plan

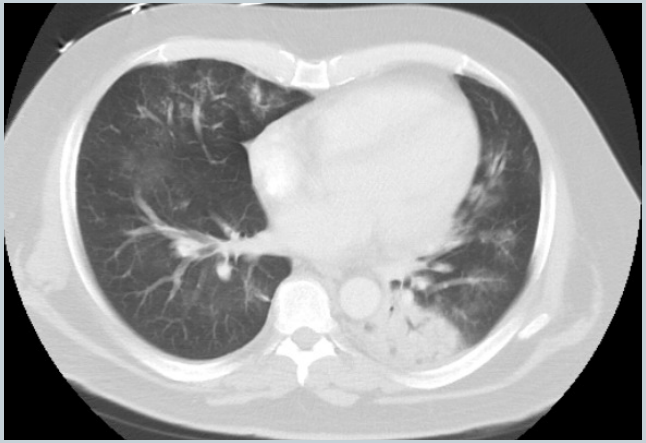
- Impression
  - Sepsis
  - Community acquired pneumonia
  - Possible vasculitis

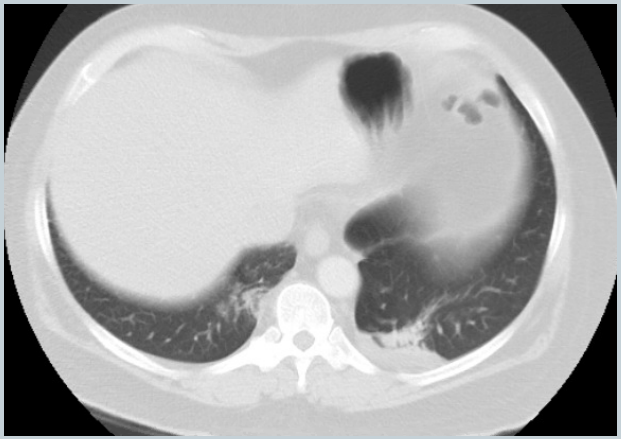
- Plan
  - 30 mL/kg fluid bolus
  - Cultures (sputum, blood, urine)
  - Ceftriaxone (2g) and azithromycin (500mg)
  - IV Vancomycin added by admitting hospitalist (MRSA nares test pending)
  - CT chest (images on next slide)

CT of Chest with Contrast









day one

CT of Chest with Contrast

- No airway obstruction or narrowing. Trace left pleural effusion. No pneumothorax. **Extensive consolidation throughout the left upper lobe with moderate adjacent ground-glass opacity**. **Similar mild to moderate consolidation throughout the dependent left lower lobe. Mild diffuse peribronchovascular ground-glass opacity throughout the right lung with small areas of tree-in-bud opacity and minimal consolidation.**
- No significant pericardial, great vessel or esophageal abnormality. No mediastinal mass. No adenopathy. No significant abnormality in the visualized upper abdomen.

Emergency Room Urinalysis

- Urinalysis
  - specific gravity 1.15 g/mL; pH 5.0
  - pH 5.5
  - Protein **100 mg/dL**
  - Glucose negative
  - Ketones **5 mg/dL**
  - Bilirubin **moderate**
  - Blood **moderate**; **RBC 10-15/hpf**
  - Nitrites **positive**; leukocyte esterase negative
  - WBC **3-5/hpf**
  - Squamous cells, granular and cellular casts all **moderate**

Hospital Course

- Develops modest oxygen requirement (4L NC)
- Develops fevers (T-max 39.5); waxing & waning
- Other vitals stable and condition seemed to stabilize
- Stopped fluids and initiated diuretics on day #3
- Still feeling weak but “a little better”
- Begins to have loose stools
- Ongoing mild tachycardia and persistent hypoxia

Laboratory Review

	Day one	Day three	
WBC	**13.3**	8.4	
Hct	**28%**	**25%**	
Hgb	**8.8**	**8.0**	
Platelets	462	371	
MCV	82	83	
Na	**127**	**131**	
K	4.5	3.9	
CO2	26	23	
BUN	25	**28**	
Creatinine	1.4	1.0	
Albumin	**2.6**	**2.1**	
AST	34	38	
ALT	17	19	
Bilirubin	**1.8**	1.0	

Additional

- COVID-19: negative
- MRSA nares: negative

Micro

- C. diff: negative
- Cultures not obtained

day three

Now What?

- Are you satisfied he is improving?
- Do you take him out of isolation?
- Do you discontinue IV vancomycin?
- Do you recommend additional diagnostics?

CT of Chest (PE protocol)

- Nondiagnostic for the assessment of pulmonary embolism due to inability to achieve adequate opacification of the main pulmonary artery despite two separate injections. No large, central pulmonary embolism is identified
- Redemonstrated **multifocal pneumonia**, similar within the left upper lobe, and **slightly worsened within the left lower lobe and right lung**
- **Slightly increased small left pleural effusion and new trace right pleural effusion**

day three

Echocardiogram

- LV: normal size; low-normal function (LVEF 50%)
- Cannot assess regional wall motion abnormalities
- RV: normal size and function
- Valves: trace mitral regurgitation, otherwise normal
- Pulmonary pressures upper limits normal (25-30 mm Hg)
- Trace pericardial effusion; no pleural effusions
- IVC: non-dilated; > 50% collapse

More Hospital Course

- Day #6: sudden worsening oxygenation
- Remains hemodynamically stable
- Oxygen escalated to high flow, then bilevel with 0.7 FiO_2

Laboratory Review

	Day one	Day three	Day six
WBC	**13.3**	8.4	**13.0**
Hct	**28%**	**25%**	**23.4**
Hgb	**8.8**	**8.0**	**7.7**
Platelets	462	371	**551**
MCV	82	83	82
Na	**127**	**131**	**134**
K	4.5	3.9	3.9
CO_2	26	23	30
BUN	25	**28**	18
Creatinine	1.4	1.0	0.8
Albumin	**2.6**	**2.1**	**2.1**
AST	34	38	
ALT	17	19	
Bilirubin	**1.8**	1.0	

Additional

- COVID-19: negative
- MRSA nares: negative

Micro

- UC: negative
- BC: negative

Day Six

- *ABG: 7.46/49/65/34/9.2-BE
- COVID-19: negative

*on bilevel with FiO_2 0.4

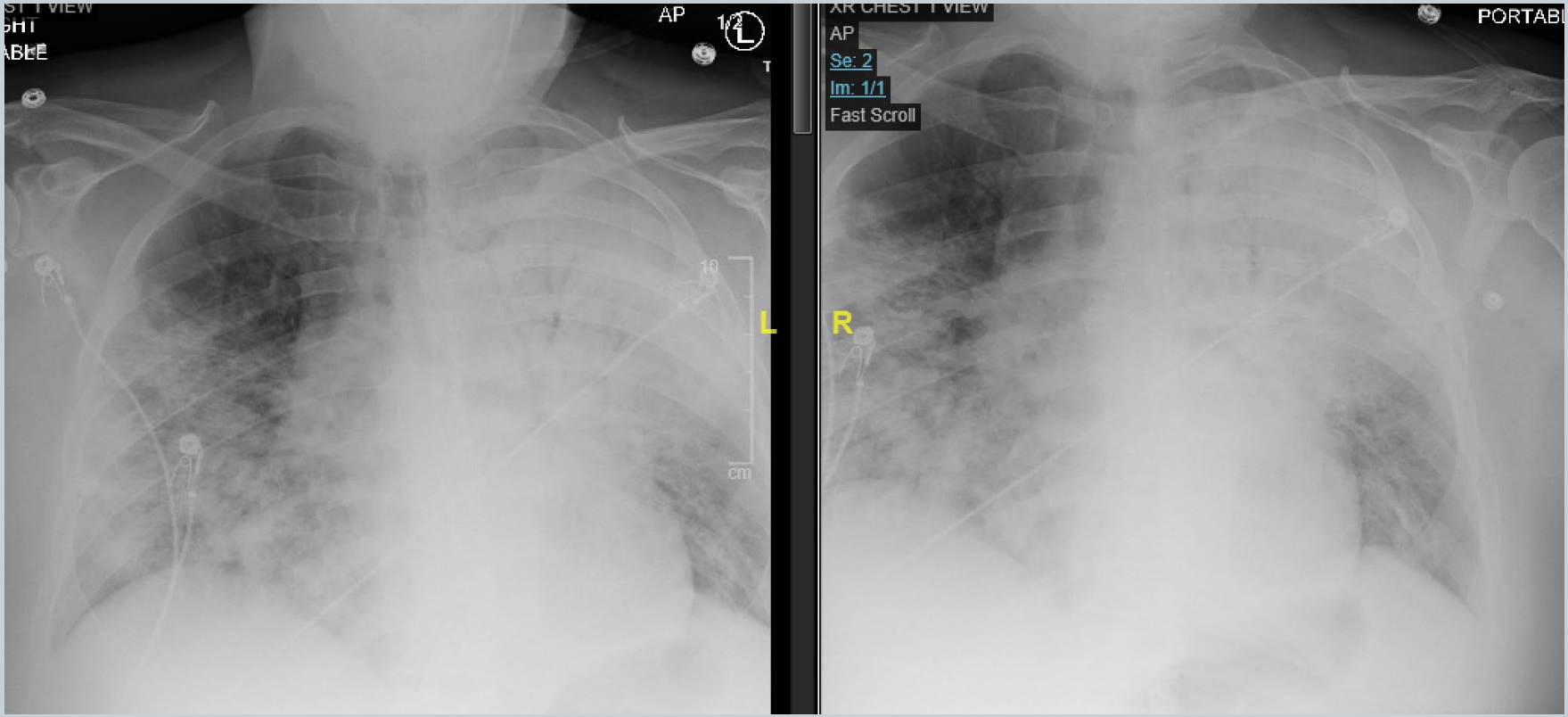
What Next?

More Hospital Course

- Day #6: sudden worsening oxygenation
- Remains hemodynamically stable
- Oxygen escalated to high flow, then bilevel with 0.7 FiO_2

- Ceftriaxone replaced with piperacillin-tazobactam
- Repeat chest radiograph obtained (next slide)
- Administered furosemide 40mg IV
- Oxygen tapered to 0.55 FiO_2

Chest Radiograph



day six

Chest Radiograph

- **Marked consolidation** of the **left upper lung** and **patchy consolidation** of the **right mid and lower lungs**, **progressive** compared to recent prior radiograph dated, and similar to CT scan. Minimal blunting of the left costophrenic sulcus indicative of small left pleural effusion. Bones and soft tissues unremarkable

What Now?

- Should this patient undergo bronchscopy?
- Should this patient be intubated?

Hospital Course

- Slowly improved over next three days (came off bilevel)
- H&H down to **6.9 & 20.5;** given 2U PRBC (day seven)
- Continued intermittent fevers
- Hospital day #9: worsening and back on bilevel

day nine

Updated Laboratory

	Day one	Day six	Day nine
WBC	**13.3**	**13.0**	**19.5**
Hct	**28%**	**23.4**	**23%**
Hgb	**8.8**	**7.7**	**7.6**
Platelets	462	**551**	**643**
MCV	82	82	82
Na	**127**	**134**	137
K	4.5	3.9	**2.8**
CO2	26	30	**39**
BUN	25	18	22
Creatinine	1.4	0.8	1.0
Albumin	**2.6**	**2.1**	**2.3**
AST	34		**59**
ALT	17		21
Bilirubin	**1.8**		1.2

Micro

- COVID-19: negative x3
- MRSA nares: negative
- Cultures: negative
- Sputum: rare yeast; 2+GPC

Inflammatory markers (day nine)

- CRP **256** -> **234**
- ESR **99** -> **133**

Immunology

- RF: **252**
- ANA negative
- ANCA pending
- Anti-GBM pending
- HIV negative
- Hepatitis negative

Transfer

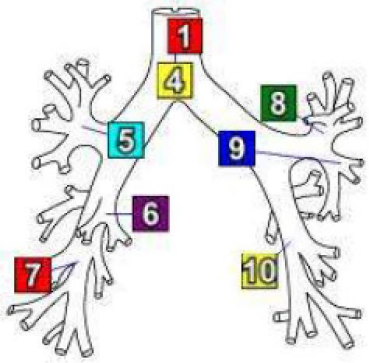
- Methylprenisolone 1g IV daily initiated
- Transfer to larger institution requested
- Intubated for transportation
- Remained hemodynamically stable
- FiO_2 needs stable (0.70)

day ten

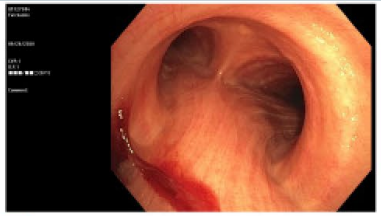
Upon Arrival

- Exam unchanged; chest radiograph unchanged
- Additional history: new numbness of left foot & great toe
- Maintain broad antimicrobials
- Bronchoscopy with biopsies and lavage is planned
- Skin biopsy planned
- CT abdomen and pelvis (when renal function allows)
- Repeat and additional lab testing performed

Bronchoscopy



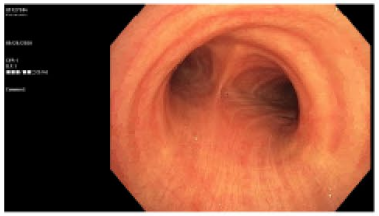
Tracheobronchial Tree



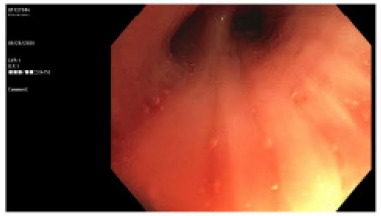
1 Trachea - blood tinged secretions

2 RUL BAL

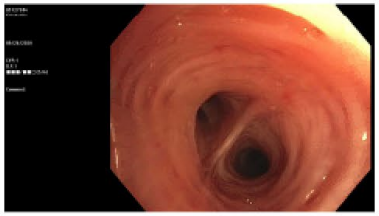
3 LUL BAL



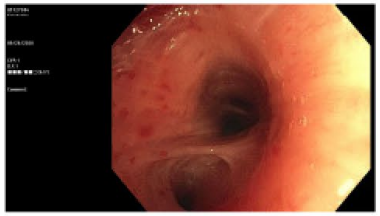
4 Trachea



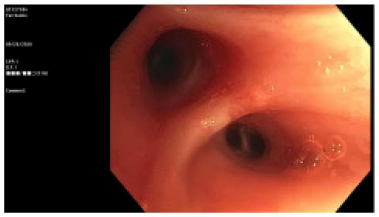
5 Right upper lobe



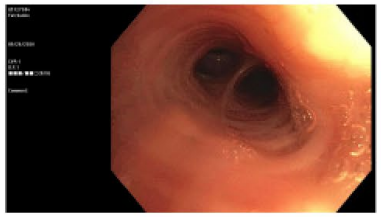
6 Right middle lobe



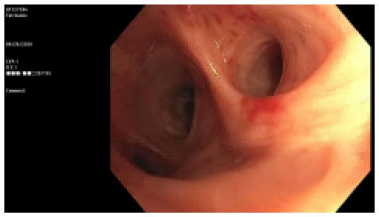
7 Right lower lobe



8 Left upper lobe



9 Left upper lobe



10 Left lower lobe

Bronchoscopy

- Bronchial mucosa and anatomy are normal
- No endobronchial lesions or secretions
- BAL blood-tinged, cellular, and cloudy (both specimens)
  - 77% PMNs, 11% epithelial cells, 11% macrophages
  - 3+ PMNs, no organisms
- Transbronchial biopsies (five) obtained

Bronchoalveolar Lavage

- What do the cell counts and gram stain results suggest?

Updated Course

- Steady clinical improvement
- Remains hemodynamically stable and afebrile
- Steady improvement in leukocytosis and renal function
- Oxygen needs tapered and extubated on day fourteen
- Bronchoscopy and additional lab results return

day fourteen

Place Your Bets!

- What are your top three diagnoses?

Bronchoscopy and BAL

- Bronchoscopy and BAL results
  - No bacterial growth
  - **200 CFU/mL yeast (C. albicans)**
  - Nocardia, Legionella, AFB, Pneumocystis all negative
  - Respiratory virus panel (including COVID-19) negative
  - Aspergillus galactomannan negative
  - Mycoplasma DNA negative, Tuberculosis PCR negative
  - **Legionella DNA isolated by PCR**

Additional Labs

- Anti-GBM negative (from before transfer)
- ACE levels normal
- Complement levels normal
- Cryoglobulins negative
- LDH mildly elevated
- Anti-phospholipid panel and lupus anticoagulant negative
- **RF elevated; anti-CCP slightly elevated**
- **SPEP: IgG kappa monoclonal component**
- **ANCA positive 1:256 (anti-PR3 positive; c-ANCA)**

Biopsy Results

- Skin
  - Leukocytoclastic vasculitis
- Bronchoalveolar lavage
  - Cytopathology negative for malignancy
- Transbronchial
  - Neutrophilic infiltration consistent with **capillaritis**
  - No granulomatous inflammation
  - Negative for neoplasm

Final Diagnosis

- Granulomatosis with Polyangiitis (GPA)
  - PR3-ANCA (c-ANCA)
- Complicated by acute lung injury with respiratory failure
- Superimposed bacterial pneumonia (Legionella)

Final Course

- Completed antibiotics (levofloxacin)
- Changed to prednisone (with Pneumocystis prophylaxis)
- Initiated rituximab (day fifteen)
- Developed acute pancreatitis (due to passed biliary stone)
- Trimethoprim-sulfamethoxazole replaced with dapsone
- Discharged to follow-up with rheumatology
- Plan for elective cholecystectomy

“I told you it’s never Lupus!”

Granulomatosis with Polyangiitis

- March 2011: New name proposed in editorial(s)
  - American College of Rheumatology (ACR)
  - American Society of Nephrology
  - European League Against Rheumatism (EULAR)
  - Shift away from “honorific eponyms” to descriptive nomenclature

- ANCA-associated vasculitides (small vessel vasculitis)
  - Granulomatosis with polyangiitis (GPA)
  - Microscopic polyangiitis (MPA)
  - Renal-limited vasculitis (RLV)
  - Eosinophilic granulomatosis with polyangiitis (EGPA)

Falk RJ et al, Arthritis Rheum. 2011 Apr;63(4):863-4

GPA: Clinical Presentation

- Generally affects older adults
  - Can present at any age
- More common among whites
  - May be more common among Asians than previously reported
- Sexes equally affected
- Time course
  - Generally develops over months
  - Can be rapid (days)
  - Relapse can present with different manifestations

GPA: Clinical Presentation

- Fever, fatigue, anorexia, weight loss
- Arthralgias
- Rhinosinusitis, cough, dyspnea
- Purpura
- Neurologic dysfunction
- Active urinary sediment

Diagnostic Criteria

- Challenging with significant clinical overlap
  - Granulomas define GPA (vs MPA), but can be missed on biopsy
  - ENT manifestations: GPA much more than MPA
  - GPA: PR3-ANCA (+) (c-ANCA; cytoplasmic staining)
  - MPA: MPO-ANCA (+) (p-ANCA; perinuclear staining)
  - EGPA: allergic rhinitis, asthma, eosinophilia, +/- ANCA (+)

- No consensus criteria
  - ACR criteria (1990; pre-MPA and pre-ANCA)
  - Chapel Hill Consensus Conference criteria (2012; define vasculitides)
  - European Medicines Agency algorithm (stepwise combination of above)
  - Stay tuned: Diagnostic and Classification Criteria in Vasculitis Study

Role of Biopsy

- Important for confirmation of the diagnosis
  - Presumptive diagnosis (with positive ANCA) can permit early treatment
  - ANCA not specific for ANCA-associated vasculitides
- Kidney biopsy
  - Often preferred and generally performed if renal manifestations
  - Pauci-immune necrotizing glomerulonephritis
- Lung biopsy
  - Generally requires thoracoscopic surgery (transbronchial ~10% yield)
  - Typically yields pulmonary capillaritis +/- granulomas
  - BAL generally non-specific alveolar hemorrhage
- Skin or nasal
  - Skin generally non-specific leukocytoclastic vasculitis
  - Nasal biopsy is of low yield

Case Specific Points

- Fairly classic presentation
  - Subacute onset with constitutional symptoms
  - ENT, Pulmonary, renal, skin involvement
- Treatment before confirmatory biopsy
  - Suspicion on clinical grounds with (+) ANCA
  - Sometimes necessary in severe cases
  - Biopsy (such as lungs) can be obtained after improvement

Thank You!

- “None of us can know what we are capable of until we are tested.”

Elizabeth Blackwell