Pathology of the Hematopoietic System

Lecture 2: Lympho and Myeloproliferative diseases
Lymph nodes
1. Cutaneous plasmacytoma
- Common benign skin masses in dogs
- Surgical excision 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

- Malignant tumour of plasma cell origin arising in the bone marrow
- Uncommon in domestic animals: dogs > cats
- Neoplastic (clonal) plasma cells secrete immunoglobulin leading to hypergammaglobulinemia:
  - Monoclonal gammopathy on serum electrophoresis
  - Hyperviscosity syndrome
  - Bence-Jones proteinuria
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

Masses may occur in any bone, but most often occur in the vertebrae.
Affected bones often have “punched” out appearance on radiographs.

Clinical diagnosis of multiple myeloma is based on finding 2 - 3 + of the following features:

- Increased plasma cells in bone marrow (30%+)
- Punched out lesions on radiographs
- Monoclonal gammopathy
- Hypercalcemia
- Light chain (Bence-Jones) proteinuria
Primary Hematopoietic Neoplasia

Hematopoietic Neoplasia

Lymphoproliferative Disease

Lymphoma

Lymphoid leukemia

Plasma cell tumours

Myeloproliferative Disease

Histiocytic Neoplasia

Myeloid leukemia

Myelodysplastic Syndrome

Mast cell tumour
## Myeloproliferative disease: Histiocytic neoplasia/proliferative disorders

<table>
<thead>
<tr>
<th>1. Cutaneous histiocytoma</th>
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<tr>
<td>• Common benign skin mass</td>
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<td>• Young dogs</td>
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<td>• Spontaneously regress</td>
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<th>2. Reactive histiocytosis</th>
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<td>• Immunoregulatory disease</td>
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<tr>
<td>• Waxing and waning, progressive</td>
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<td>• <strong>Cutaneous histiocytosis</strong></td>
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<tr>
<td>• Affects the skin</td>
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<tr>
<td>• <strong>Systemic histiocytosis</strong></td>
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<tr>
<td>• Affects skin and viscera</td>
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3. Histiocytic sarcoma

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

3. Disseminated histiocytic sarcoma (= malignant histiocytosis)

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

Courtesy of Dr A Lopez, AVC

Histiocytic sarcoma, hilar and mesenteric lymph nodes
3. Disseminated histiocytic sarcoma (= malignant histiocytosis)

- **Histology**: Masses / diffuse infiltrates composed of atypical histiocytes
- May be avidly hemophagocytic causing a non-regenerative anemia
Mast cells are widely distributed in the connective tissues - however they originate in bone marrow

**Cutaneous mast cell tumours**
- Common skin tumours of dogs

**Alimentary mast cell tumour**
- Intestinal or gastric masses

**Systemic mastocytosis**
- Involves primarily the hematopoietic organs
Systemic mastocytosis – visceral mast cell tumours

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

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
Myeloproliferative disease: Mast cell neoplasia

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

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Normal lymph node, cow
Lymph node: General response to injury

Two basic responses: Decrease in size or increase in size

**Small lymph nodes**
- Lymphoid atrophy
- Lymph node degeneration
- Lymph node hypoplasia

**Enlarged lymph nodes**
- Lymphadenitis
- Lymphoid hyperplasia
- Hyperplasia of the monocyte/macrophage system
- Primary neoplasia
- Secondary neoplasia
**Lymph node: Lymphadenopathy (lymphadenomegaly)**

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

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**Enlarged lymph nodes**

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* 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: Acute lymphadenitis

Gross lesions:
- Enlarged, soft, wet, red lymph nodes
- Often bulging and hyperemic on cut surface
- Exudates are usually serous or hemorrhagic

Mesenteric lymphadenitis

Popliteal lymphadenitis

Courtesy: Dr C Legge
Lymph node: Chronic lymphadenitis

- With chronicity the lymph nodes become large, irregular, and firm due to fibrosis
- Chronic suppurative 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
  • Response to pyogenic bacteria
  • Can fistulate to the skin surface
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
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
Lymph node: Nodular granulomatous lymphadenitis

Bovine Tuberculosis: *Mycobacterium bovis*

**Gross:** Enlargement of the lymph node with multiple discrete yellow-tan gritty (caseated) nodules

Image: Cornell Veterinary Medicine
• **Histology**: Granulomas with central necrosis and mineralization surrounded by epithelioid macrophages and multinucleated giant cells

Bovine Tuberculosis: *Mycobacterium bovis*
Lymph node: Nodular granulomatous lymphadenitis

Bovine Tuberculosis: *Mycobacterium bovis*

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

- Can be localized or generalized
- Immunological reaction = response to antigen presentation or circulating interleukin levels
  - Lymph nodes draining site of local infection or vaccination
  - Also occurs during early stages of lymphadenitis

Gross:

- Moderate enlargement of the node(s) = Lymphadenopathy
- May bulge on cut section
Histology:
- Proliferation of lymphoid follicles with prominent germinal centers*
- Increased T cells in the paracortex
- +/- Increased plasma cells in the medullary cords
Primary lymph node neoplasia = Lymphoma

Covered in primary hematopoietic neoplasia*
Lymph node metastasis:

• Common with carcinomas, melanomas, mast cell tumors…
• May see lymph node enlargement
• Variable effacement of normal architecture

One basis of staging tumor malignancy

• Stage 0: regional node normal
• Stage 1: regional node enlarged but still freely moveable
• Stage 2: regional node enlarged and fixed
Metastasis of mammary carcinoma to a lymph node

Images: Courtesy of Dr Hanna, AVC
Questions?