Granulomatosis with Polyangitis

(Wegener’s Granulomatosis)

Adam M. Parker, M4
University of Mississippi
School of Medicine
October 2013

To view Speaker Notes – see separate link
Background

- Wegener’s Granulomatosis is a systemic disease characterized by necrotizing granulomatosus vasculitis that classically involves the upper respiratory tract, lower respiratory tract, and kidneys.

- **1897**: Peter McBride (Scotland) first describes the disease

- **1931**: Heinz Klinger adds to McBride’s findings

- **1936 & 1939**: Friedrich Wegener (Germany) clearly defines the disease and is thus credited with its discovery

- **1985**: c-ANCA is discovered (cytoplasmic antineutrophil cytoplasmic antibody)

- **2011**: renamed “Granulomatosis with Polyangiitis” after Wegener’s association with the Nazi party is widely publicized
Epidemiology

- **Incidence**: 1-2 cases per 100,000 population

- **Age**: most commonly presents between 30-50 y.o. (variable)

- **Sex**: Male = Female

- **Race**: Caucasian (90%)
Etiology

- Exact etiology is unknown
  - Autoimmune (antineutrophil cytoplasmic antibodies)
  - S. aureus colonization
  - Drugs
  - Environmental toxins
  - Genetic factors
Prognosis (Systemic GPA)

- **Untreated**
  - fatal
  - ~80% mortality rate within first year

- **With Treatment**
  - ~90% 5-year survival rate
  - Disease remission is possible, but 50% of patients experience flare-ups or relapse within 2 years.
Pathology

- Proteinase-3 is a serine protease enzyme that’s associated with the primary (azurophilic) granules located in the cytoplasm of neutrophils.

- c-ANCAs target proteinase-3, and this interaction is believed to result in neutrophil activation (e.g. endothelial adhesion) and degranulation.

- Results in localized or systemic small vessel necrotizing vasculitis with granulomatous inflammation that involves small to medium sized vessels.
Presentation

- **Head and Neck Involvement (70% = initial S/Sx’s)**
  - **Sinonasal** (80%)
    - Recurrent and Chronic Rhinosinusitis that is unresponsive to traditional treatment (**most common presentation**)
    - Nasal obstruction, septal perforation, recurrent epistaxis
    - Saddle-nose deformity (late complication)
  - **Otologic**
    - Most commonly serous otitis media +/- CHL
    - Acute and Chronic OM (+/- Mastoiditis)
    - SNHL (involvement of CN VIII or Cochlea)
Presentation

- **Larynx and Trachea**
  - Subglottic ulcerations and stenosis (20% of cases)
    - Biphasic stridor, dyspnea, hoarseness
    - BV supply

- **Pulmonary Disease**
  - Develops in 80% of cases (present in 40% of presenting patients at)
  - Cough, stridor, hemoptysis, dyspnea
  - Bilateral, cavitating infiltrates or nodules

- **Renal Disease**
  - Develops in 75% of cases
  - May be subclinical until renal failure develops
  - Crescentic Glomerulonephritis (RPGN)
Differential Diagnoses

- Churg-Strauss Syndrome (p-ANCA)
- Microscopic Polyangiitis (p-ANCA)
- Sarcoidosis
- Rheumatoid Arthritis
- Fungal Infection
- Mycobacterial Infection
Workup & Diagnosis

- **Clinical presentation**

- **Biopsy (Gold Standard)**
  - Pulmonary > Renal > Nasal.
  - Necrotizing vasculitis with granulomatous inflammation (multinucleated giant cells and palisading histiocytes)
  - Higher false-negative results seen with nasal biopsies.

- **c-ANCA**
  - Specificity: as high as 98%
  - Sensitivity: varies with disease activity
    - 90% (active systemic), 60% (localized), and 30% (remission)
  - Titer may be used to follow disease course (controversial)
Workup and Diagnosis cont’d

- **Culture**
  - Rule out infectious etiologies (Fungal, TB)

- **CXR**
  - Assess for pulmonary involvement

- **Urinalysis**
  - Assess for renal involvement

- **Other**: Sinus films, BMP, ESR, CRP, Autoimmune Panel, VDRL or RPR.
Treatment

- **Induce Remission**
  - Cyclophosphamide, Methotrexate, or Azathioprine
  - Corticosteroids (e.g. Prednisone)

- **Prophylaxis**
  - Bactrim

- **Resistant Disease**
  - Rituximab
  - Infliximab, Etanercept, Lefunomide

- **Saline irrigations +/- antibiotics**
Subglottic Stenosis

- May resolve with medical treatment alone
- Serial dilation with steroids +/- Mitomycin-C
- Tracheotomy (severe airway compromise)
- Laser therapy, local resection, and laryngotracheal reconstruction are less efficacious in the treatment of SGS secondary to Wegener’s Granulomatosis.
References


