Conceptual Approach to the Immunocompromised Patient
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Lecture Objectives
- How a patient's immune system and response determines the clinical manifestation of various infectious insults
- 3 Major immune systems strategies to protect the lungs from disease
- Some helpful imaging clues that will limit the possibilities

My Literature Research Assistant

Patient 1: 46 Year Old With Cough And Confirmed H1N1

Patient 2: H1N1 With An Organizing Pneumonia Reaction

Patient 3: 28 yo Female 15 Months Post BMT: Fevers Over 3 Days
4 Days Later on Antibiotics: Fevers Persist and Increased Dyspnea

Diffuse Alveolar Damage – Why The Difference?

Concept 1: Host Response
- Individuals have a unique genetic and immunological characteristics
- Therefore, 1 infection can have variable clinical manifestations by...
  - Inducing different responses by the patients, some mild, others more aggressive

Example: Aspergillus

BALANCE OF DISEASE: UBIQUITOUS ORGANISM

Manifestation of Aspergillus Depends on Immune Status
14 Year Old with Known Asthma
Received Nasal H1N1 Vaccine 9 Days Prior:
Severe Asthma Exacerbation → Respiratory Failure
Hyper-immune Response?

Influenza A (H1N1) → Strep Pneumonia

Staphylococcal Pneumonia: Post Seasonal Influenza Infection 2008

Concept 2: Dynamic Immune Susceptibility
- One infection/lung disease further alters a person’s immune system, such that other opportunistic infections can then flourish
- Viral infection → Secondary Bacterial
- Graft vs. Host Diseases/DAD → Th-1 to Th-2 activation: Aspergillus

Concept 3: Unsettled Feelings Toward The “Immune-Compromised” Patient
- The differential: “It could be anything”
- Understanding the different defects within a patient’s immune system will allow the radiologist to anticipate which pulmonary complications are most likely to arise.
- What are imaging manifestations that would help us narrow the differential?

The Lung’s Immune Protection
- A Multitiered immune system defends the lungs against challenges
- The systems are multilayered, redundant and tightly controlled to avoid excessive inflammation
- General categorization is divided into the Local Mechanical Defenses and an Activated Systemic and Specific Response system (Cellular and Humoral Defense)
Local Defenses: The “Lineup”

- **Local Airway Mechanical Factors**: Nasal filter, cilia, mucus (particles 5-10 micrometers), cough/sneeze reflex
- **Local Alveolar Immune System**: Pulmonary Macrophages (< 5 micrometers), Lymphatic Drainage
- **General Activated System**: Neutrophils and Eosinophils (More aggressive inflammation)

Round 1: Local Airway Protective System: Defects

- Dyskinetic cilia Syndrome, Cystic Fibrosis
- Asthma & Viral infections
- Recurrent Aspiration
- IgG and IgA deficiency
- Weakened cough
- Tracheobronchial malacia
- Results in a greater pathogen burden

Airway Barrier/Cough Reflex Breakdown: Pathogens

- Most common are bacterial: Staphylococcus aureus, Haemophilus and Pseudomonas species
- Results in linear scarring, recurrent bronchitis, bronchiolitis and eventually...
- Bronchiectasis (A common consequence)

Diagnosis: “COPD”: Recurrent Admissions for Bronchitis and Bacterial Pneumonia – Why?

Kartagener Syndrome
Cystic Fibrosis: The Type of Bronchiectasis is NOT as Clinically Important as the Extent

Widespread Bronchiectasis From IgG Deficiency

Localized Bronchiectasis
Unlikely From a Systemic or Activated Immune Abnormality

Round 2: Local Alveolar Immune System: Particles < 5 Micrometers
- Alveolar Macrophages are always present and have a restrained inflammatory reaction compared to circulating Macrophages (Reduce lung damage)
- 3 Known Functions: Clearing debris, destroying foreign pathogens and signals other immune cells when overwhelmed
- Mainly functions through phagocytosis and lysosomes enzymes

Alveolar Macrophages: Defects
- Compromised phagocytic function leads to recurrent infections, granulomatous formation and prolonged clearance of inflammation
- Most common infections: S. aureus, Streptococcus, Pseudomonas, Haemophilus
- Excessive surfactant may accumulate (Alveolar proteinosis) – Mycobacterium, Aspergillus and Nocardia infections (Altered local environment and immune activation)

Defective Alveolar Macrophages
- Viral infections
- Transplants, especially lung
- Dehydration and Alcohol abuse
- Uremia
- Chronic Granulomatous disease of childhood
- Silicosis
**Round 3: Alveolar Activated General Immune Defenses**

- When previously mentioned systems become overwhelmed, macrophages signal the neutrophils and eosinophils to quickly arrive in the affected areas.

- The neutrophils and eosinophils induce a greater inflammatory reaction, resulting in more local damage – counterbalanced by alpha 1-proteinase inhibitor.

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**Impaired Function or Neutropenia:**

- Chemotherapy, hematological malignancies and solid organ/bone marrow transplants.


- Acquired in community: Streptococcus and Haemophilus.

- Opportunistic ubiquitous fungi: Aspergillus or Mucormycosis (slower evolution of the clinical and imaging manifestations).

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**53 yo With PAP: Secondary Chronic Necrotizing Aspergillus**

- Microenvironment has been altered (Th-1 → Th-2).

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**52 yo 30 Days Post BMT for Leukemia with Persistent Fevers**

- 37 yo With Fevers: 140 days Post Allo BMT

- Septic Emboli With Aspergillus in Camouflage
Day 110 Post Allo BMT:
Angio-Invasive Aspergillus
Aspergillus usually occurs > 100 Days after
BMT: NOT WITHIN FIRST 30 DAYS

Halo Sign Is An Early
CT Finding of Angio
Invasive Aspergillus
Crescent sign: Later Finding &
More Specific

Leukemia: Day 85 Post BMT
Non-Responsive
to Therapy: Went
to Surgical Resection -
Mucormycosis

Round 4: Specific Activated System
- Humoral system: B-lymphocytes produce
  antibodies, which facilitate macrophage
  engagement
- Cellular system: T-lymphocytes help
  activate the B-cell lymphocytes, generate
  a delayed-type hypersensitivity reaction, cytotoxic activity and tumor surveillance
- Both are dependent, on each another –
therefore they will be considered together

B-Cell/T-Cell Mediated Immune System: Diseases
- Splenectomy
- Combined Immunodeficiency Syndrome
- HIV/AIDS
- Chronic Corticosteroid Therapy
- Lymphoproliferative/Leukemia diseases
- Transplants: Solid organ and bone
  marrow* (*Neutrophil dysfunction & Th-2 → Aspergillus)
- Chemotherapy and cyclosporine

B-Cell/T-Cell Mediated
Immunosuppression: YIKES!
- Bacteria: Streptococcus, Haemophilus
  Rhodococcus equi, Legionella & Nocardia
  (acquired in community) Staphylococcus,
  Pseudomonas & Klebsiella (acquired in hospital)
- Granulomatosis: Mycobacteria, Cryptococcus,
  Coccidioidomycosis, Histoplasmosis
- Virus: CMV, Varicella-Zoster, Influenza,
  Parainfluenza, Adenovirus & RSV
- Pneumocystis pneumonia
Imaging Can Help!

- **Consolidation**: Strep, Staph, Haemophilus, Pseudomonas, Klebsiella, Legionella
- **Nodular/Mass-like Consolidation**: Nocardia, Aspergillus (BMT); Varicella (Diffuse distribution)
- **Necrotizing Consolidation**: Rhodococcus, Granulomatous infections, Cryptococcus
- **Diffuse Airway (Tree-in-bud)**: Influenza, RSV, Parainfluenza, Adenovirus
- **Ground Glass**: Pneumocystis, CMV, Influenza

Leukemia: Pseudomonas Pneumonia (Acquired in Hospital)

42 Year Old with Advanced HIV: Fever over 7 Days. Presents with Left Sided Chest Pain

Hemolytic Anemia: Fever With Mass Developed in 1 Month. CT Guided Biopsy: Nocardia

Necrotizing Multifocal Legionella Pneumonia

HIV Patient with a Cough (Works on a Farm)
220 Days Post Allo BMT: Fever Has Graft vs. Host Disease

Influenza (2004)
What Other Complications Should We Look For?

HIV Patient: Radiograph and HRCT Localized “Tree-in-bud”

32 Year Old Male With AIDS: Ground Glass with Cysts PCP

BMT: 90 Days Post Transplant with Shortness of Breath and Fever

Looking “Underneath” Our Conventional Teachings
38 yo Female With Stage 1 Sarcoidosis Has Recurrent Fevers X 3 Months

Cryptococcus gattii Is Her Immune System Normal?  
March 2007       March 2008  
Lab Results Did Not Demonstrate Any Immune Abnormality

Immune Concepts: Summary

- An infection can have variable clinical manifestations based on the unique genetic and immunological characteristics of each person.

- An infection/lung disease further alters a person’s immune system, such that other opportunistic infections can then flourish.

Multilayered Pulmonary Immune Systems - Summary

- Mechanical barriers: Initial Defense
- Alveolar Macrophages: Always Present
- General Activated System: Neutrophils and Eosinophils
- Activated Specific Response Systems: Humoral and Cell-mediated Immune systems

Thank You gosselin@OHSU.edu