INSTRUCTOR'S GUIDE
TUBERCULOSIS
CASE STUDY #97

Parts I and II will be given to students prior to the small group.

Lecture

Acute, Chronic and Granulomatous Inflammation

PART I

Objectives

Following the discussion of this case, the students should:

1. Understand the immunopathogenesis of tuberculosis infection
   - Tubercle bacilli are inhaled into terminal alveoli
   - Ingested by macrophages
   - Multiply in phagolysosome
   - Macrophages fuse and become Langerhans Giant cells
   - Reactive granuloma formation
   - Central necrosis of granuloma with release of tubercle bacilli
   - Spread of bacilli to regional lymph nodes
   - Hematogenous spread
   - Healing with fibrosis or calcification vs further dissemination
   - Infection put into check “quiescent state”
   - Patient becomes immunocompromised and bugs begin to multiply
   - More granuloma formation, patient ultimately dies of tissue destruction and necrosis.

   The development of cell mediated, or type IV, hypersensitivity to the tubercle bacillus probably explains the organisms destructiveness in tissues. The hypersensitivity reaction controls 95% of disease.

2. Understand the mechanisms of granuloma formation and the morphology of caseating and non-caseating granulomas.
   - Bacteria ingest macrophages → antigens stimulation epithelioid conversion ↑ size. Class II MHC + CD4 T cell → cytogen protection → delayed hypersensitivity → sensitized T cells + epithelioid cells + giant cells → granuloma formation and ultimately to central necrosis of these granulomas
3. Understand causes of granulomatous inflammation and be able to construct a differential diagnosis for this case.
   • Mycobacterial infections, fungal infections, sarcoid, Chrons disease, Q fever, *Coxiella burnetii*, brucellosis, syphilis, leprosy, cat scratch disease, schistosomiasis, foreign body reaction.

4. Understand the differences between primary and secondary tuberculosis and miliary tuberculosis and be able to describe the morphologic appearance of lesions in tissues.
   • 1° pulmonary infection ± regional lymphoid 90+% resolve. 2° = reactivation disease = pulmonary or other remote sites, usually associated with immunocompromise.
   • 1° TB
     ➢ asymptomatic pneumonitis ± mediastinal involvement
     ➢ PPD+ in 2-4 weeks due to cell-mediated hypersensitivity
     ➢ 95° to heal without sequelae
   • Miliary TB
     ➢ Usually develops at the time of 1° TB, most commonly seen in children
     ➢ Weight loss, fever, nonspecific findings including meningeal disease
     ➢ Hematogenous spread → small granulomas all over body in all tissues “millet seed” appearance.
     ➢ Rapidly fatal if not treated
   • Reactivation TB
     ➢ TB predilection for upper lobe cavitary lesions, coin lesions, hemoptysis
     ➢ Very infectious
     ➢ Chronic wasting, fever, weight loss, drenching sweats
     ➢ May reactivate from non-pulmonary sites of quiescence

5. Understand the categories of individuals at risk for tuberculosis and be able to describe how the disease may differ among these different risk groups.
   • Malnutrition, poverty, poor medical care
   • Race – Africans, American Indians, Blacks, Eskimos
   • Males > Females
   • Chronic Illness
     ➢ DM
     ➢ ETOH abuse
     ➢ Immunosuppression
   • Increased age

**PART II**

1. Patient’s Risk Factors for TB
   • Untreated 1° TB (5% of patients aren’t able to clear infection)
   • Older age (71 years)
2. Signs/Symptoms of TB
   - Nonspecific findings – fatigue, pallor, anemia
   - Confusion (possible meningeal TB)
   - SOB with respiratory distress – severe pulmonary involvement
   - Spleen enlarged
   - Testicle with calcified mass
   - Bone marrow involvement anemia, thrombocytopenia, granulomas in biopsy
   - LDH ↑ 2⁰ lung tissue destruction, spleen, other tissues
   - Nodulo-reticular pattern in lung (extensive involvement)
   - Fibro-nodular involvement upper lung (some old changes)

TB CASE # 97
Slide Key

1. High-power view of a TB granuloma. Necrotic center →
   Epithelioid macrophages (pale, large nuclei) & Langhans type giant cells which
   surround the necrotic center →
   Peripherally = lymphs (smaller, darker nukes vs. macrophages).

2. Close up view of Langhans type giant cells. Note peripheral orientation of nuclei
   (classic morphology).

3. This is a very, very high power view of a TB granuloma stained with an acid-fast
   stain. You can see the red snappers that are within the epithelioid cells.

4. Bone marrow bx. Much fat – typical for “older” person. Big red area is probably
   hemorrhage due to biopsy trauma. *Point to many granulomata. Loaded.

5. Brain – and it’s obviously not a bx! I don’t know if this belongs to our patient. You’re
   looking at the undersurface- (POINT) frontal, occipital & temporal lobes, cerebellum,
   brainstem. Focus on this thick, white covering that overlies the brainstem. This
   presumably represents TB meningitis.

6. Closer view

7. What’s this organ? Cross section of spinal cord. Cord itself looks OK, but Meninges
   are markedly thickened. Hard to appreciate here, but there are lots of pink/red
   “blotches” speckled throughout the meninges. These are granulomata. Very
   impressive.