Bone Marrow Disorders of Nonhematopoietic Elements

January 5, 2004
I. Storage disorders
II. Noninfectious granulomas
III. Disorders of bone marrow stroma
IV. Metabolic bone disease
V. Metastatic tumors
I. Lipid Storage Disorders

- Hereditary lysosomal enzyme deficiency
  - Autosomal recessive
- Partially degraded lipids accumulate in macrophages
  - Liver, spleen, bone marrow, etc.
  - Organomegaly, cytopenias
Gaucher’s Disease

- Enzyme deficiency = Glucocerebrosidase
- Accumulate = Glucocerebroside
- 3 clinical forms, all AR
  - Type I - adult
  - Type II - acute infantile, neuronopathic
  - Type III - subacute juvenile, neuronopathic
Gaucher’s Disease

- Gaucher cell
  - “Wrinkled cigarette paper”
  - PAS positive
Pseudo-Gaucher Cell

- Indistinguishable from true Gaucher cell
- Conditions with high cell membrane turnover
  - CML, Hemoglobinopathies, Myeloma
  - Increased burden of glucocerebrosides
Pseudo-Gaucher Cell

- MAI infection
- Macrophages packed with organisms
  - Negatively staining organisms mimics striations of Gaucher cells.
Niemann-Pick Disease

- Enzyme deficiency = Sphingomyelinase
- Accumulate = Sphingomyelin
- 3 clinical forms, all AR
  - Type A - early onset
  - Type B - adult, no cerebral involvement
  - Type C - late onset
Niemann-Pick Disease

- Foamy macrophages
  - “Bubbly” appearance
  - Weak PAS+
  - Oil Red O and Sudan black positive
- Sea blue histiocytes
Sea Blue Histiocytes

- Macrophages contain ceroid
  - Lipofuscin-like pigment
  - H&E, yellow-brown
  - Geimsa, bright blue green
  - PAS positive

- High turnover states - CML, ITP, SCD

- Lipidoses and hyperlipidemia
Sea Blue Histiocytes
II. Noninfectious Granulomas

- Lipogranuloma
- Sarcoidosis
- Reactive (sarcoid-like) granuloma
Lipogranuloma

- Focal aggregate of macrophages with lipid vacuoles
- +/-Inflammatory cells
- Rare MNGC
Sarcoidosis

- Epitheloid granulomas in lung and other organs
  - Bone marrow involvement 17%
  - LAD, Spleenomegaly, lymphopenia
Sarcoidosis

- Epitheloid histiocytes
  - Small, noncaseating
  - “Naked” granulomas
- MNGC
### Table 24.1 Etiology of Bone Marrow Granulomas

<table>
<thead>
<tr>
<th>Noninfectious Bone Marrow Granulomas</th>
<th>Infectious Bone Marrow Granulomas</th>
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<tbody>
<tr>
<td><strong>Sarcoidosis</strong></td>
<td>Mycobacterial and fungal infections</td>
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<td><em>Mycobacterium tuberculosis</em></td>
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<td><em>Mycobacterium avium-intracellular</em></td>
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<td><em>Bacillus of Calmette and Guerin</em></td>
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<td><em>Mycobacterium leprae</em></td>
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<td><em>Histoplasma capsulatum</em></td>
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<td><em>Cryptococcus neoformans</em></td>
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<td><em>Coccidioides immitis</em></td>
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<td><em>Saccharomyces cerevisiae</em></td>
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<td><em>Aspergillus</em></td>
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<td><strong>Drugs</strong></td>
<td>Bacterial, rickettsial, and mycoplasmal infections</td>
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<td><em>Brucellosis</em></td>
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<td><em>Tularemia</em></td>
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<td><em>Rocky Mountain spotted fever</em></td>
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<td><em>Q-fever</em></td>
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<td><em>Mycoplasma pneumoniae</em></td>
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<td><strong>Autoimmune and hypersensitivity disorders</strong></td>
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<td><em>Rheumatoid arthritis</em></td>
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<td><em>Systemic lupus erythematosus</em></td>
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<td><em>Hypersensitivity pneumonitis</em></td>
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<td><em>Primary biliary cirrhosis</em></td>
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<td><em>Crohn’s disease</em></td>
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<td><strong>Neoplasms</strong></td>
<td>Protozoan infections</td>
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<td><em>Toxoplasma gondii</em></td>
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<td><em>Leishmania donovani</em></td>
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<td>Viral infections</td>
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<td><em>Infectious mononucleosis</em></td>
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<td><em>Cytomegalovirus</em></td>
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<td><em>Viral hepatitis</em></td>
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III. Disorders of Bone Marrow

Stroma

- Bone marrow infarction
- Serous fat atrophy
Bone Marrow Infarction

- Coagulative necrosis
- Associated with neoplastic process, vasocculsive disorders and hemoglobinopathies
Bone Marrow Infarction

- Homogenously staining
- Ghost cells
Serous Fat Atrophy

- AKA gelatinous transformation
- Associated with starvation and wasting diseases
- Homogenous extracellular substance with watery appearance
IV. Metabolic Bone Disease

- Osteopetrosis
  - (Albers-Schonberg or marble bone disease)
- Osteomalacia
- Renal osteodystrophy
- Paget’s disease
  - (Osteitis deformans)
Osteopetrosis

- Functional defect in osteoclasts
  - Abnormal accumulation of dense bone
- AR - severe, infancy
  - Hematopoietic failure
- AD - frequently asymptomatic
Osteopetrosis

- Dense bone
- Persistence of cartilaginous cores
Osteomalacia

- Defective mineralization of bone
  - Vitamin D deficiency
- Hyperosteooidosis
  - Increased unmineralized osteoid
Renal Osteodystrophy

- Chronic renal insufficiency
  - Deficiency of active vitamin D
    - Hyperosteoidosis
  - 2º hyperparathyroidism
    - Increased osteoclast activity - irregular scalloping of bony trabeculae and peritrabecular fibrosis
    - Osteitis fibrosa cystica
Renal Osteodystrophy

- “Scalloping” of bony trabeculae
- Peritrabecular fibrosis
Paget’s Disease

- Disordered bone remodeling
  - Thickened trabeculae
  - Irregular cement lines “mosaic” pattern
  - Osteoblasts and osteoclasts prominent
V. Metastatic Tumors

- Adults
  - Breast, prostate, lung and GI carcinoma
- Pediatric
  - Neuroblastoma
- Clues: unexplained fibrosis or necrosis
Metastatic Tumors

Prostate Carcinoma

Artifact