Granulomatous lung disease: how pathologic findings add value to clinical and radiologic information

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“Clinical correlation”

Pathology matters

Case 1. Clinical/radiologic information

- 48/F: fever, admitted for pneumonia
- H/O
  - multiple sclerosis
  - elevated CPK, rhabdomyolysis
  - butterfly rash on face + extremities (dermatomyositis)
  - coagulopathy (PAI-1 deficiency)
  - severe pneumonia 1y ago
  - Chest CT: multiple lung nodules, extensive nodularity and ground-glass infiltrates in RUL, RLL

Clinical/radiologic impression: Pneumonia, suspect vasculitis
Nodules and ground-glass infiltrates

Nodules in lung adjacent to bronchioles

Organizing pneumonia

Suppurative granuloma

Suppurative granuloma

Suppurative granuloma
Differential diagnosis of lung granulomas

- Infection
  - Mycobacterial
  - Fungal
- Non-infectious
  - GPA, EGPA
  - Sarcoidosis
  - Talc granulomatosis
  - Particulate matter aspiration
  - Others

Differential diagnosis of suppurative lung granulomas

- Blastomycosis
- Coccidioides
- Aspergillus
- Sporothrix
- NTM
- GPA (Wegener)
- Particulate matter aspiration

Suppurative foreign-body granulomas with food particulate material

Background of organizing pneumonia

Diagnosis: Organizing particulate matter aspiration pneumonia

Pulmonary Disease due to Aspiration of Food and Other Particulate Matter: A Clinicopathologic Study of 59 Cases Diagnosed on Biopsy or Resection Specimens

- Debilitated patient
- Right lower lobe infiltrate
- Swallow eval abnormal
- Acute bronchopneumonia at autopsy
- Intact skel muscle/vegetable
- Food within bronchial lumen

Not the aspiration pneumonia you learned about in medical school

Classic teaching:
- Acute aspiration pneumonia
  - Relatively functional
  - Any lobe, often nodules
  - Swallow eval may be normal
  - Organizing pneumonia + granulomas in lung biopsy
  - Degenerated vegetable/filler
  - Food within granulomas

Organizing particulate matter (“chronic”) aspiration pneumonia
  - Relatively functional
  - Any lobe, often nodules
  - Swallow eval may be normal
  - Organizing pneumonia + granulomas in lung biopsy
  - Degenerated vegetable/filler
  - Food within granulomas
Vegetable particles in various stages of degeneration

Case 2. Clinical/radiologic information

- 68/F with hemoptysis
- Radiology: large cavitary lesion surrounded by small satellite lesions throughout LUL
- Serum QuantiFERON-TB: negative
- Serology for p-ANCA: weakly positive (1:20)
- LUL apical segmentectomy: ?Wegener’s

Clinical/radiologic impression: Large cavitary lesion

Geographic necrosis (necrosis with irregular contours)

Necrotizing granulomatous inflammation
- Basophilic dirty necrosis
- “Distinctive” giant cells

Necrotic blood vessel (but not necrotizing vasculitis)

Vasculitis without necrosis
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Which histologic feature is most specific for GPA (Wegener’s)?

Histologic features in infectious granulomas vs GPA

Mycobacterial disease
Histoplasmosis GPA (Wegener’s)

Acid-fast bacteria

Geographic variation in culture-confirmed mycobacterial disease and proportion of culture-confirmed TB

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Case 3. Clinical/radiologic information
- 32/M with fatigue, shortness of breath, night sweats, productive cough
- History of neurosarcoidosis (granulomas on prior lung biopsy)
- Lung nodules decreased with prednisone, started on infliximab
- Served in Afghanistan, Iraq; lumbar puncture negative
- New large cavitary mass

Clinical/radiologic impression: Sarcoid? Infection? Tumor?

Follow-up
- Cultures from "lung tissue" grew MAI

What did we learn?
- ANCA+ does not necessarily mean GPA (Wegener’s)
- Basophilic necrosis, giant cells, vasculitis all occur in mycobacterial/fungal infections
- Examine your special stains carefully

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Diagnosis: Necrotizing granulomatous inflammation (mycobacteria present)

Suppurative necrosis

Granulomatous inflammation with fungal organisms

Broad-based budding
Thick cell wall
Nuclear material
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**Diagnosis:** Suppurative granulomatous inflammation (fungal organisms present, Blastomyces favored)

After the biopsy...
- Blastomyces serology: negative
- Histoplasma serology positive (1:32)
- Cultures from biopsy grew *Blastomyces* 7 days after biopsy

![White to khaki colonies](image1)

Narrow-diameter hyaline septate hyphae. A simple conidium is produced at the terminus of a simple, short conidiophore

What did we learn?
- Fungal serology is not always accurate
- Histology is often the first to detect fungi; usually faster than cultures
- Histology can identify organism or narrow the differential

Case 4. Clinical/radiologic information
- 56/M with blood-tinged sputum, malaise, nasal crusting, epistaxis, night sweats, MPO-ANCA +
- Seen 12 years ago for similar complaints; enlarged lymph node 16 years ago with granulomas
- Spontaneous resolution of clinical and lung radiologic findings without treatment; few self-limited episodes since then
- Radiology: new bilateral infiltrates and hilar lymphadenopathy

Clinical/radiologic impression: GPA vs. sarcoidosis

What did we learn?
- Fungal serology is not always accurate
- Histology is often the first to detect fungi; usually faster than cultures
- Histology can identify organism or narrow the differential

*Multiple new ground glass infiltrates and nodules and solid nodules greatest in the mid and upper lung zones in a perilymphatic and peribronchovascular distribution. Differential possibilities are sarcoidosis or vasculitides such as Wegener granulomas.*
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- Suppurative granuloma
- Karyorrhexis

- Distinctive giant cells

- Giant cell embedded in organizing pneumonia

- Necrotizing vasculitis
  - Eccentric

- Necrotizing vasculitis: Movat pentachrome
  - Mixed neutrophil-histiocyte infiltrate
  - Karyorrhexis
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**Diagnosis: Granulomatosis with polyangiitis (Wegener’s)**

**What did we learn?**

- GPA cases that come to biopsy are usually clinically atypical in some way
- Negative ANCA
- Absence of full triad (lung, ENT, kidney)
- Atypical radiologic features
- Pathology can be diagnostic if
  - Necrotizing granulomas + necrotizing vasculitis

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**Case 5. Clinical/radiologic information**

- 59/M with cough, low grade fever, body aches, dyspnea
- History of ulcerative colitis, on prednisone
- Radiology: new bilateral infiltrates and hilar lymphadenopathy
- Received antibiotics and steroids

**Clinical/radiologic impression: Sarcoidosis**

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**Transbronchial biopsy:**

“Non-necrotizing granulomatous inflammation

Correlation with the clinical and microbiology results is suggested”

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After transbronchial biopsy...

- Diagnosed with sarcoidosis → IV methylprednisolone
- Worsening dyspnea, fever, hypoxia, tachycardia
- cough, low grade fever, body aches, dyspnea
- Chest CT: confluent airspace opacities
- Radiology: new bilateral infiltrates and hilar lymphadenopathy

**Clinical/radiologic impression: Infection? IBD-related?**

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Progressive disease, multiple small new and enlarging nodules, smooth septal thickening, peribronchial consolidation

Lymphadenopathy

Pericardial Effusion
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Suppurative granuloma

GMS: fungal organisms

Morphology not typical of Aspergillus or Mucor

Dilated and constricted portions

Pseudohyphaes?

Yeasts?
Diagnosis: Necrotizing granulomatous inflammation with pseudohyphae-like and other fungal elements

Follow-up
- After biopsy: sputum, BAL, pericardial fluid, lung biopsy tissue positive for Candida (confirmed by PCR on FFPE lung biopsy at CDC)
- Amphotericin → Micafungin
- Symptoms and infiltrates resolved; alive 32M after lung biopsy

What did we learn?
- Clinical impression of sarcoidosis can be erroneous
- Candida can rarely cause clinically significant pneumonia characterized by suppurative granulomas

Take Home Message

What did I learn at #USCAP2017?

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Suppurative granulomas
Think: fungal infection, GPA, particulate matter aspiration

Clinical correlation is good, but...

- Clinical information can be misleading or non-specific
- In cases with suppurative granulomas, look for key pathologic findings:
  - Microorganisms
  - Necrotizing vasculitis
  - Particulate matter

Pathology matters

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