
به نام خداوند
جان آفرین
حکیم سخن
در زبان آفرین

Current Concept of ; Pulmonary Renal Syndrome Red Urine and Sputum?

Fooman, Iran
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Behrooz Broumand, M.D.

Iran
PERSEPOLIS

What do the lungs and kidneys have in common?

- *Detailed and extensive amount of micro-vasculature across a large surface area*
- *Basement membrane (which has special antigens)*
- *Exchange of materials across a thin barrier.*
- *Both clean the body of waste material and manage the delicate balance of other materials.*

هر نفسی که فرو می رود ممدّ حیاتست

وچون برمی آید مفرّح ذات

سعدی

AKI and Pulmonary Dysfunction

- Coexistence of AKI and acute lung injury is associated with **high mortality** of up to **80%**
- Increased pulmonary vascular permeability, lung edema,alveolar hemorrhage,and leukocyte trafficking
- **Bidirectional interaction** between kidney and lung
- Intraluminal and not interstitial neutrophils are contributing to lung injury

Pulmonary Renal Syndrome

- Characterized by:
  - Diffuse Alveolar hemorrhage
  - Glomerulonephritis
- Manifestation of underlying disease
- Has a differential diagnosis of its own

AKI and Pulmonary Dysfunction

- **IL-6** is a direct mediator of AKI induced increase in vascular permeability, leukocyte trafficking, and increased edema following bilateral IRI or nephrectomies

- Administration of the anti-inflammatory cytokine **IL-10** before bilateral nephrectomy **reduced** lung injury and inflammatory markers

Causes of Pulmonary Renal Syndromes

- ANCA associated Vasculitis: ~ 60%
  - ~~Wegeners~~ noncaseating Granulomatosis with Polyangiitis (PGA):
  - Microscopic Polyangitis
  - Churg Strauss Syndrome
- Goodpasture's syndrome ~ 20%

OTHERS:

- SLE
- Uremic Lung
- Pneumonia with Infectious GN

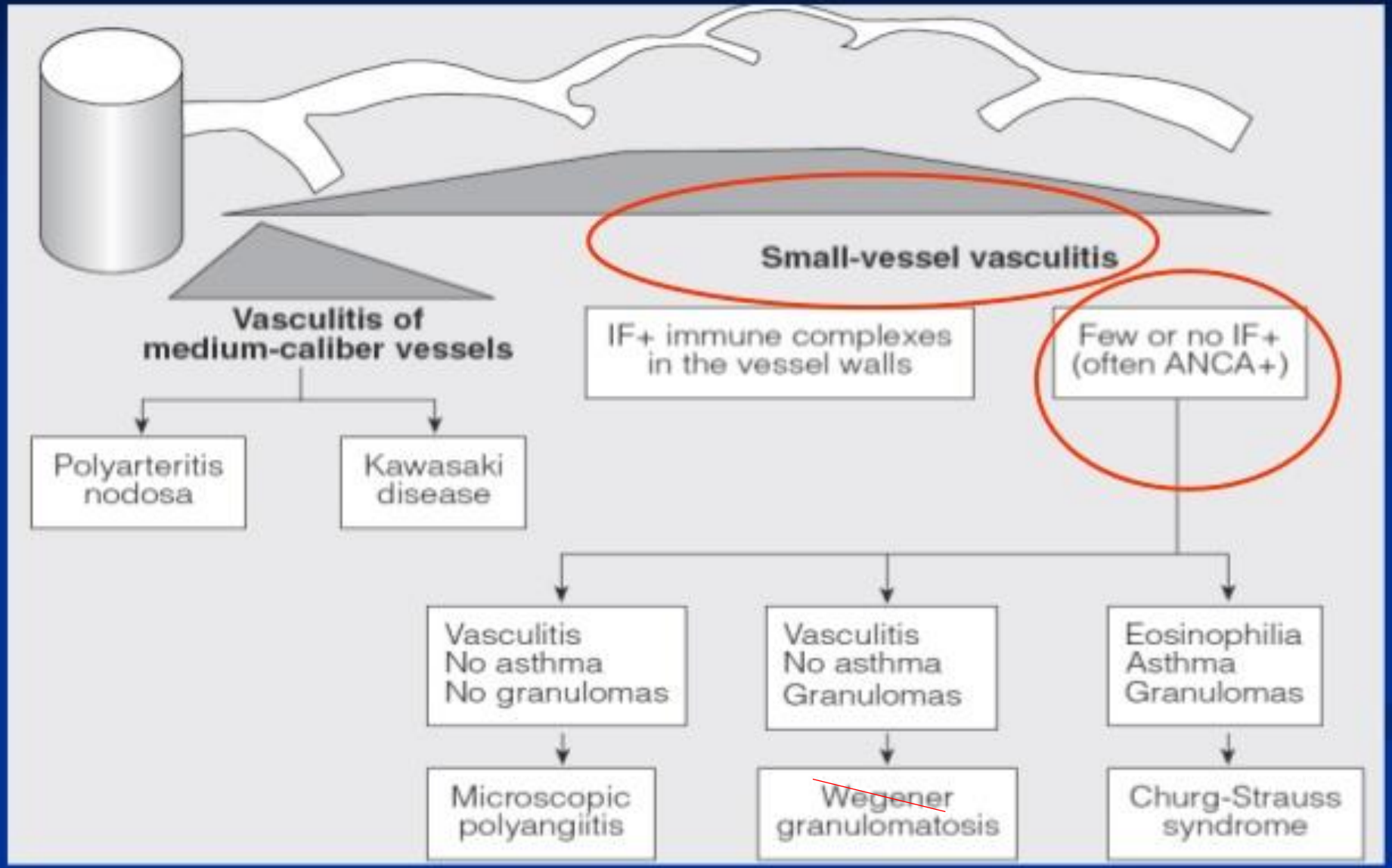
Basis of Classification

- A variety of mechanisms are implicated in the pathogenesis of this syndrome i.e. antibody mediated diseases, immune complex mediated and others i.e. drugs
- Underlying pulmonary pathology is small-vessel vasculitis involving arterioles, venules and, frequently, alveolar capillaries
- Underlying renal pathology is a form of focal proliferative glomerulonephritis
- Immunofluorescence helps to distinguish between antibody mediated and immune complex mediated diseases

Facts to keep in mind

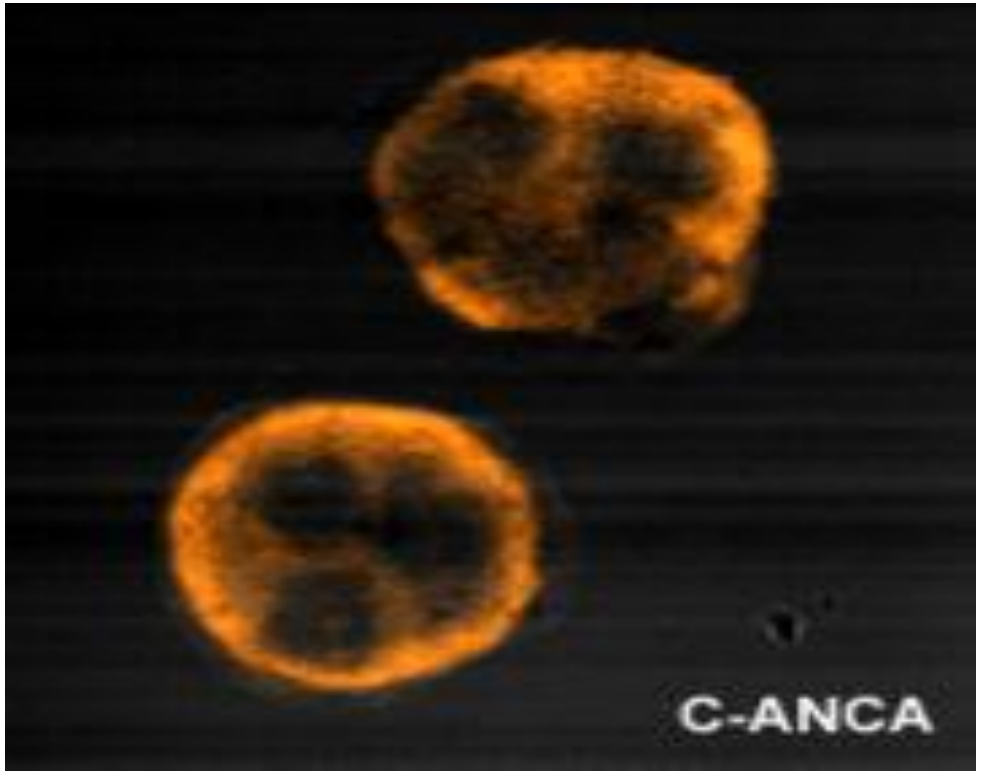
- Pulmonary Renal syndromes can be FATAL.
- If bleeding is occurring from both the lungs and kidneys then these patients need to be in the ICU and get treatment FAST otherwise they will die.
- In difficult cases with vague symptoms, sometimes an early renal biopsy can make all the difference

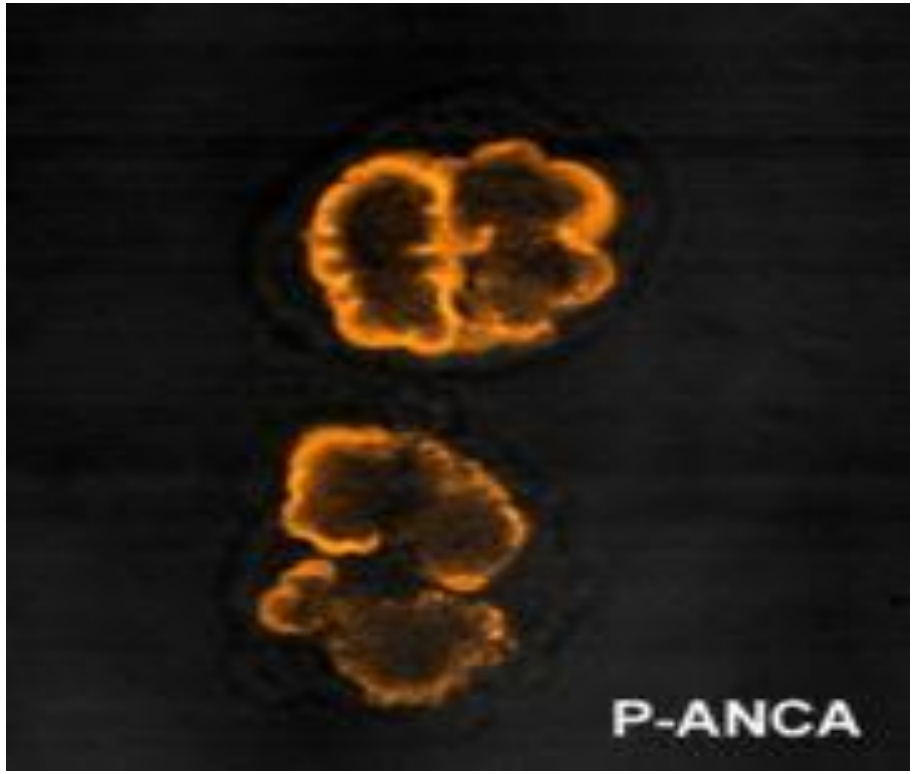
Classification Based On Vessels Size



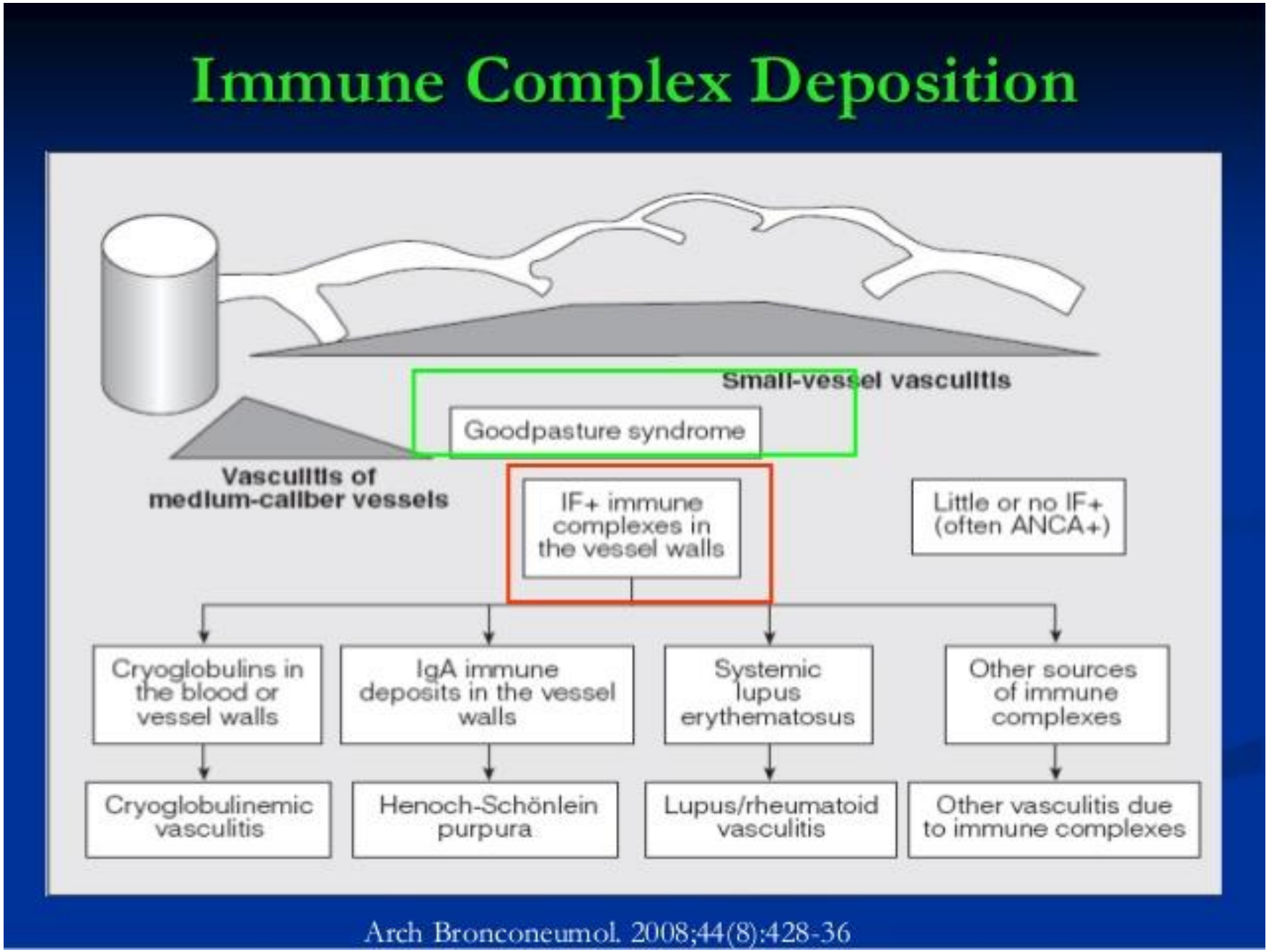
Arch Bronconeumol. 2008;44(8):428-36

ANCA





An Immunological Emergency



Antibody mediated Vs Immune Complex Disease

SPECIFIC CAUSE	FREQUENCY	SUGGESTIVE DIAGNOSTIC FEATURES	SUGGESTIVE SEROLOGIC FEATURES
Goodpasture syndrome	20%–100% of patients develop alveolar hemorrhage (more likely in smokers and in men)	Smoking, hydrocarbon exposure, pulmonary-renal syndrome	Antiglomerular basement membrane antibody positivity Linear immunoglobulin G glomerular membrane deposits
Systemic lupus erythematosus	Up to 11% of patients have diffuse alveolar hemorrhage at onset (more commonly than any other connective tissue disorder)	Fever, arthralgia, rash	ANA positivity Anti-dsDNA antibodies Decreased C3 and C4

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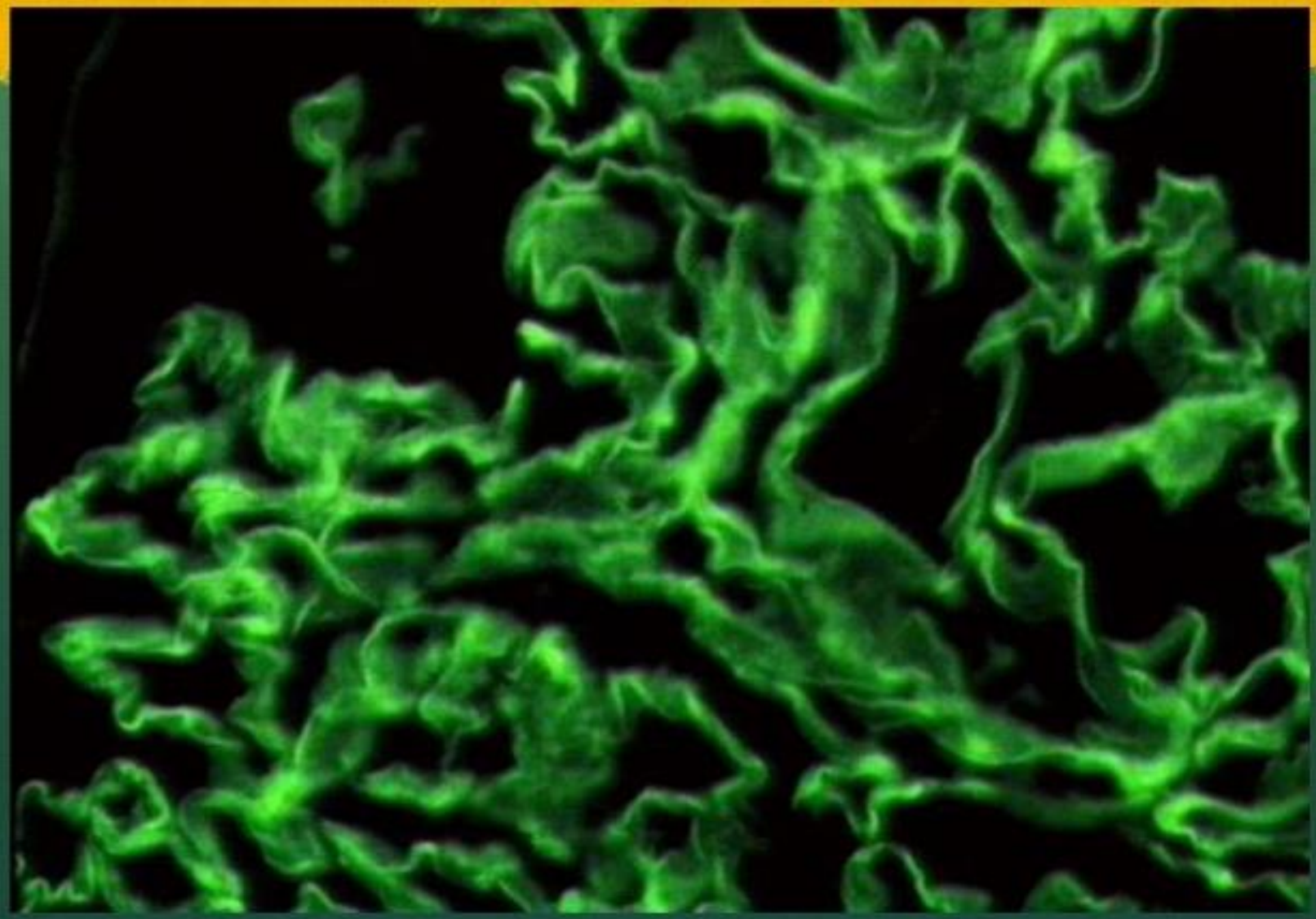
Goodpasture's: Linear immunoflorence



Presentation and Diagnostic Workup

- Fever, cough and dyspnea, often acute or sub acute(<1wk)
- Hemoptysis may be absent in 1/3 of patients
- When hemoptysis is present, one must exclude infection, left heart failure, severe mitral stenosis, pulmonary embolism and drug exposure (PTU and Cocaine) as possible etiologies so thorough history is extremely important
- CXR and Chest CT show diffuse bilateral infiltrates often impossible to differentiate form infection or acute pulmonary edema
- Early bronchoscopy is most helpful and serves two purpose, document hemorrhage and exclude airway lesions as source of bleeding and BAL fluid cultures exclude infection

The basic pathology

LUNGS: Diffuse alveolar hemorrhage (DAH)

- Acute onset of symptoms
- 2/3 have at least mild Hemoptysis if not more gross bleeding
- X-ray and CT scans are usually abnormal: Alveolar and interstitial opacities, or even fibrosis type appearance may be seen
- If severe – many of them need intubation

KIDNEYS: Rapidly Progressive Glomerlo-Nephritis

- Acute Renal Failure
- Oliguria <400ml/day
- RBC casts and RBC on UA

Wegener's Granulomatosis

LUNG, UPPER AIRWAY (sinus, nasopharynx) , and RENAL involvement.

- Necrotizing Vasculitis of SMALL VESSELS (arterioles AND veins)
  .
- Renal Biopsy shows SEGMENTAL NECRTIZING Glomerulonephritis and Rapidly Progressive GN in later stages
- Non-Caseating Granuloma formation – rarely in the kidney, mostly in lung/sinuses.
- If no renal involvement it is called LMITED Wegeners – but kidneys usually get involved later.
- Chest X-Ray may show: Nodules, persistent infiltrates, cavities
- Cause unknown – has been associated with Silica exposure.

~~Wegener's~~ Granulomatosis

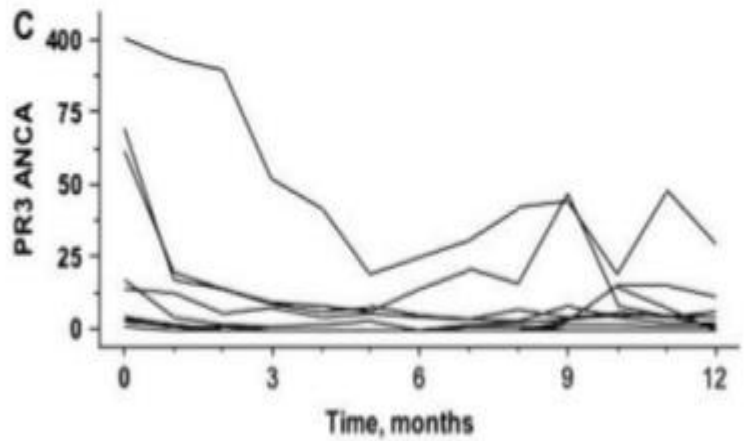
noncaseating Granulomatosis with Polyangiitis (PGA)

- Signs and Symptoms: Fever, Rhinorrhea, Sinus pain, Sinus ulcers, Hemoptysis, SOB, Hematuria, Proteinuria, Cutaneous purpura.
- Lung biopsy has highest yield.
- More common in people with apha-1 antitrypsin deficiency → which inhibits PR3
- Rx: STEROIDS + CYCLOPHOSPHAMIDE .
- Plasmapharesis is not established - may or may not be used initially depending on severity
- 25% will relapse → REPEAT ABOVE TREATMENT and give Methotrexate OR Azathioprine to maintain remission.

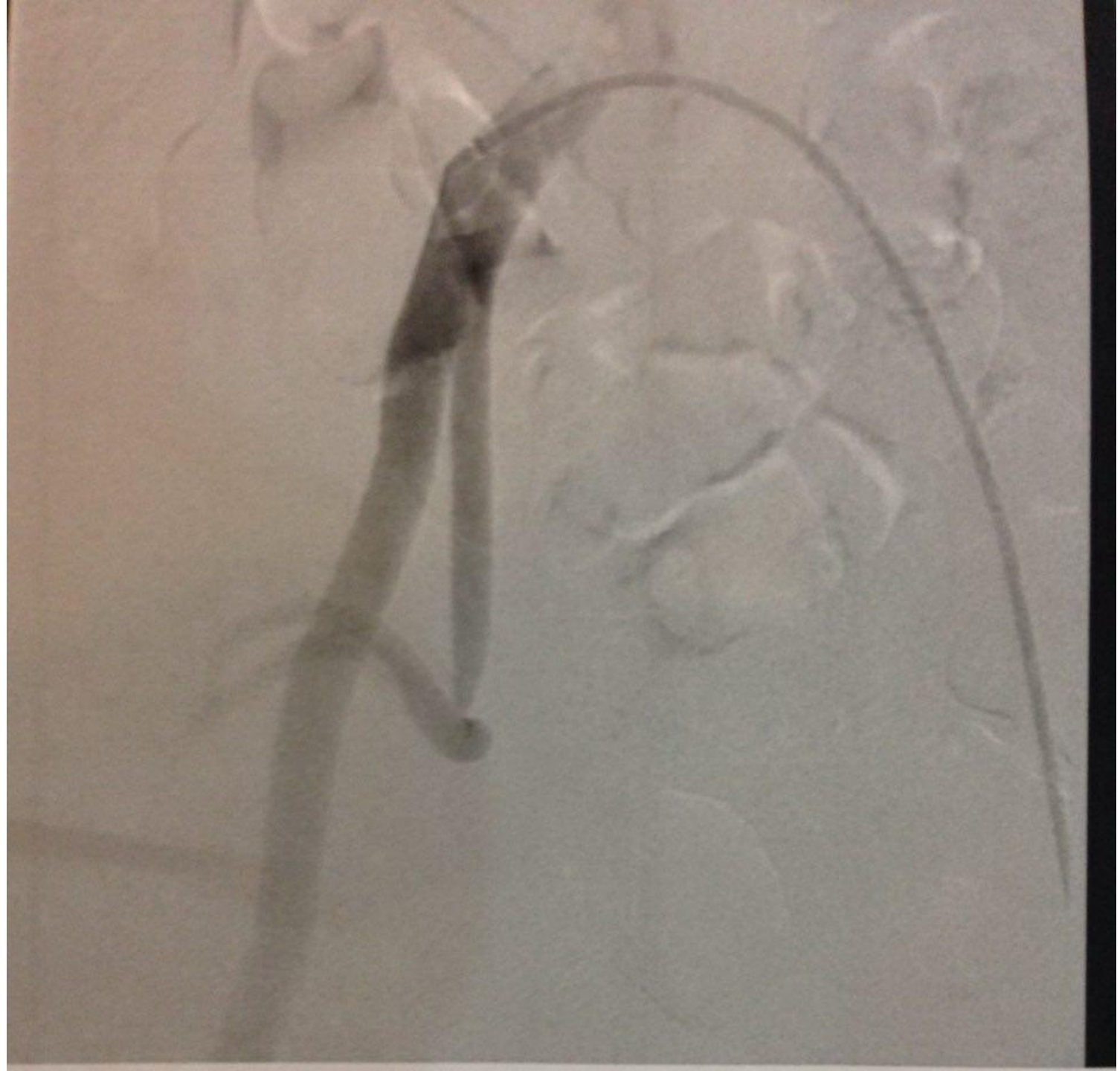
A prospective open-label pilot trial

- 10 patients with active severe ANCA - vasculitis, and resistance to (or intolerance of) cyclophosphamide

- The regimen consisted of oral prednisone (1 mg/kg/d) and four weekly infusions of rituximab (375 mg/m2)



Transplanted kidney in a Pt. Diagnosed as noncaseating Granulomatosis with Polyangiitis (PGA):
44 Y/O White female diagnosed as ANCA Associated Vasculitis at age 24Y/O underwent Renal Tx, at age 26 and developed ARF six years post Tx . Work up revealed RAS of Tx kidney at the anastomosis site of donated RA to R Iliac artery of Tx Recipient. Patient AKI and hypertension improved with increasing the dose of corticosteroid. Repeat Angiography less stenosis.



Microscopi polyangitis

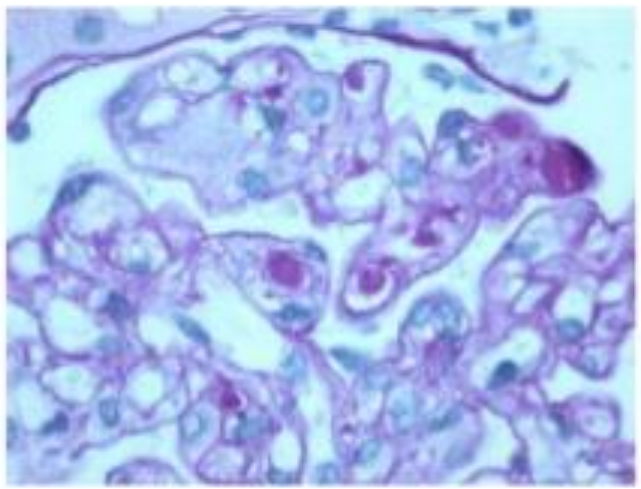
- Necrotizing vasculitis, glomerulonephritis, and pulmonary capilaritis.
- Very similar to Wegener's Granulomatosis – Except that there are NO GRANULOMAS on biopsy.
- Lungs are involved only 50% of the time and upper airway is rarely involved – and these involvements are rarely severe
- Used to be included in P.A.N – no longer – involves the lungs – and PAN does Not. Also not associated with HBV, but PAN is.
- Can also cause GI vasculitis , cutaneous vasculitis and Mononeurtis complex.
- Rx: similar to Wegener's – STEROIDS + IMMUNOSUPPRESSANT. Plasmapharesis is not established – may or may not be used depending on severity.
- Relapse also occurs – 35% of the time – treated the same – repeat and give maintenance therapy with MTX or Azathioprine

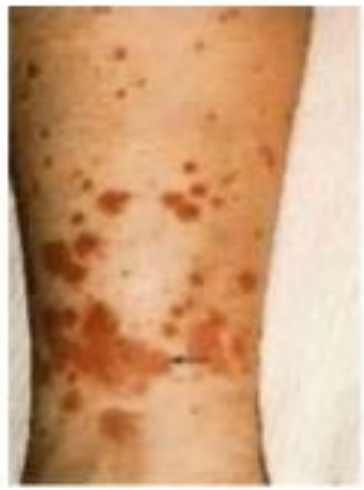
Churg Strauss Syndrome

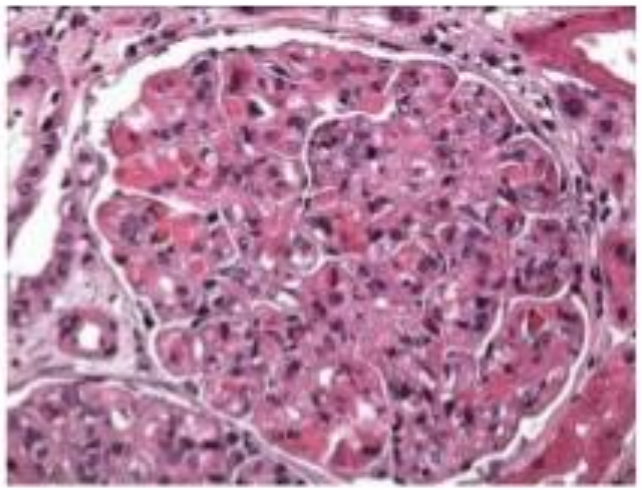
- Small vessel vasculitis with focal segmental necrotizing glomerulonephritis.
- Rare "allergic state" with systemic inflammation associated with Asthma, Hypergammaglobulinemia, RF+, raised IgE levels, and EOSINOPHILS
- Rare: about 1 in 3 million
- Has been associated with Asthma treated with Leukotriene antagonists.
- Symptoms: Lung involvement dominates and may preceded others by years: Cough, infiltrates, severe asthma, 1/3 have pleural effusions – high in eosinophils.
- GN (45%), Rhinitis, mononeuritis, Skin involvement (50%) , GI vasculitis and Cardiovascular inflammation resulting in MI (most frequent cause of death in Churg Strauss)

Mixed cryoglobulinemia

- Immune complex mediated small to medium vessel vasculitis associated with neuropathy, arthritis, rash and proliferative glomuronephritis
- HCV triggers B-cell expansion with production of IgG-IgM cryoglobulins
- Antiviral therapy, steroid, cyclophosphamide and plasma exchange are commonly used in HCV related cryoglobulinemia

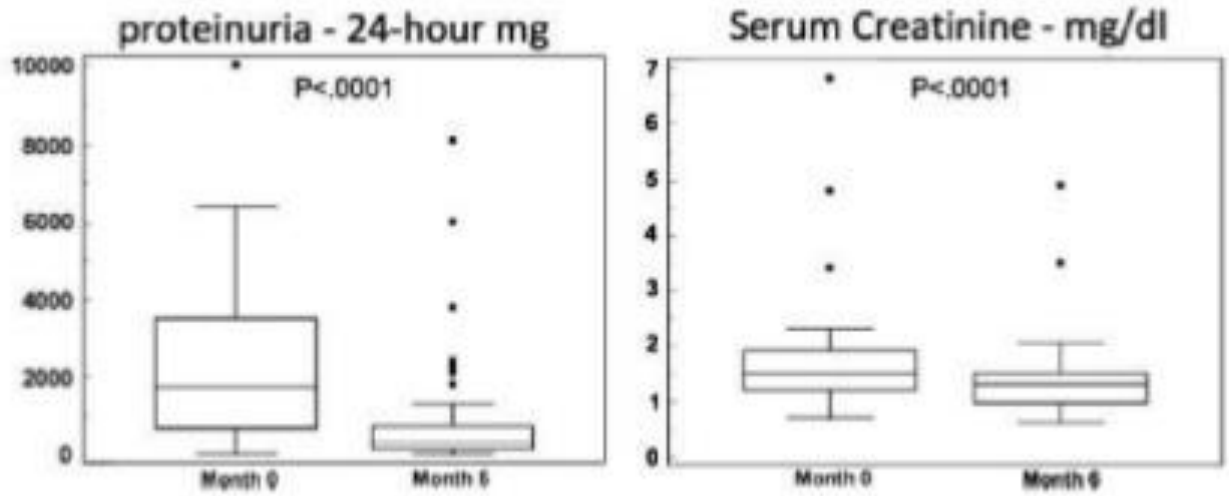






Multicenter retrospective study

- 87 HCV patients with active cryoglobulinemic vascuilitis treated with rituximab monotherapy 375 mg/m2 weekly x 4doses and followed up for 6 months



9.2.3: For patients with HCV and mixed cryoglobulinemia (IgG/IgM) with nephrotic proteinuria or evidence of progressive kidney disease or an acute flare of cryoglobulinemia, we suggest either plasmapheresis, rituximab, or cyclophosphamide, in conjunction with i.v. methylprednisolone, and concomitant antiviral therapy. (*2D*)

Goodpastures syndrome…

Young Men in 20s:

- Explosive, sudden onset.
- Sudden anemia
- More lung involvement than in older age group
- Hemoptysis - specially if smokers
- Dyspnea,
- Hematuria
- Better prognosis than older age group

Goodpasture's syndrome…

Older Age Group: 60-70s , M and F

- Prolonged asymptomatic renal injury
- May present with oliguria – Poor prognosis
- Lung disease may range from mild dyspnea to outright pulmonary hemorrhage
- Urgent kidney biopsy if we suspect this disease and there are mild or no lung signs

Goodpasture's syndrome

TREATMENT AND PROGNOSIS:

Plasmapharesis + Steroids + Immunosuppressants

(and supportive care if needed: ventilator , dialysis)

Signs of Poor Prognosis:

- Biopsy shows >50% crescent and advanced fibrosis, (specially seen in long standing asymptomatic disease in older folks)
- Cr 5-6 mg/dl
- Oliguria
- If needs urgent dialysis at presntation → may not even respond to plasmapheresis or steroids

Goodpasture's … treatment and prognosis

- Even if kidney disease does not respond to plasmapharesis – lung disease does and it can be lifesaving.
- 8-10 treatments of plasmapharesis is needed
- At the same time Prednisone or IV methylprednisolone, PLUS Cyclophosphamide should be started together → cyclophosphamide for at least first 2 weeks
- Kidney transplant can be considered – but wait 6 months for antibodies to clear out.

Pauci-immune Vasculitis

SPECIFIC CAUSE	FREQUENCY	SUGGESTIVE DIAGNOSTIC FEATURES	SUGGESTIVE SEROLOGIC FEATURES
~~Wegener~~ granulomatosis	Capillaritis in about one-third of patients	Glomerulonephritis, sinusitis, multiple cavitary pulmonary infiltrates, granulomata	c-ANCA positivity
Churg-Strauss syndrome	27%–77% of patients have radiographic abnormalities, but diffuse alveolar hemorrhage is very rare	Asthma, peripheral eosinophilia, cutaneous lesions, mononeuropathy or polyneuropathy, granulomata, tissue eosinophilia	p-ANCA positivity
Microscopic polyangiitis	Half of patients with pulmonary involvement present with diffuse alveolar hemorrhage	Systematic manifestations (glomerulonephritis, fever, myalgia, arthralgia) are more common than pulmonary disease (found in 40% of cases); necrotizing vasculitis	p-ANCA positivity

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Lupus Nephritis

- Immune complex deposition in the glomeruli + Complement cascade activation. If Antiphospholipid antibodies are present then thrombotic microangiopathy also occurs
- In Lung: Pleuritis , pleural effusion, diaphragmatic dysfunction, atelectasis, pulm vascular disease with pulm hemorrhage, uremic pulmonary edema.

Lupus Nephritis ….

Classification of SLE with Reference to Glumerulonephritis

Class	Renal Histology (type of lupus nephritis)	Prognosis for Renal Function
I	Minimal mesangial	Excellent
II	Mesangial proliferative	Good
III	Focal	Moderate
IV	Diffuse	Moderate-Poor
V	Membranous	Moderate
VI	Advanced sclerosing	Poor

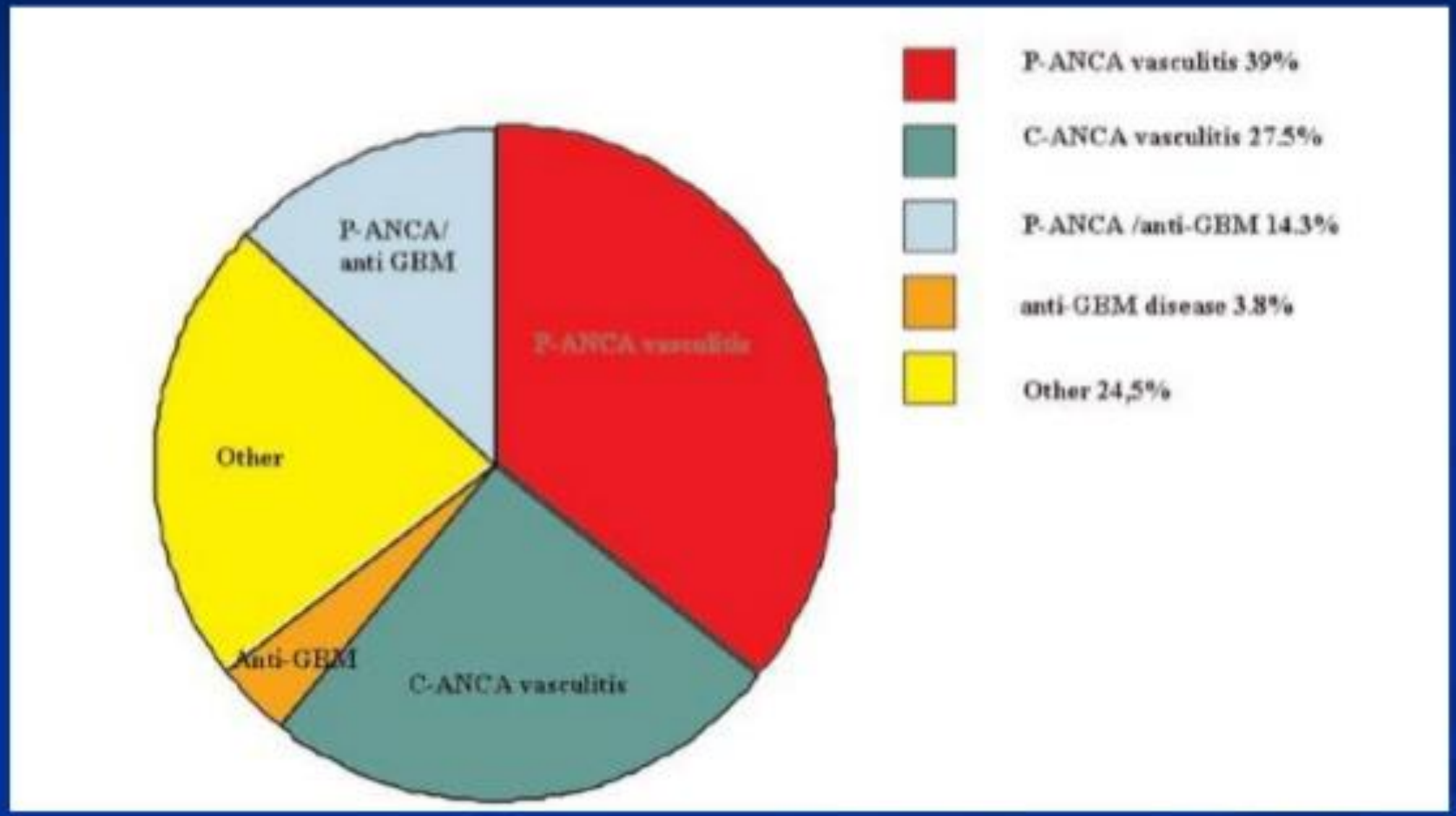
Uremic Lung / Uremic Pulmonary Edema

- Occurs in severe renal failure, ESRD , specially when HTN also present.
- Due to the actual Uremia itself – usually when Cr Clearance <10ml/min. Fluid, electrolyte, metabolic changes – No single toxin has been identified as the cause yet.
- There is increase in pulmonary capillary permeability due to uremia effects – causing protein rich fluid to enter the lungs from the capillaries – causes Uremic Pulmonary Edema.
- CXR shows perihilar edema, though peripheries are clear.
- Correction or uremia with or without Dialysis can correct the flow dynamics of the pulmonary vasculature and improve

Infectious GN

- Very rarely – If Strep pharyngitis and Strep pneumonia occur – pulmonary symptoms may still be present by the time Renal RPGN starts …

Relative Frequencies of Vasculitis

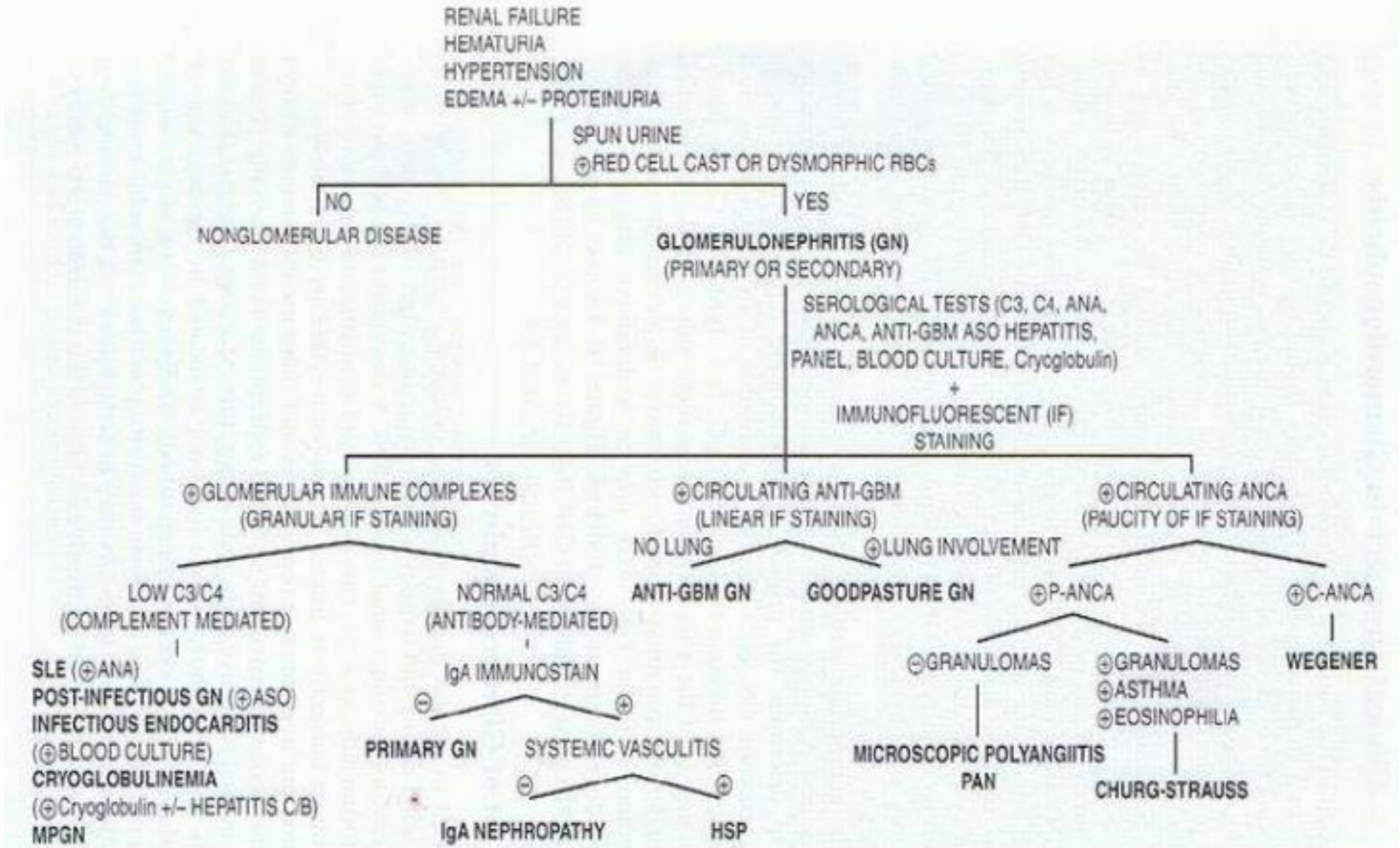


Critical Care Vol 11 No 3 Papiris *et al.*

Pulmonary Renal Syndromes

- Pulmonary–renal syndrome in drug-associated ANCA-positive vasculitis
  - Propylthiouracil
  - D-Penicillamine
  - Hydralazine
  - Allopurinol
  - Sulfasalazine
- Pulmonary–renal syndrome in anti-GBM-postive and ANCA-positive patients
- Pulmonary–renal syndrome in autoimmune rheumatic diseases (immune complexes and/or ANCA mediated)
  - Systemic lupus erythematosus
  - Scleroderma (ANCA?)
  - Polymyositis
  - Rheumatoid arthritis
  - Mixed collagen vascular disease
- Pulmonary–renal syndrome in thrombotic microangiopathy
  - Antiphospholipid syndrome
  - Thrombotic thrombocytopenic purpura
  - Infections
  - Neoplasms
- Diffuse alveolar haemorrhage complicating idiopathic pauci-immune glomerulonephritis

Critical Care Vol 11 No 3 Papiris *et al.*


RENAL FAILURE
HEMATURIA
HYPERTENSION
EDEMA +/– PROTEINURIA
SPUN URINE
⊕RED CELL CAST OR DYSMORPHIC RBCs
NO
NONGLOMERULAR DISEASE
YES
GLOMERULONEPHRITIS (GN)
(PRIMARY OR SECONDARY)
SEROLOGICAL TESTS (C3, C4, ANA, ANCA, ANTI-GBM ASO HEPATITIS, PANEL, BLOOD CULTURE, Cryoglobulin)
+
IMMUNOFLUORESCENT (IF) STAINING
⊕GLOMERULAR IMMUNE COMPLEXES (GRANULAR IF STAINING)
⊕CIRCULATING ANTI-GBM (LINEAR IF STAINING)
⊕CIRCULATING ANCA (PAUCITY OF IF STAINING)
NO LUNG
⊕LUNG INVOLVEMENT
LOW C3/C4 (COMPLEMENT MEDIATED)
NORMAL C3/C4 (ANTIBODY-MEDIATED)
ANTI-GBM GN
GOODPASTURE GN
⊕P-ANCA
⊕C-ANCA
SLE (⊕ANA)
POST-INFECTIOUS GN (⊕ASO)
INFECTIOUS ENDOCARDITIS (⊕BLOOD CULTURE)
CRYOGLOBULINEMIA (⊕Cryoglobulin +/– HEPATITIS C/B)
MPGN
IgA IMMUNOSTAIN
⊖GRANULOMAS
⊕GRANULOMAS
⊕ASTHMA
⊕EOSINOPHILIA
WEGENER
⊖
⊕
PRIMARY GN
SYSTEMIC VASCULITIS
MICROSCOPIC POLYANGIITIS
PAN
CHURG-STRAUSS
⊖
⊕
IgA NEPHROPATHY
HSP

Differential Diagnosis and Treatment

- Microscopic polyangitis
- Churg-Strauss Syndrome
- Pneumonia

  Legionalla or PCP,
  Nosocomial infection

- Pulse dose steroids x3
- Plasmapheresis
- Hold Cytoxan concern for infection-pending cultures
- Broad spectrum antibiotics
- IV Cytoxan started after Renal biopsy
- Resulted in favorable outcome

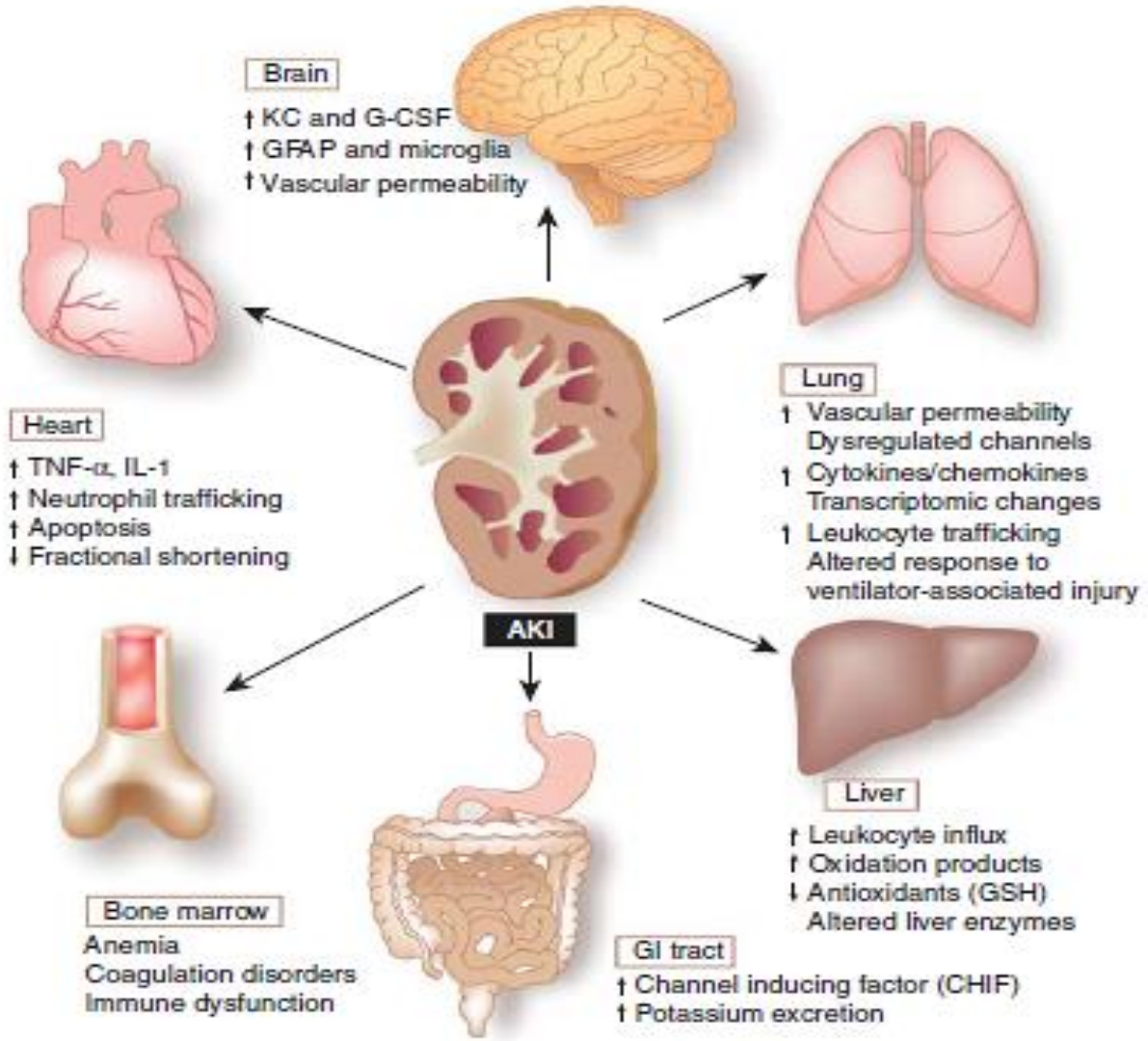


Figure 1 | Distant organ consequences of AKI. AKI, acute kidney injury; G-CSF, granulocyte colony-stimulating factor; GFAP, glial fibrillary acidic protein; GI, gastrointestinal; GSH, glutathione; IL, interleukin; KC, keratinocyte-derived chemokine; TNF, tumor necrosis factor.
Note: Used with permission from Scheel *et al.*[64]

AKI and Pulmonary Dysfunction

- In patients with AKI that require **mechanical ventilation**, the **mortality rate** for AKI was **higher** than for those not requiring mechanical ventilation

- Mechanical ventilation may **induce AKI**

< **arterial blood gases**

< **systemic and renal blood flow**

< **pulmonary inflammatory reactions** releasing cytokines

AKI and Pulmonary Dysfunction

- Both **hypoxemia** and **hypercapnia** together or separately can induce reductions in renal blood flow
- ***Mechanical ventilation,****especially* with increasing positive end-expiratory pressure

< decreasing cardiac output, preload, pulmonary vascular volume, resistance and right ventricular afterload

< alter renal blood flow , the distribution of cortical and medullary blood flow

Doctor with Matula

Summary of Diagnostic Workup

- It is a life threatening condition which requires early intervention to prevent high mortality
- Concurrent infection, severe anemia and long mechanical dependence are poor prognostic markers
- Aim for an early bronchoscopy to document hemorrhage and exclude infection
- Biopsy (open lung or renal with IF) can be extremely helpful and reassuring

- Common practice to use of Pulse dose steroids and Cytoxan in life threatening renal and pulmonary involvement
- There is good data early use of plasma exchange followed by IVIG in life threatening and treatment resistant cases
- Plasma exchange has been helpful in situations with concomitant need for anticoagulation

Evaluating PAH and Hematuria

Are you dealing with a systemic vasculitis	Y/N
Is there evidence of oral and nasal inflammation	Y/N
Any history of Asthma, eosinophila or paranasal sinus disease	Y/N
Is there palpable purpra, arthritis or/and abdominal pain	Y/N
Does patient has bilateral pulmonary infiltrates + bronchoscopy with hemorrhagic BAL	Y/N
Oral and genital ulceration, uveitis and skin lesions	Y/N
Is there history of D-penicillamine or PTU use or BMT	Y/N
Risk factors for pneumonia with renal failure, in an immunosuppressed host (bacterial/viral or PCP)	Y/N
Is there new congestive heart failure with prior hx renal disease	Y/N

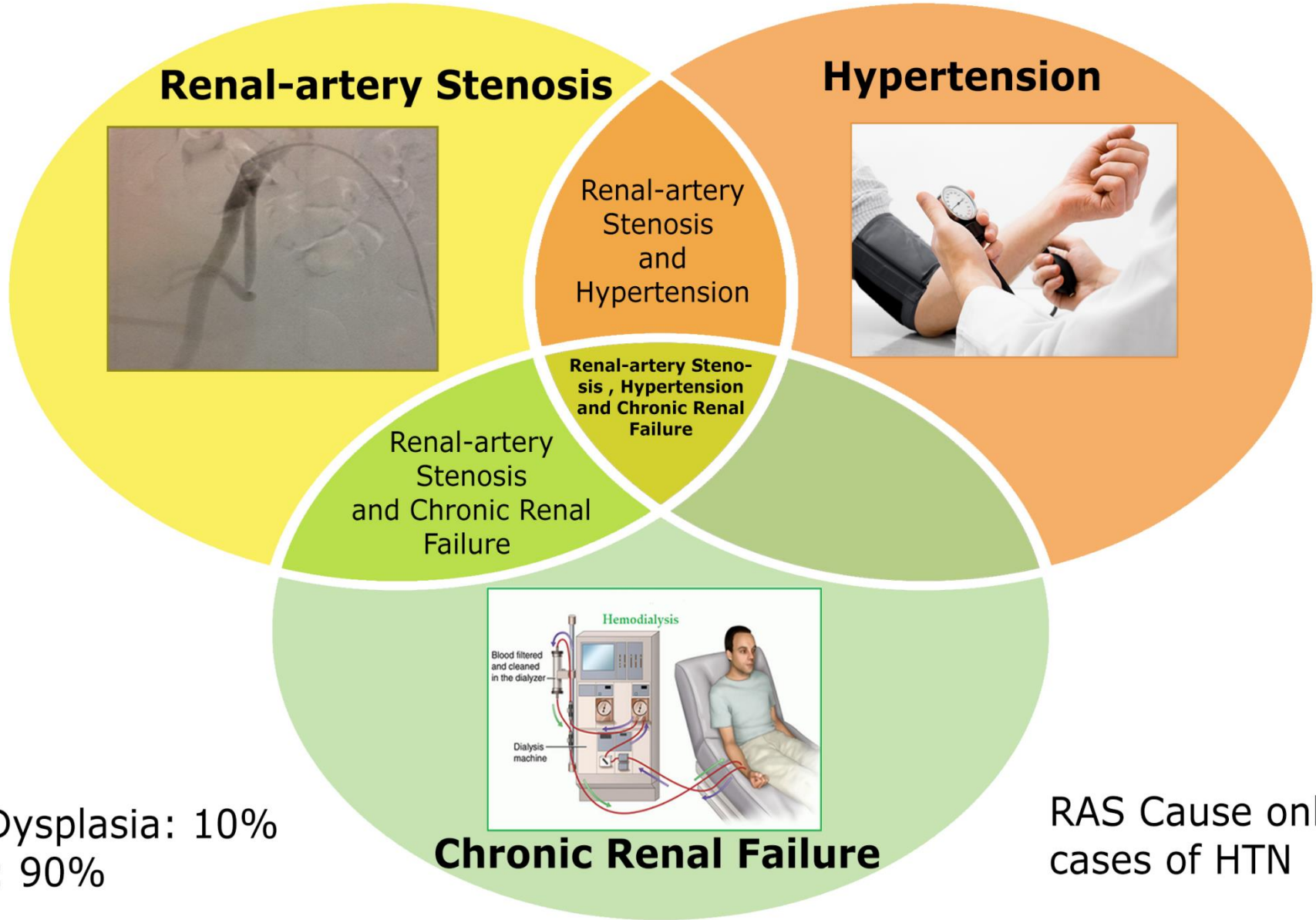
Evaluating PAH and Hematuria

Any evidence of MAHA (HUS/TTP): HPT, LDH, DAT, Peripheral smear, Low PLT	Y/N
Possibility of a bleeding diathesis: DIC , Coags, coumadin	Y/N
Is there nephrotic proteinuria → Pulmonary Embolism	Y/N
Serologies Lupus: ANA, ENA, DsDNA, C3,C4 Pauci-Immune: ANCA, Pr3, MPO, AGBM Immune complex Vasculitis: Cryo, RF, viral hepatitis Antiphospholipid syndrome: DRVVT,CAB, B2GP1	Y/N
Tissue biopsy showing necrosis, vasculitis, granulomatous inflammation	

Differential Diagnosis and Treatment

- Lupus nephritis flare with pulmonary hemorrhage
- TTP or HUS
- End-stage renal disease with congestive heart failure
- Legionalla pneumonia
- Nephrotic syndrome with hypercoagulable state causing a pulmonary embolus

- Pulse steroids
- Plasmapheresis
- Broad spectrum antibiotics
- IVIG
- Cytoxan
- Rituxan
- IVIG
- Cellcept



Causes of RAS:
Fibromuscular Dysplasia: 10%
Atherosclerosis: 90%

RAS Cause only 1% of all cases of HTN

Clinical Pathology Conference: Pulmonary

"A case I've Never Seen…"

Jonathan Mock, MD
Dept of Internal Medicine
Scott and White Memorial Hospital

The Case

- Chief Complaint:
  - 82 year old Caucasian female who presents with fatigue

- History of Present Illness:
  - She has had complaints of fatigue and “weakness” for approximately one year.
  - The weakness is to the point she cannot ambulate without assistance.
  - She has fallen multiple times, but has never lost consciousness.
  - She has had a poor appetite and has intermittent periods of nausea and vomiting with associated mid-epigastric abdominal pain that is not related to oral intake.
  - She has lost 20 pounds unintentionally in one year
  - She denies hematemesis, melena, and hematochezia.

The Case

- History of Present Illness Continued:
  - The patient has a long standing history of COPD and bronchiectasis with periods of productive cough. These are usually successfully treated with antibiotics.
  - Over the past year, she has been treated numerous times for bronchiectasis, with no significant change in symptoms.
  - She does not feel that her current symptom complex is related to her pulmonary disease.
  - She currently denies cough, chest pain, shortness of breath, hemoptysis, fevers, and chills.
  - She does report sinus drainage over the last several months with associated frontal headaches that have been quite bothersome.
  - The patient had vertebroplasty performed approximately 6 months ago for T9 and L1 compression fractures. Unfortunately, she did not have significant improvement in her strength or pain. She feels her pain may be contributing “some” to her problems.

The Case

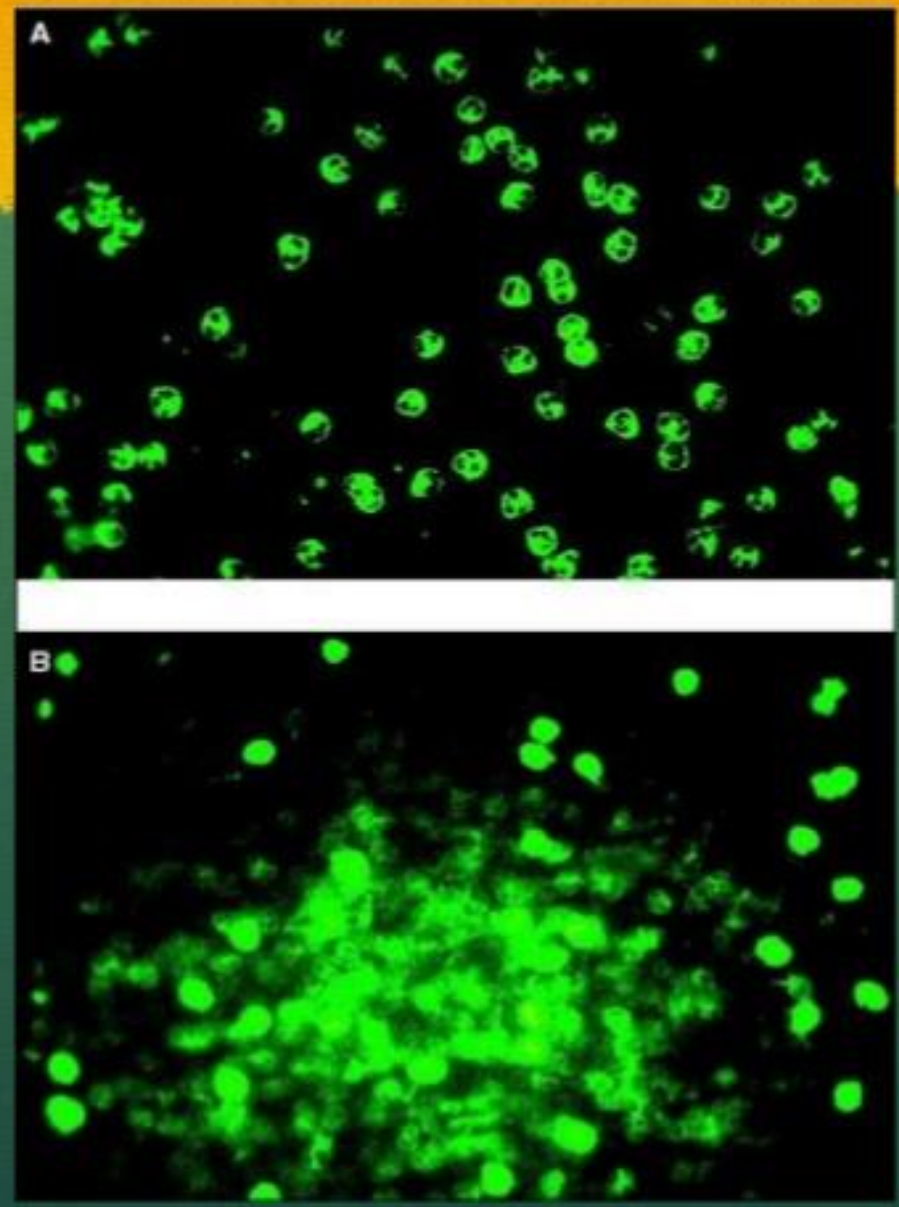
- Past Medical History:
  - Chronic Obstructive Pulmonary Disease
  - Bronchiectasis
  - Hypertension
  - Hyperlipidemia
  - Hypothyroidism
  - Osteoporosis
  - Macular Degeneration
  - Cataracts
  - Diverticulosis
  - Cholelithiasis

The Case

- Past Surgical History:
  - Vertebroplasty
  - Cataract Surgery
- Family History:
  - Father died of gastric cancer in his 60's
  - Mother died of heart failure in her 80's
- Social History:
  - No history of alcohol or illicit drugs
  - "Very Brief" smoking history many years ago

C ANCA above

P ANCA below



The Case

- Allergies:
  - No Known Drug Allergies
- Medications:
  - Atenolol 25 mg by mouth daily
  - Synthroid 50 mcg by mouth daily
  - Actonel 35 mg by mouth weekly
- Review of Systems:
  - No rash
  - No photosensitivity
  - No oral ulcers
  - Otherwise per HPI

The Case

- Physical Exam:
  - VS: T 96.7, BP 170/90, P 90, R 16, O2Sat: 95% on RA
    Wt 101 lbs
  - Gen: A&O x 3, NAD
  - HEENT: NC/AT, PERRLA, EOM intact, Oropharynx clear
  - Neck: No JVD, No lymphadenopathy, No thyromegaly
  - CV: Regular rhythm, No murmurs/gallops/rubs
  - Lungs: Clear to Ausc bilaterally. No wheezes, rales,
    or rhonchi
  - Abd: Soft, NT, ND, Normoactive BS, No organomegaly
  - Ext: No clubbing, cyanosis, or edema
  - Skin: No rashes
  - Rectal: Normal tone, Guaiac negative

The Case

- Labs:
  - CMP:

    Na: 137
    K: 3.4
    Cl: 101
    C02: 21
    Creat: 4.7 (6 mos prior: 0.8)
    BUN: 79
    Glu: 106
    Ca : 8.2
    Alb: 2.6
    Phos: 6.6

  - CBC:

    WBC: 13,700 (85% Granulocytes)
    Hgb: 7.8
    MCV: 85.9
    Plt: 288,000

  - UA:

    100 Protein
    10-19 WBCs
    >50 RBCs
    2+ Blood
    Neg Leukocyte Esterase
    Neg Nitrites

The Case

- Labs Continued:

  - A Few Extras:
    TSH: 0.45
    ESR: 120
    Complements WNL
      C3: 93
      C4: 39
    ANA: Negative
    PPD: Negative

  - CT Abdomen (6 mos PTA):
    Diverticulosis and Cholelithiasis

  - CT Chest:
    Bronchiectasis with centrilobular nodules and interstital densities

  - Renal US:
    Normal Kidney size with no obstruction present

Problem List

COMPLAINTS

Weakness/Fatigue

Weight Loss

Nausea

Vomiting

Abdominal Pain

Diminished Appetite

Sinus Drainage

Headache

Back Pain

Cough

PAST HISTORY

Hx of COPD
Hx of Bronchiectasis
Hx of HTN
Hx of Hyperlipidemia
Hx of Hypothyroidism
Osteoporosis
Compression Fx
Diverticulosis
Cholelithiasis
Macular Deg/Cataracts

LABAROTORY DATA

Abnormal CT Chest:
    Bronchiectasis with Centrilobular Nodules and Interstitial Densities
Renal Failure
Active Urine Sediment
Mild Metabolic Acidosis
Elevated ESR
Hyperphosphatemia
Normocytic Anemia
Leukocytosis
Hypoalbuminemia

How to Proceed

- Multiple ways to organize thought processes and initiate workup.
  - Weight Loss
  - Cough
  - Abdominal Complaints
  - Anemia
  - ESR
  - Renal Failure with active Urine Sediment
  - Differential for Fatigue

Problem List

COMPLAINTS	PAST HISTORY	LABAROTORY DATA
Weakness/Fatigue	Hx of COPD	Abnormal CT Chest:
Weight Loss	Hx of Bronchiectasis	Bronchiectasis with Centrilobular
Nausea	Hx of HTN	Nodules and Interstitial Densities
Vomiting	Hx of Hyperlipidemia	Renal Failure
Abdominal Pain	Hx of Hypothyroidism	Active Urine Sediment
Diminished Appetite	Osteoporosis	Mild Metabolic Acidosis
Sinus Drainage	Compression Fx	Hyperphosphatemia
Headache	Diverticulosis	Elevated ESR
Back Pain	Cholelithiasis	Anemia
Cough	Macular Deg/Cataracts	Leukocytosis
		Hypoalbuminemia

Severe Systemic Illness

Glomerulonephritis

Pulmonary Involvement

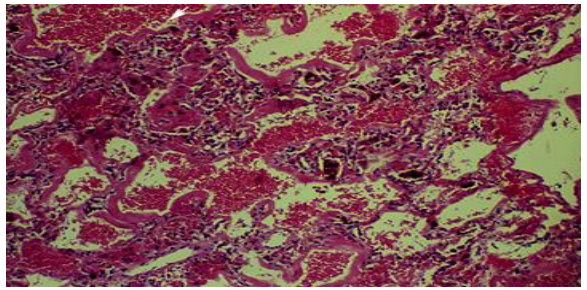
Pulmonary-Renal Syndrome

Diffuse Alveolar Hemorrhage

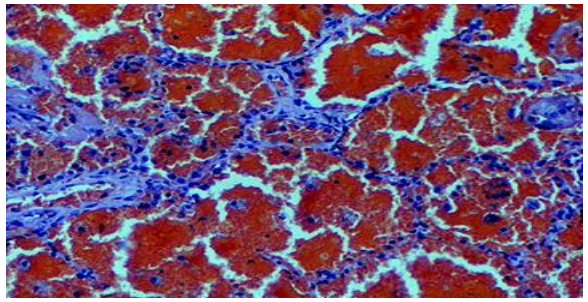
- Patients can present with constellation of symptoms initially including cough, fever, hemoptysis, and dyspnea.
- Can present with severe respiratory distress
- Onset is usually abrupt but can resolve/recur.
- Suspect DAH:
  - Presence of Hemoptysis (Absent in 1/3 of patients)
  - Radiographic Abnormalities (Alveolar opacities, Interstitial opacities, Fibrosis)
  - Unexplained drop in Hematocrit

Diffuse Alveolar Hemorrhage

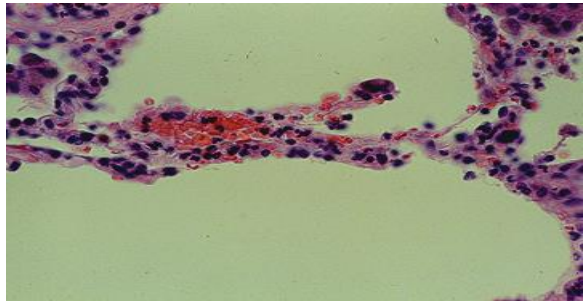
- Diffuse Alveolar Damage: Edematous septa but no inflammation



- Bland Alveolar Hemorrhage: Hemorrhage without alveolar destruction or inlammation



- Pulmonary Capillaritis: Neutrophilic infiltration of the alveolar wall and hemorrhage with resulting

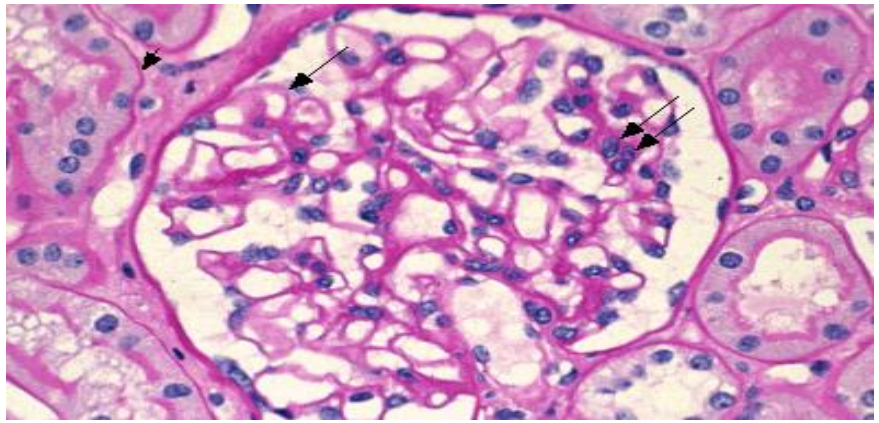


Glomerulonephritis

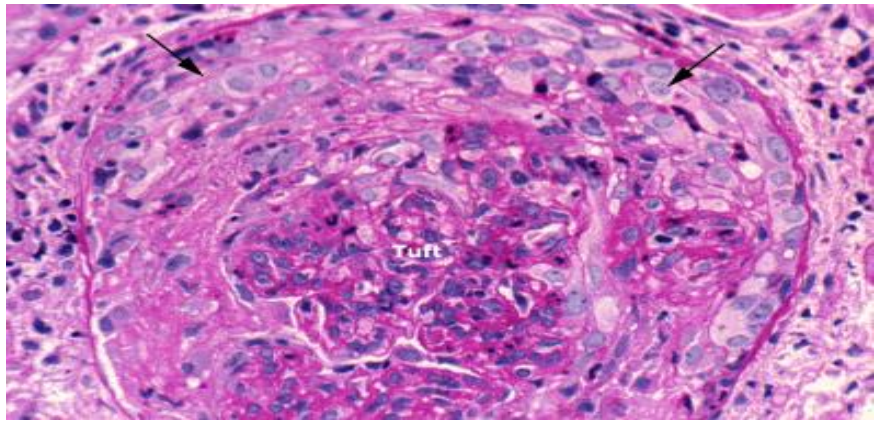
- Acute Nephritic Syndrome: Days to Weeks
- Rapidly Progressive Glomerulonephritis: Weeks to Months (Crescentic Glomerulonephritis is pathologic entity)
- RPGN Usually classified by mechanism of injury:
  - **Antibodies against GBM** (10%-20%): *Linear Immunofluorescent Pattern*
    Goodpasture's
  - **Pauci-Immune (45%-50%):** *Negative Immunofluorescent Pattern*
    ANCA associated Vasculitides
  - **Immune Complex Mediated (30%-45%):** *Granular Immunofluorescent Pattern*
    Cryoglobulinemia
    Henoch-Schonlein Purpura
    SLE
    IgA nephropathy
    Post-Infectious GN
    Membranoproliferative GN Antibodies against GBM (10%-20%)

Glomerulonephritis

- Crescents form as a response to severe glomerular injury
- Decreased GFR may result in increased extracellular volume causing edema and HTN.
- UA: hematuria, red cells/casts, variable level of proteinuria



Normal Glomerulus



RPGN/Crescentic GN

Differential of Pulmonary Renal Syndrome

- Goodpasture's Disease
- Systemic Vasculitis
  - Wegener's Granulomatosis
  - Microscopic Polyangiitis
  - Churg-Strauss syndrome
  - Cryoglobulinemia
  - Henoch-Schonlein Purpura
- Connective Tissue Disease
  - Polymyositis/Dermatomyositis
  - Progressive Systemic Sclerosis
  - SLE
- Primary Glomerular Disease
  - IgA nephropathy
  - Post-Infectious GN
  - Membranoproliferative GN

Goodpasture's Disease

- History:
  - 1918: Ernest Goodpasture described massive hemoptysis and acute renal failure in an 18 year old male.
  - Goodpasture's Disease:
    - Clinical complex of Anti-GBM nephritis and lung hemorrhage.
    - Alveolar Hemorrhage occurs in 60-70% of Anti-GBM disease

- Epidemiology:
  - Incidence: 0.5-1 cases per 1,000,000
  - Responsible for 1-5% of cases of GN
  - Can affect all age groups
  - Bimodal Distribution:
    - Ages 30-40 (Male: Female = 6:1) — HEMOPTYSIS ⇨
    - >60 (Male = Female) — RENAL DZ ⇨
  - Disease has higher prevalence in Caucasians

Goodpasture's Disease

- Pathogenesis:
  - Antibodies directed against specific antigenic targets that reside primarily in the Glomerular Basement Membrane and Alveolar Membrane
  - Antigen is the alpha-3 chain of Type IV Collagen (NC1 Domain)
  - Also reside in eye, cochlea, NMJ, and choroid plexus
  - There are Multiple thoughts on inciting stimuli (Ex: Tobacco, Hydrocarbon exposure, Pnuemonia, URI)
  - Genetic Susceptibility appears positively related to HLA- DR15. HLA DR1 and DR7 appear to have protective effect.
  - Anti-GBM Abs trigger cell mediated inflammatory response.
  - Concentration of Abs does not directly correlate with disease activity.

Goodpasture's Disease

- Clinical Presentation:
  - Pulmonary Sx:
    - Cough, SOB, Hemoptysis
    - Presentation with hemoptysis is declining. (Secondary to Smoking?)
    - Usually pulmonary involvement does not predominate
    - Can even be asymptomatic with alveolar hemorrhage
  - Renal Sx:
    - Fairly rapid renal failure that rarely resolves spontaneously
  - Can have malaise, weight loss, and fever though constitutional symptoms usually not prominent

Goodpasture's Disease

- Laboratory Findings:
  - CXR:
    - Alveolar opacities/infiltrates secondary to hemorrhage
    - Interstitial changes after hemorrhage
  - PFTs reveal an increased DLCO
  - Nephritic Sediment with Non-nephrotic proteinuria
  - Fe Deficiency Anemia
  - ANCA: 10-38% are ANCA + (usually p-ANCA). These patients have better treatment outcomes.
  - Normal Complement Levels

Goodpasture's Disease

- Diagnosis:
  - Anti-GBM Abs:
    - Usually IgG
    - Specific immunoassays with >90% sensitivity

      ELISA

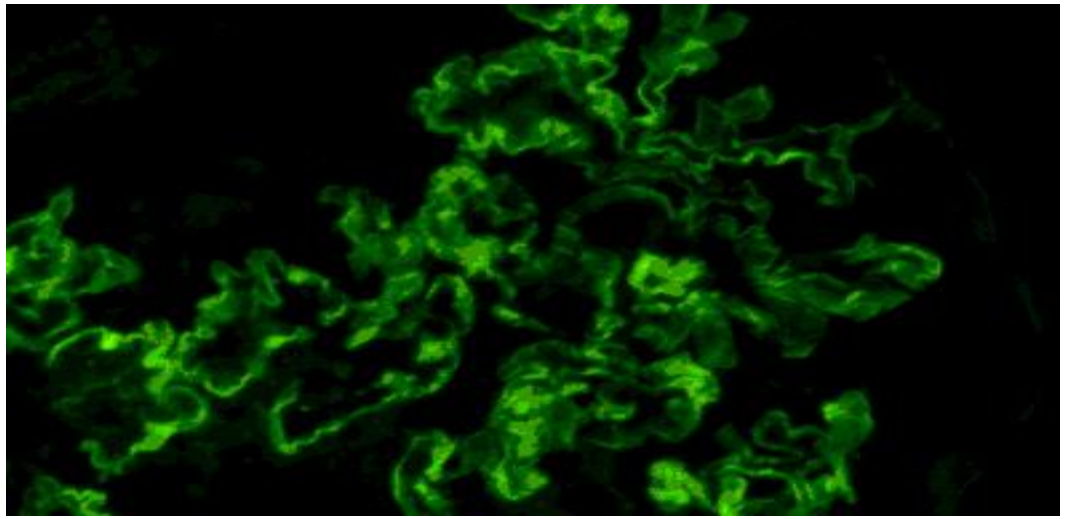
      Western Blot (Confirmatory, High False +, Low False -)
  - Indirect immunofluorescence:
    - Looking for IgG deposits after pts serum added to normal renal tissue
  - Renal Biopsy

Goodpasture's Disease

- Renal Biopsy:
  - Light Microscopy:

    Diffuse proliferative glomerulonephritis with focal necrotizing lesions and crescents
  - Electron Microscopy: Inflammatory change without immune deposits
  - Immunofluoresence Microscopy:

    "Linear ribbon like" deposition of IgG along GBM



Goodpasture's Disease

- Prognosis:
  - Histology on biopsy helps assess prognosis as renal involvement occurs in stages:
    - Mesangial expansion
    - Focal and Segmental Glomerulonephritis leading to necrosis
    - Glomeruli develop crescents which are at same stage
    - Scarring
  - If crescents exist in >50% of glomeruli, then usually survival <2 yrs
  - Without treatment, 80% get ESRD within 1 year
  - Prognosis improves with earlier treatment
  - Better response to treatment if ANCA +

Our Patient…

- Goodpasture's Disease
- Systemic Vasculitis
  - Wegener's Granulomatosis
  - Microscopic Polyangiitis
  - Churg-Strauss Syndrome
  - Cryoglobulinemia
  - Henoch-Schonlein Purpura
- Connective Tissue Disease
  - Polymyositis/Dermatomyositis
  - Progressive Systemic Sclerosis
  - SLE
- Primary Glomerular Disease
  - IgA Nephropathy
  - Post-Infectious GN
  - Membranoproliferative GN

Our patient has Many Systemic Sx

Vasculitis Overview

- Leukocytes cause reactive damage to blood vessels (Bleeding, Tissue Ischemia, and/or Necrosis)
- 1866: Kussmaul and Maier published report of necrotizing arteritis. Labeled it periarteritis nodosa.
- 1950s: Started to realize some forms seemed to affect certain size vessels.
- Systemic Vasculitis rare: Incidence of 20-100/Million
- Usually see Multi-Organ Dysfunction and Systemic Complaints (Fatigue, Weakness, Fever, Arthralgias)
- Certain syndromes affect certain tissues
- Though syndromes exist, there is significant overlap between each.

Primary Vasculitis Classification

- Large: (Aorta and largest branches)
  - Takayasu's Vasculitis
  - Giant Cell/Temporal Arteritis

- Medium: (Renal, Hepatic, Coronary, Mesenteric)
  - PAN
  - Kawasaki's
  - Behcet's

- Small: (Capillaries, Arterioles, Venules)
  - Wegener's Granulomatosis — ANCA Related
  - Microscopic Polyangiitis — ANCA Related
  - Churg-Strauss Arteritis — ANCA Related
  - Henoch-Schonlein Purpura
  - Cryoglobulinemic Vasculitis

ANCA

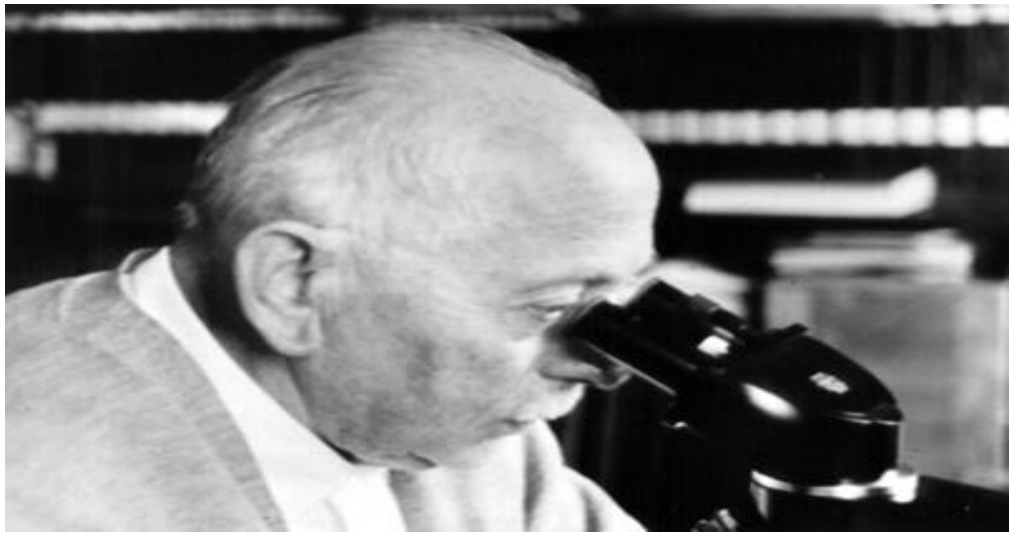
- Discovered in 1982
- ANCA = Anti-Neutrophil Cytoplasmic Antibodies
- Proteinase 3 (PR3) and Myeloperoxidase (MPO) are in granules of neutrophils/monocytes.
- Abs can have PR3 or MPO as their antigens.
- Immunofluorescence:
  - C-ANCA: Staining is diffuse through cytoplasm; Mostly PR3 Abs
  - P-ANCA: Staining is perinuclear; Mostly MPO Abs
- Ethanol Fixation results in MPO relocation to perinuclear position.

Differential of Pulmonary Renal Syndrome

- Goodpasture's Disease
- Systemic Vasculitis
  - **Wegener's Granulomatosis**
  - Microscopic Polyangiitis
  - Churg-Strauss Syndrome
  - Cryoglobulinemia
  - Henoch-Schonlein Purpura
- Connective Tissue Disease
  - Polymyositis/Dermatomyositis
  - Progressive Systemic Sclerosis
  - SLE
- Primary Glomerular Disease
  - IgA Nephropathy
  - Post-Infectious GN
  - Membranoproliferative GN

Wegener's Granulomatosis

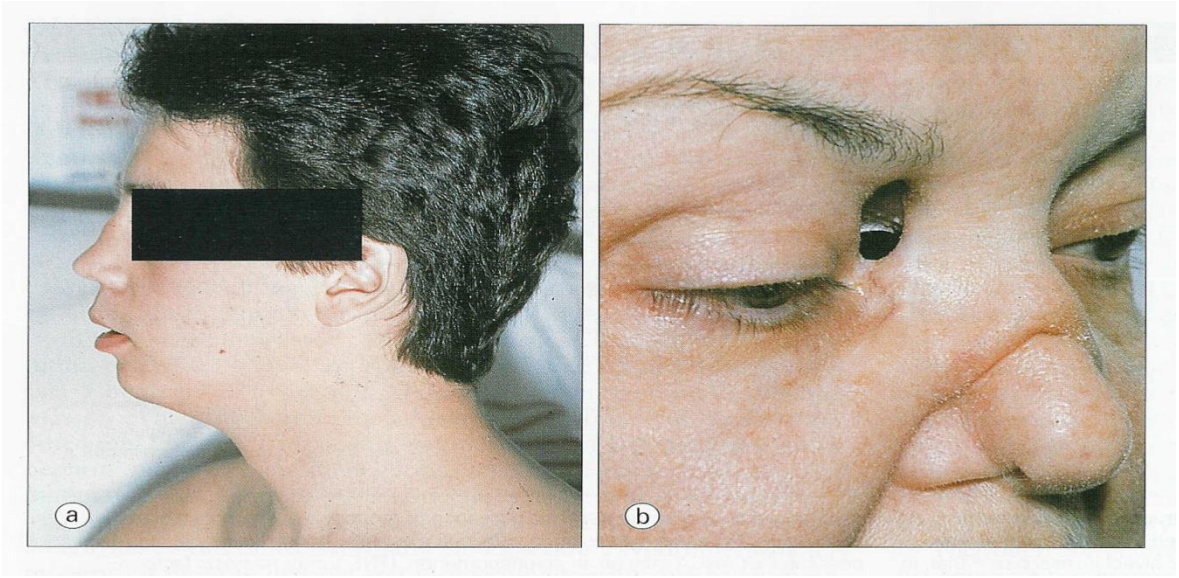
- History:
  - 1931: Heinz Klinger reports a 70 year old physician with sx of fever, sinusitis, pulmonary vasculitis, and nephritis.
  - 1936: Friederic Wegener describes clinical presentation in 3 patients. (1907-1990; Dedicated Nazi)
- Epidemiology:
  - Prevalence in US estimated at 3 per 100,000
  - Male : Female = 1 : 1
  - 80-97% are Caucasian
  - Mean age at diagnosis: 41-56



Wegener's Granulomatosis

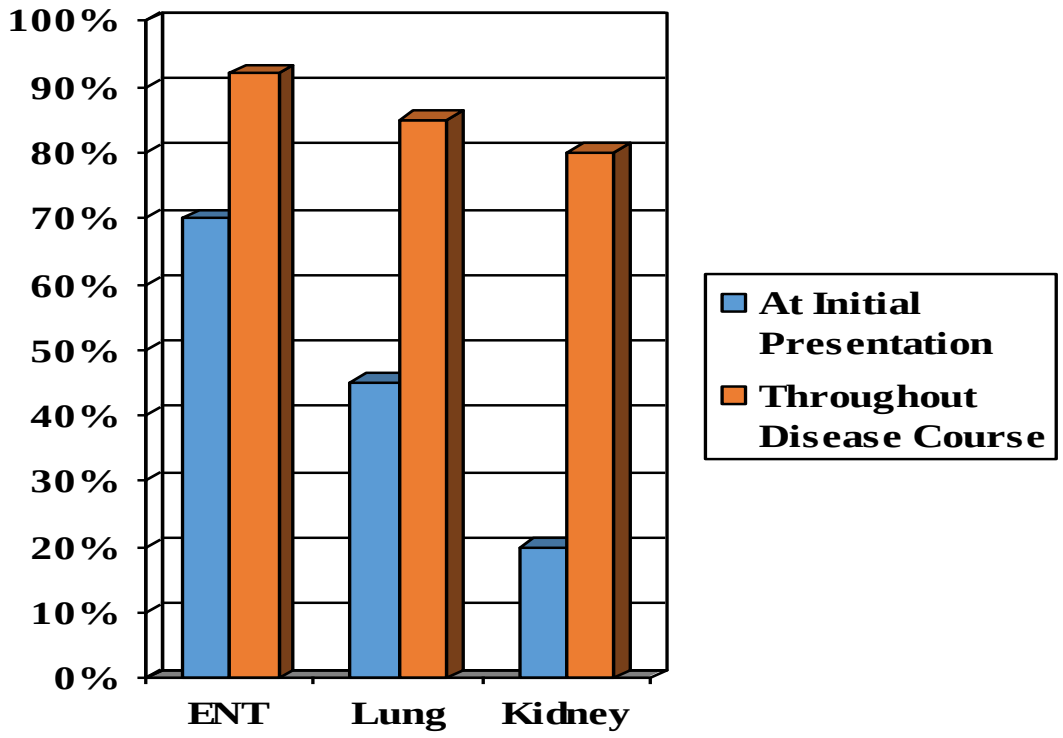
- Pathogenesis:
  - Tissue injury occurs from antibodies directed against neutrophil/monocyte granular proteins
  - Granulomatous inflammation occurs
  - No specific inciting agent is known.
  - Flares do seem to follow infections and symptoms are similar
  - No genetic markers are clearly over-represented in patients with WG.

Wegener's Granulomatosis



- Clinical Presentation:
  - Persistent Rhinorrhea
  - Purulent Nasal Discharge
  - Sinus Pain
  - Hoarseness
  - Stridor
  - Earache
  - Nasal Deformity
  - Proptosis
  - Cough
  - Dyspnea
  - Hemoptysis
  - Fever (23% at onset)
  - Weight Loss (15% at onset)
  - Anorexia
  - Malaise

Wegener's Granulomatosis



- About 50% have no lung involvement at presentation.
- Lung involvement:
  - Infiltrates
  - Nodules
  - Hemoptysis
  - Pleuritis
- 33% with lung involvement are asymptomatic.
- About 80% have no renal involvement at presentation.

Klippel, 1998

Wegener's Granulomatosis

- Laboratory Findings:
  - Leukocytosis
  - Thrombocytosis
  - Normochromic/Normocytic Anemia
  - Elevated ESR (Correlates with disease activity in 80% of pts)
  - Normal Complement Levels

  - CXR: Can have varying presentation.
    - Nodules
    - Cavitary lesions
    - Alveolar opacity
    - Interstitial changes
    - Pleural opacities

Wegener's Granulomatosis

- Diagnosis:
  - ANCA:
    - C-ANCA (Abs against Proteinase 3)
    - P-ANCA (Abs against MPO) in 1-5%
    - Sensitivity with wide report range 30-99%. Lower end relates to organ limited.disease.
    - Specificity of 90-98% with active disease.
  - Biopsy
    - Necrotizing granulomatous vasculitis

Wegener's Granulomatosis

- Prognosis:
  - Poorer outcomes with advanced age, severe renal impairment, DAH.
  - Mortality >75% if untreated with median survival of 5 months. Drastic improvement since 1970s in mortality.
  - Permanent morbidity:
    - CKD 42%
    - Hearing Loss 35%
    - Nasal Deformity 28%
    - Tracheal Stenosis 13%
    - Severe Infection 50% (Treatment)

Differential of Pulmonary Renal Syndrome

- Goodpasture's Disease
- Systemic Vasculitis
  - Wegener's Granulomatosis
  - **Microscopic Polyangiitis**
  - Churg-Strauss Syndrome
  - Cryoglobulinemia
  - Henoch-Schonlein Purpura
- Connective Tissue Disease
  - Polymyositis/Dermatomyositis
  - Progressive Systemic Sclerosis
  - SLE
- Primary Glomerular Disease
  - IgA Nephropathy
  - Post-Infectious GN
  - Membranoproliferative GN

Microscopic Polyangiitis

- History:
  - 1948: Davson differentiated from PAN in regards to whether glomeruli affected
  - 1994: Microscopic Polyangiitis preferred over Microscopic Polyarteritis

- Epidemiology:
  - Incidence of 2.4 per million
  - Male: Female = 1.8:1

Microscopic Polyangiitis

- Clinical Presentation:
  - Systemic, multi-organ complaints along with constitutional symptoms.
  - Pulmonary involvement in approximately 30-50%.
  - Milder upper respiratory disease than pts with WG
  - Necrotizing glomerulonephritis is common (79%)
- Laboratory Findings:
  - ANCA: + P-ANCA in 50-75% and + C-ANCA in 10-15%
- Diagnosis:
  - Biopsy reveals necrotizing vasculitis and nongranulomatous inflammation

Differential of Pulmonary Renal Syndrome

- Goodpasture's Disease
- Systemic Vasculitis
  - Wegener's Granulomatosis
  - Microscopic Polyangiitis
  - **Churg-Strauss Syndrome**
  - Cryoglobulinemia
  - Henoch-Schonlein Purpura
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  - Membranoproliferative GN

Churg Strauss Syndrome

- History:
  - 1951: Realization that syndrome was pathologically different from Polyarteritis Nodosa and characterized by asthma, eosinophilia, and granuloma formation.
  - “Allergic Angiitis and Granulomatosis”
- Epidemiology:
  - Prevalance data not extremely accurate. Rare disease.
  - Male:Female = 1:3
  - Mean age at diagnosis: 40
- Clinical Presentation:
  - Triad: Asthma, Hypereosinophilia, Necrotizing Vasculitis
  - Can also present in these same 3 phases.
  - Pulmonary infiltrates are seen in 62-77% of patients
  - Pulmonary Hemorrhage and GN may occur, though much less common.

Churg Strauss Syndrome

- Laboratory Findings:
  - ANCA: + P-ANCA in 35-75%, + C-ANCA in 10%
  - Eosinophilia

- Diagnosis:
  - Biopsy:
    - Necrotizing vasculitis with granulomas with eosinophil rich infiltrate

Differential of Pulmonary Renal Syndrome

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  - Post-Infectious GN
  - Membranoproliferative GN

Cryoglobulinemia

- Epidemiology:
  - Prevalence estimated at approximately 1:100,000
  - Skewed by patients with chronic infections/inflammation (Hepatitis C)

- Pathogenesis:
  - Cryoglobulins are antibodies that precipitate from serum in cold conditions.
  - Vasculitis results from deposition of cryoglobulin containing immune complexes
  - Different Types:
    - Type I: Monoclonal, Lead to hyperviscosity
    - Type II,III: “Mixed” with both IgG and IgM

Cryoglobulinemia

- Clinical Presentation:
  - Palpable Purpura that is recurrent
  - Neuropathy, GN, Arthralgias
- Labs:
  - Decreased complement levels
  - Spurious leukocytosis/thrombocytosis in cold sample
- Diagnosis:
  - Demonstration of circulating cryoglobulins.
  - Biopsy reveals cryoprecipitate.

Differential of Pulmonary Renal Syndrome

- Goodpasture's Disease
- Systemic Vasculitis
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  - Churg-Strauss Syndrome
  - Cryoglobulinemia
  - **Henoch-Schonlein Purpura**
- Connective Tissue Disease
  - Polymyositis/Dermatomyositis
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  - SLE
- Primary Glomerular Disease
  - IgA Nephropathy
  - Post-Infectious GN
  - Membranoproliferative GN

Henoch-Schonlein Purpura

- Epidemiology:
  - Well described in adults though not as common
  - Adult incidence reported at 1.2 per million
- Pathogenesis:
  - Exact cause is unknown
  - Numerous infectious/chemical inciting agents proposed
- Clinical Manifestations:
  - Tetrad: Palpable Purpura, Arthritis, Abdominal Pain, and Glomerulonephritis (IgA Nephropathy)
  - Case reports of Massive Pulmonary Hemorrhage
- Lab Findings:
  - Increased serum IgA (50-70%)
  - Normal Serum Complement Levels
- Diagnosis:
  - Biopsy reveals IgA deposition in vessel walls (Kidney, Skin)

Small Vessel Vasculitis

TABLE 4. APPROXIMATE FREQUENCY OF ORGAN-SYSTEM MANIFESTATIONS IN SEVERAL FORMS OF SMALL-VESSEL VASCULITIS.*

ORGAN SYSTEM	HENOCH–SCHÖNLEIN PURPURA	CRYOGLOBULINEMIC VASCULITIS	MICROSCOPIC POLYANGIITIS	WEGENER'S GRANULOMATOSIS	CHURG–STRAUSS SYNDROME
			percent		
Cutaneous	90	90	40	40	60
Renal	50	55	90	80	45
Pulmonary	<5	<5	50	90	70
Ear, nose, and throat	<5	<5	35	90	50
Musculoskeletal	75	70	60	60	50
Neurologic	10	40	30	50	70
Gastrointestinal	60	30	50	50	50

*Approximate frequencies are estimated from data in previous reports.[49-65]

Jennette, 1997

Our Patient…

Goodpasture's Disease

Systemic Vasculitis
- Wegener's Granulomatosis
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- Churg-Strauss Syndrome
- Cryoglobulinemia
- Henoch-Schonlein Purpura

Connective Tissue Disease
- Polymyositis/Dermatomyositis
- Progressive Systemic Sclerosis
- SLE

Primary Glomerular Disease
- IgA Nephropathy
- Post-Infectious GN
- Membranoproliferative GN

Our patient has Many Systemic Sx

No asthma, No eosinophilia, PRS Rare
Complement levels normal, PRS Rare
No palpable purpura, PRS Rare

Polymyositis/Dermatomyositis

- Chronic inflammation of striated muscle/skin resulting in painless proximal muscle weakness

- Pulmonary Manifestations:
  - Can have Diffuse alveolitis/interstitial fibrosis with nonproductive cough.
  - Usually have asymptomatic interstitial lung disease
  - Case reports of initial presentation being pulmonary

- Renal Manifestations:
  - Has been associated with GN though this is very rare

Klippel, 1998

Systemic Sclerosis

- Disease characterized by fibrosis and immune system activation.
- Common Clinical Features:
  - Raynaud's, Skin Thickening, Subcutaneous Calcinosis, Telangiectasias
- Pulmonary Manifestations:
  - Pulmonary involvement in the form of fibrosis is very common.
  - Pulmonary hemorrhage less common
- Renal Manifestations:
  - Most important is scleroderma renal crisis with rapidly progressive renal failure
  - Can present with this before skin thickening

Klippel, 1998

Systemic Sclerosis

- Pulmonary Renal Syndrome rare though is documented.
  - 2001: Review of 11 cases of SS who developed PRS.
  - Earliest case developed within 6 months after initial diagnosis.
  - All patients died within 12 months

Bar, 2001

SLE

- Auto-immune disease with inflammation, vasculitis, and immune complex deposition that occurs throughout the body
- 1982 Criteria for Classification:
  - Malar Rash
  - Discoid Rash
  - Photosensitivity
  - Oral Ulcers
  - Arthritis
  - Serositis
  - Renal Disorders
  - Neurologic Disorders (Seizures, Psychosis)
  - Hematologic Disorders
  - Immunologic Disorders (Anti-dsDNA, Anti-Sm, Antiphospholipid)
  - Antinuclear Antibodies

SLE

- Pulmonary Involvement:
  - Pleural effusions/Lupus Pneumonitis are common manifestations.
- Renal Involvement:
  - Signature organ affected with presence in 1/2 to 2/3 of patients.
- Pulmonary Renal Syndrome:
  - Alveolar Hemorrhage is rare
  - Histologically seen as diffuse bland hemorrhage
  - Mechanism thought to be apoptosis secondary to immune complex deposition

Hughson, 2001

Our Patient…

- Goodpasture's Disease
- Systemic Vasculitis
  - Wegener's Granulomatosis
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  - Progressive Systemic Sclerosis
  - SLE
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  - Post-Infectious GN
  - Membranoproliferative GN

Our patient has Many Systemic Sx

No asthma, No eosinophilia, PRS Rare
Complement Levels Normal, PRS Rare
No palpable purpura, PRS Rare

No Sx
No Sx
Complement Levels Normal, ANA Neg

Renal Disease

- RPGN Classification:
  - Antibodies against GBM (10%-20%)
    - Goodpasture's — Complement Normal
  - Pauci-Immune Disease(45%-50%)
    - ANCA associated Vasculitides — Complement Normal
  - Immune Complex Mediated (30%-45%)
    - Cryoglobulinemia — Complement Low
    - Henoch-Schonlein Purpura — Complement Normal
    - SLE — Complement Low
    - IgA nephropathy — Complement Normal
    - Post-Infectious GN — Complement Low
    - Membranoproliferative GN — Complement Low

- Complement levels help further classify: Normal or Low

IgA Nephropathy

- Pathogenesis:
  - Results from globular deposits of IgA in the mesangium and glomerular capillary wall
  - Spectrum of Henoch-Schonlein Purpura
- Epidemiology:
  - May present at any age. Peaks in 20s and 30s.
  - Constitutes >45 % of primary GN
- Clinical Presentation:
  - Classic presentation is URI with gross hematuria
  - Can have asymptomatic hematuria/proteinuria
  - Pulmonary involvement rare.
- Diagnosis:
  - Biopsy: Mesangial deposition of IgA

IgA Nephropathy

- Case Reports exist of associated Alveolar hemorrhage:
  - 2001: 10th known adult case of IgA nephropathy and pulmonary hemorrhage published.
  - Involved 36 year old male.
  - Workup for other causes for alveolar hemorrhage were negative.
  - Only finding was IgA deposits on biopsy.

Fung, 2001

Our Patient…

Goodpasture's Disease	Our patient has Many Systemic Sx
Systemic Vasculitis	
Wegener's Granulomatosis	No asthma, No eosinophilia, PRS Rare
Microscopic Polyangiitis	Complement Levels Normal, PRS Rare
Churg-Strauss Syndrome	No palpable purpura, PRS Rare
Cryoglobulinemia	
Henoch-Schonlein Purpura	
Connective Tissue Disease	
Polymyositis/Dermatomyositis	No Sx
Progressive Systemic Sclerosis	No Sx
SLE	Complement Levels Normal, ANA Neg
Primary Glomerular Disease	
IgA Nephropathy	Pulmonary Involvement Rare
Post-Infectious GN	Complement Levels Normal
Membranoproliferative GN	Complement Levels Normal

Our Patient…

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Small Vessel Vasculitis

TABLE 4. APPROXIMATE FREQUENCY OF ORGAN-SYSTEM MANIFESTATIONS IN SEVERAL FORMS OF SMALL-VESSEL VASCULITIS.*

ORGAN SYSTEM	HENOCH–SCHÖNLEIN PURPURA	CRYOGLOBULINEMIC VASCULITIS	MICROSCOPIC POLYANGIITIS	WEGENER'S GRANULOMATOSIS	CHURG–STRAUSS SYNDROME
			percent		
Cutaneous	90	90	40	40	60
Renal	50	55	90	80	45
Pulmonary	<5	<5	50	90	70
Ear, nose, and throat	<5	<5	35	90	50
Musculoskeletal	75	70	60	60	50
Neurologic	10	40	30	50	70
Gastrointestinal	60	30	50	50	50

*Approximate frequencies are estimated from data in previous reports.[49-65]

Jennette, 1997

Our Patient…

Diagnosis:

Wegener's Granulomatosis

- *Consistent with fatigue, weakness, weight loss, sinus drainage, anemia, elevated ESR, and normal complement levels..*
- *Would expect C-ANCA to be positive*

Diagnostic Test:

Renal Biopsy

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