Pathology of the Hematopoietic System

Lecture 2: Lympho/Myelo-proliferative diseases, Lymph nodes and Thymus
Primary Hematopoietic Neoplasia

Hematopoietic Neoplasia

Lymphoproliferative Disease

Lymphoma

Lymphoid leukemia

Plasma cell tumours

Histiocytic Neoplasia

Myeloid leukemia

Myelodysplastic Syndrome

Mast cell tumour
Plasma cell tumours

1. Cutaneous Plasmacytoma
   - Common skin masses in dogs
   - Surgical excision is usually curative

2. Extramedullary Plasmacytoma
   - Arising at sites other than BM / skin
   - Often affect the GI tract
   - More aggressive, may metastasize to the lymph nodes
3. Multiple Myeloma

- Uncommon in domestic animals: dogs > cats
- Malignant tumour of plasma cell origin arising in the bone marrow
- Neoplastic (clonal) plasma cells secrete immunoglobulin leading to hypergammaglobulinemia:
  - Monoclonal gammopathy on serum electrophoresis
  - Hyperviscosity syndrome
  - Bence-Jones proteinuria
Masses may occur in any bone, but most often occur in the vertebrae. Can see hypercalcemia due to ↑ osteoclastic activity *

3. Multiple Myeloma

- **Gross:** Pale pink to dark red gelatinous masses replace bone marrow – typically multiple masses!
- **Histologically:** Sheets of round cells – with plasmacytoid morphology
Clinical diagnosis of multiple myeloma is based on finding 2-3+ of the following features:

- Increased plasma cells in bone marrow
- Punched out lesions on radiographs
- Monoclonal gammopathy
- Hypercalcemia
- Light chain (Bence-Jones) proteinuria

Affected bones often have “punched” out appearance on radiographs.

Clinical signs: lameness, pain, lethargy, paraplegia

Slowly progressive

Stained image of bone with lesions.

Courtesy of Dr. A Matthews, AVC
Hematopoietic Neoplasia

Myeloproliferative Disease

Lymphoproliferative Disease

Lymphoma

Lymphoid leukemia

Plasma cell tumours

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Mast cell tumour
# Histiocytic Proliferative Disorders

1. **Cutaneous histiocytoma**
   - Common benign skin mass
   - Young dogs
   - Spontaneously regress

2. **Reactive histiocytosis**
   - Immunoregulatory disease
   - Waxing and waning, progressive
   - Cutaneous histiocytosis
   - Affects the skin
   - Systemic histiocytosis
   - Affects skin and viscera

[http://vetmedicine.about.com/od/diseasesandconditions/tp/Lumps-Bumps.htm](http://vetmedicine.about.com/od/diseasesandconditions/tp/Lumps-Bumps.htm)
3. Histiocytic Sarcoma

- Malignant neoplasia of macrophages or dendritic cells
- Breed predispositions
  - Bernese Mountain dog, Rottweiler, Flat-coated Retriever
- Can be solitary of multiple:
  - Solitary lesions
    - Surrounding joints, subcutis
    - Lymph nodes, spleen or liver
  - Multiple lesions
    - Disseminated histiocytic sarcoma = Malignant histiocytosis
3. Disseminated histiocytic sarcoma (= malignant histiocytosis)

- Aggressive multisystemic disease
- Tumour masses in several organs: spleen*, bone marrow*, lymph nodes*, lung, skin
- Splenomegaly, hepatomegaly

Histiocytic sarcoma, hilar and mesenteric lymph nodes

Courtesy of Dr A Lopez, AVC
3. Disseminated histiocytic sarcoma (= malignant histiocytosis)

- **Histology**: Masses / diffuse infiltrates composed of atypical histiocytes
  - May be avidly hemophagocytic causing a non-regenerative anemia
Mast cell neoplasia

Mast cells are widely distributed in the connective tissues - however they originate in bone marrow

1. Cutaneous mast cell tumour
   • Common skin tumours of dogs

2. Alimentary mast cell tumour
   • Intestinal or gastric masses

3. Systemic mastocytosis
   • Involves primarily the hematopoietic system
3. Systemic mastocytosis = Visceral mast cell tumours

- Primarily involves the hematopoietic system
  - Spleen, bone marrow
- Rare in animals: cats
- **Gross:** Splenomegaly +/− nodular surface
Mast cell neoplasia

3. Systemic mastocytosis = Visceral mast cell tumours

- Primarily involves the hematopoietic system
  - Spleen, bone marrow
- Rare in animals: cats
- Gross: Splenomegaly +/- nodular surface

Can see diffuse hepatic enlargement
Mast cell neoplasia

3. Systemic mastocytosis = Visceral mast cell tumours

**Histology:**
Cords and sheets of mast cells efface the parenchyma
Secondary Bone Marrow Neoplasia

- Results of metastasis of a tumour from a distant site to the bone marrow
- Can be a carcinoma or a sarcoma

Metastasis of a malignant pheochromocytoma to the rib, dog

Image Courtesy of Dr A Lopez
Myelophthisis

- Replacement of hematopoietic tissue within the bone marrow by abnormal tissue

- Fibrosis → Myelofibrosis
- Neoplastic cells → leukemia, lymphoma, histiocytic sarcoma etc.
- May result in pancytopenia due to competition for space/nutrients

Dog: Replacement of bone marrow by lymphoma
Lymphoid Tissue: Lymph nodes
Lymph nodes

Function:
• Filtration of lymph
• Immune response

Structure:
• Outer cortex → follicles (mostly B cells)
• Inner cortex → paracortex (mostly T cells)
• Medulla → mostly B cells and macrophages

Lymph circulation:
• Afferent lymphatics → subcapsular sinuses → trabecular sinuses → medullary sinuses → efferent lymphatics → thoracic duct

Modified from Pathologic Basis of Veterinary Disease
Lymph nodes

**Function:**
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**Lymph circulation:**
- Afferent lymphatics ➔ subcapsular sinuses ➔ trabecular sinuses ➔ medullary sinuses ➔ efferent lymphatics ➔ thoracic duct
Lymph node: General response to injury

Two basic responses: Decrease in size or increase in size

Enlarged lymph nodes
- Lymphadenitis
- Lymphoid hyperplasia
- Hyperplasia of the monocyte/macrophage system
- Primary neoplasia
- Secondary neoplasia

Small lymph nodes
- Lymphoid atrophy
- Lymph node degeneration
- Lymph node hypoplasia
Lymph node: General response to injury

**Lymphadenopathy**
- Enlargement of the lymph node(s) of unknown cause
- Can be localized or generalized

**Enlarged lymph nodes**

- Lymphadenitis
- Lymphoid hyperplasia
- Hyperplasia of the monocyte/macrophage system
- Primary neoplasia
- Secondary neoplasia

Enlargement of the right retropharyngeal LN sheep
Lymph node: Inflammation

Lymphadenitis

- An inflammatory response to an infectious agent within the node

- As opposed to reactive hyperplasia which is an antigen driven immunologic response

Acute Lymphadenitis

- Usually the result of a regional lymph node draining a site of inflammation and becoming infected

Cervical and sternal lymphadenitis with sepsis
Lymph node: Chronic lymphadenitis

- With chronicity the lymph nodes become large, irregular, and firm due to fibrosis
- Chronic suppurrative lymphadenitis
- Chronic granulomatous lymphadenitis

*Rhodococcus equi* in a foal
Lymph node: Chronic suppurative lymphadenitis

- Gross lesions:
  - Swollen lymph node with pus-filled center = Lymph node abscess
- Can fistulate to the skin surface
- Response to pyogenic bacteria

From Pathologic Basis of Veterinary Disease
**Equine Strangles**

- *Streptococcus equi* subsp *equi*
- Inflammation of the URT → abscesses in the mandibular, retropharyngeal and parotid Lnn
- May fistulate to the surface
- Can spread to the viscera → “Bastard Strangles”
Pathogenesis:
• Usually enters via contamination of shear wounds; rarely by inhalation
• Drains to regional lymph nodes
  – Superficial nodes more often affected than internal nodes
    • Prescapular LN
    • Prefemoral LN

Caseous lymphadenitis: *Corynebacterium pseudotuberculosis*
• Chronic suppurative lymphadenitis in sheep & goats
• Ulcerative lymphangitis in horses and cattle
• Pectoral abscesses in horses
Lymph node: Chronic suppurative lymphadenitis

Caseous lymphadenitis: *Corynebacterium pseudotuberculosis*

Goat, caudal mediastinal lymph nodes: lymph node abscesses
*Lymph node: Chronic suppurative lymphadenitis*

**Caseous lymphadenitis: *Corynebacterium pseudotuberculosis***

- Chronic suppurative inflammation, caseous necrosis & fibrosis
- As lesion progresses → characteristic concentric laminations**

With time, there may be systemic involvement with abscesses in the internal organs
### Lymph node: Granulomatous lymphadenitis

#### Nodular granulomatous lymphadenitis
- Mycobacterium bovis
- Mycobacterium avium subsp. paratuberculosis
- Actinobacillus lignieresii
- Migrating parasitic larva

- Focal or multifocal
- Often white-yellow nodules
- +/- caseous necrosis/mineralization

#### Diffuse granulomatous lymphadenitis
- Porcine Circovirus type 2
- Histoplasma capsulatum
- Blastomyces dermatitidis
- Cryptococcus neoformans

- Enlarged, pale, dry, firm lymph nodes
- Loss of architecture

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![Image of lymph node with granulomatous changes]

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Lymph node: Nodular granulomatous lymphadenitis

Bovine Tuberculosis: *Mycobacterium bovis*

- **Gross:** Enlargement of the lymph node with single to multiple discrete yellow-tan gritty (caseated) nodules
- Can disseminate to the organs

Image: Cornell Veterinary Medicine
Lymph node: Nodular granulomatous lymphadenitis

Bovine Tuberculosis: *Mycobacterium bovis*

- **Histology**: Granulomas with central necrosis and mineralization surrounded by epithelioid macrophages and multinucleated giant cells
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Lymph node: Nodular granulomatous lymphadenitis

Bovine Tuberculosis: *Mycobacterium bovis*

- **Histology**: Granulomas with central necrosis and mineralization surrounded by epithelioid macrophages and multinucleated giant cells

Acid fast bacilli within macrophages
Lymph node: Diffuse granulomatous lymphadenitis

Postweaning multisystemic wasting syndrome (PMWS): Porcine Circovirus type 2

• **Gross:** Diffuse enlargement of the mesenteric lymph nodes
Lymph node: Diffuse granulomatous lymphadenitis

Postweaning multisystemic wasting syndrome (PMWS):
Porcine Circovirus type 2

• Histology: Granulomatous infiltration of the node with large botryoid intracytoplasmic viral inclusions
**Gross:**
- Moderate enlargement of the node(s) = Lymphadenopathy
- May bulge on cut section

**Benign Reactive Hyperplasia**
- Immunological reaction = response to antigen presentation or circulating interleukin levels
- Causes lymph node enlargement
- Can be localized or generalized
- Lymph nodes draining site of local infection or vaccination
- Also occurs during early stages of lymphadenitis
Histology:
- Proliferation of lymphoid follicles with prominent germinal centers*
- Increased T cells in the paracortex
- +/- Increased plasma cells in the medullary cords
Questions?