Granulomatosis with Polyangiitis (Wegener’s)

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Agenda

- Patient presentation
- Overview of granulomatosis with polyangiitis (Wegener’s), abbreviated GPA
- Review spectrum of pulmonary findings
Patient presentation

• 26y/o male graduate student with shortness of breath and small volume hemoptysis
• Fevers, nosebleeds, fatigue, drenching nightsweats, weight loss
• Past medical history: childhood asthma
• Physical exam: T 100.7F, scattered lung crackles, serous otitis media
• Chest radiograph in Emergency Department
Our patient: Initial chest x-ray
Our patient: Initial chest x-ray, findings

- Diffuse, dense, nodular, perihilar opacities
- Peripheral RUL opacity
Our patient: Broad Differential Diagnosis

- **Infectious**
  - Tuberculosis
  - Multifocal bacterial pneumonia
  - Pneumocystis pneumonia
  - Atypical/viral/fungal pneumonia

- **Autoimmune**
  - Granulomatosis with polyangiitis (Wegener’s)
  - Microscopic polyangiitis
  - Churg-Strauss Syndrome
  - Anti-GBM antibody disease (Goodpasture’s)

- **Neoplastic**
  - Lymphoma
  - Bronchus-associated lymphoid tissue lymphoma (BALT)
  - Leukemia
  - Kaposi’s sarcoma
  - Metastatic disease
Our patient: Initial work-up

- WBC 11.9, Hct 31, Plt 385
- ESR 86, Cr 1.1
- U/A: 8 RBCs/hpf
- PPD negative, HIV negative
Our patient: Axial chest CT, C+, superior level

- Peripheral RUL consolidation
- Bilateral peribronchial and perihilar opacities
- Air bronchograms
Our patient: Axial chest CT, C+, soft tissue window

- Peripheral RUL consolidation
- Early central necrosis
- Air bronchograms
Our patient: Axial chest CT, C+, middle level

- Bilateral peribronchial and perihilar opacities
- Air bronchograms

No lymphadenopathy
Our patient: Axial chest CT, C+, inferior level

- Bilateral peribronchial and perihilar opacities
- Air bronchograms

No lymphadenopathy
Our patient: Coronal chest CT, C+

- Peripheral RUL consolidation
- Bilateral peribronchial and perihilar opacities
- Air bronchograms
Our patient: Differential Diagnosis, Revisited

- **Infectious**
  - Tuberculosis
  - Multifocal bacterial pneumonia
  - Pneumocystis pneumonia
  - Atypical/viral/fungal pneumonia

- **Autoimmune**
  - Granulomatosis with polyangiitis (Wegener’s)
  - Microscopic polyangiitis
  - Churg-Strauss Syndrome
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- **Neoplastic**
  - Lymphoma
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  - Metastatic disease
Our patient: Initial Management

• Broad spectrum antibiotics
• C-ANCA positive, anti-proteinase-3 positive
• *Diagnosis: Granulomatosis with polyangiitis (Wegener’s)*
• Methylprednisolone was begun
• Endobronchial and transbronchial biopsies showed acute and chronic inflammation but no vasculitis
Granulomatosis with Polyangiitis (Wegener’s)

- Vasculitis of small arteries and veins
- Necrotizing granulomas
- C-ANCA and anti-proteinase 3 positive

• Thick vessel wall with inflammatory infiltrate
• Giant cells of granuloma

Adkinson: Middleton’s Allergy: Principles and Practice, 7th ed.
Why the long name “Granulomatosis with polyangiitis (Wegener’s)”?
Friedrich Wegener (1907-1990)

- German pathologist
- Published cases of necrotizing granulomatous inflammation in 1939
- Lieutenant Colonel of the National Socialist Party
- Little evidence detailing wartime activities, but complicity in Nazi war crimes is suspected by some
- Never faced trial or charges, files are now lost

Woywodt, Rheumatology 2006
Wegener’s granulomatosis: A nominal controversy

• In April 2011 the American College of Rheumatology recommended that Wegener’s granulomatisis be called “Granulomatosis with polyangiitis (Wegener’s)” due to the controversy surrounding Friedrich Wegener’s wartime activities, and following a recent trend to replace eponyms with more descriptive names.

• In a few years, “(Wegener’s)” will be dropped from the end of the new name.

• GPA is an appropriate abbreviation

Falk, Annals of Rheumatic Disease, 2011
GPA: Clinical Manifestations

Systemic Symptoms
(Malaise, anorexia, weight loss, arthralgias, weakness, fevers)

**Upper Airway (90%)**
- Nasal discharge
- Sinusitis
- Mucosal ulceration
- Serous otitis media
- Subglottic tracheal stenosis

**Lung (90%)**
- Cough
- Hemoptysis
- Dyspnea
- Stridor
- Wheezing

**Kidney (80%)**
- Hematuria
- Proteinuria
- RBC casts
Now let’s examine the wide spectrum of imaging findings seen in granulomatosis with polyangiitis (Wegener’s)
Companion patient 1: Classic GPA on Chest x-ray

- Multiple, peripheral, rounded opacities, 2-4cm
- 25% cavitate

Allen, BJR, 2007
Companion patient 2: Classic GPA on axial CT, C+

- Solid nodules
- Cavitating nodules with thick walls and irregular inner borders
- Halo sign (focal alveolar hemorrhage)

Frazier, Radiographics, 1998
Companion patient 3: Pulmonary Hemorrhage in GPA on Chest x-ray

- Multiple, peripheral, rounded opacities
- Diffuse pulmonary hemorrhage

Allen, BJR, 2007
Companion patient 4: Pulmonary hemorrhage in GPA on axial CT, C+

- Diffuse ground glass change

Allen, BJR, 2007
Companion patient 5: Spiculated nodules and feeding vessel in GPA on axial CT, C+

- Solid nodules
- Spiculations
- Feeding vessel

Ananthakrishnan, AJR, 2009
GPA: Summary of Imaging Findings

- Lung parenchyma
  - *Multiple nodules (93%), subpleural or diffuse*
    - *Solid (75%) or cavitating (25%)*
    - Rarely with spiculation or feeding vessel
  - Consolidation (30%)
    - Diffuse, peripheral, or peribronchial
    - Ground glass attenuation (25%), diffuse or “halo sign”
    - Septal and non-septal lines

- Tracheobronchial tree
  - Bronchial wall thickening (50%)
  - Bronchiectasis (20%)

- Pleura
  - Pleural effusion (15%)
  - Pleural thickening (15%)

- Lymph nodes
  - Hilar or mediastinal lymphadenopathy (15%)

Lohrmann, EJR, 2005
Our patient: Review of coronal CT, C+

- Peripheral RUL consolidation
- Bilateral peribronchial and perihilar opacities
- Air bronchograms
Our patient: Chest x-ray post-treatment

- Improved on steroids
- Rituximab as outpatient
- Gradual resolution of dyspnea and fatigue
- Steroid taper
- Clear chest x-ray by week 6
GPA: Prognosis

• 85-90% of patients achieve complete remission with initial immunosuppressive therapy
• Relapse occurs in 25-80% of patients, risk factors include:
  – C-ANCA/PR3 seropositivity
  – Lung involvement
  – Upper respiratory tract involvement
• Methotrexate or azathioprine maintenance therapy for 12-18 months reduces the risk of relapse

Stone, UpToDate, 2011
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References


• Woywodt, A, EL Matteson. Wegener’s granulomatosis—probing the untold past of the man behind the eponym. Rheumatology 2006; 45(10): 1303-1306.