

Lymphadenopathy

This is defined as a regional or generalized lymph node enlargement of unknown or unspecific cause. Local enlargement of L/nodes usually reflects a pathologic process limited to the drainage area.

Lymphadenitis

Lymphadenitis is inflammation of the lymph nodes. This may be non-specific, local or general. Functioning as a filter, the lymph node affected by any irritant that may be present in the area it drains. The following are the irritants that may cause non-specific lymphadenitis:

- (a) Irritant chemicals, (b) Soluble toxins from trauma and burns, and
- (c) Bacteria, Depending on the nature of the exudates, lymphadenitis may be acute, serous, hemorrhagic, supportive or chronic.

Acute Serous Lymphadenitis: This condition is common in the nodes draining lymph from acutely infected or inflamed areas. In some septicemia all the nodes in the body may be affected e.g. Anthrax, Pastenurellosis, swine Erysipelas, dog cholera, salmon disease. Mesenteric nodes may be affected by the absorption of irritants from the gastro intestinal tract.

Microscopically, the affected node is enlarged, moist and reddened.

Microscopically, hyperemia and edema are noticed. due to proliferation of the lymphatic parenchyma and reticulo endothelial tissue, the lymph sinuses are filled with lymphocytes, mononuclear (derived from the RE, system) plasma cells and a few neutrophils

Hemorrhagic lymphadenitis. Occurs when the irritant is stronger than in the serous variety. The best example is Anthrax. The exudates in the gland are mixed with blood. Microscopically lymph sinuses contain large number of erythrocytes.

Suppurative lymphadenitis: Pyogenic bacteria cause suppurative lymphadenitis. The common organisms producing this are: *Streptococcus equi* in horses (strangles) *Corynebacterium ovis* (caseous lymphadenitis in sheep).

Macroscopically pus may be found in the nodes.

Microscopically, the predominant cell of the greatly infiltrating leucocytes is the neutrophils. There is necrosis and liquefaction of the parenchyma and several small purulent foci may be present which may coalesce to form a big abscess.

Chronic lymphadenitis: Grossly the affected nodes are large, hard and dry. This is seen in Johne's disease in which mesenteric lymph nodes are involved.

Microscopically, there is hyperplasia of the R. E. system with numerous endothelial cells becoming rounded, swollen and cast off into the lymph sinuses that are much distended. To this picture is given the name of "sinus catarrh" Macrophages predominate, Reactive hyperplasia of the lymph nodules is also present. Fibrosis that occurs is the cause of hardness.

Specific lymphadenitis:

Lymphadenitis is a characteristic lesion of the following diseases.

- (a) Tuberculosis
- (b) Glanders
- (c) Actinobacillosis
- (d) Johne,s diseases
- (e) Salmon poisoning in dogs
- (f) Strangles in horses
- (g) Caseous lymphadenitis in sheep
- (h) Bovine lymphangitis and lymphadenitis caused by *Pastcurella pseudotuberculosis rodentium*.
- (i) Brucellosis in guinea pigs
- (j) Tularemia in rodents
- (k) Epizootic lymphadenitis.
- (l) helminthic larvae – Pentastoma and other helminthic larvae in mesenteric lymph nodes of cattle; lungworm larvae in the bronchial nodes.

Note that a-d result into granulomatous lymphadenitis with caseation and calcification

Neoplasms – Primary benign tumors of lymph nodes are not common. But primary malignant neoplasms such as lymphosarcoma – are common.

Secondary tumors that are common in the lymph nodes are: carcinoma, malignant melanoma and occasionally sarcoma, which invade the lymph vessels.

Lymphoid Nodules

Lymphoid atrophy – Causes include:

Viral infections.

Malnutrition

Cachexia

Aging

Anti-neoplastic chemotherapeutic drugs.

Toxins

Irradiation and Lymphoid hyperplasia caused by antigenic stimulation

SPECIFIC DISEASES OF THE HAEMOPOIETIC SYSTEM

Specific Diseases of this system include

1. Equine combined immunodeficiency.
2. Caseous lymphadenitis
3. Histoplasmosis
4. Anthrax
5. Streptococcal Adenitis in swine (in Dogs)
6. Tularaemia
7. Leishmaniasis
8. Theileriosis
9. Tick – Borne fever
10. Bovine Petechial fever
11. Myeloproliferative disease.

1. **Equine combined immunodeficiency.** (Equine CID)

This is genetic disorder occurring in Arabian foals. It is inherited as an autosomal or recessive trait, meaning that both the sire and dam are carriers of the defective gene in this disorder, there is failure of functional B and T- lymphocytes production, so foals are remarkably susceptible to a variety of microbial agents and usually die before 5 months of age. Adenoviruses that are typically resisted by a normal foal are major causes of death in foals with CID. The viral infection is frequently complicated by various bacteria and protozoan infections that typically result in pneumonia.

Affect foals frequently have profuse nasal discharge, unthrifty hair coat, loss of condition, pneumonia and occasionally diarrhea.

Confirmatory diagnosis of CID include persistent lymphopaenia, absence of serum IgM and maternally derived IgG declines to very low concentration by approx 3 months of age. Hypoplastic lymphoid tissue, varying degree of neutrophilia with left shift and mild anaemia occur and probably result from chronic inflammation.

P/M Findings

Gross: Severe bronchopneumonia in combination with small thymus, spleen, and lymph nodes. The thymus may be difficult to identify or may consist of a few isolated lobules within the mediastinal fat.

Microscopically, the thymus usually consists of a few island of lymphocyte – like cells and thymus corpuscles. The spleen is smaller than normal because of a marked reduction in the white pulp owing to absence germinal centers and peri- arteriolar lymphoid sheaths. Peripheral Lymph nodes and internal Lymph nodes may be small and difficult to identify because of the absence of lymphocytes.

X – Linked severe combined immuno deficiency (XSCIA) has been reported in Basset hounds. It has also been observed in Russell terrier and Welsh Corgi breeds of dogs.

2 **Caseous Lymphadenitis**

- (1) Caseous Lymphadenitis: is a specific lymphadenitis of sheep and goats caused by *Corynebacterium Pseudotuberculosis(ovis)*. This organism also causes ulcerative lymphagitis and pectoral abscesses in horses. It is suspected that the organism lives within the intestine and enters the skin through wounds contaminated with soil containing fecal material or purulent discharges. In sheep abscesses occur in superficial lymph nodes and these may rupture and discharge thick, green pus.

The pathogenicity of *C. pseudotuberculosis* is related to the production of heat-labile toxin, which causes increased vascular permeability and which may be identical to the haemolytic phospholipase which the organism produces and a surface lipid which is leukotoxin. The leukotoxin surface lipid allows persistence within inactivated macrophages in which the organism is effectively a facultative intracellular parasite.

Pathogenesis and Pathology

The disease in goat can be more severe than that in sheep, with the most frequent lesion being in the lymph nodes of the head and neck. The disease is widespread in goat and differs from that in sheep in the distribution of the abscesses. In goats the mandibular lymph nodes followed by the parotid L/nodes are most often involved suggesting that the organism is acquired through the bucal mucosa as well as through the skin wound. Lymphadenitis in sheep is almost always follows a wound infection usually a shear wound. The organic can penetrate the intact shin of freshly dehorned sheep and may be transmitted by dipping fluids. Docking and castration wound and

the umbilicus are of minor importance. Occasionally, the infection may be acquired by ingestion, as indicated by confinement of the lesions to the lymph nodes draining the buccal cavity and less commonly the organism is inhaled producing lung abscesses.

Summarily, the sequence of events in progressive caseous lymphadenitis is infection of a superficial wound, spread of infection to the local lymph nodes which suppurate and then lymphogenous and haematogenous extension to produce abscesses in internal organs.

The initial lesion in lymphoid tissues is a diffuse lymphadenitis which is probably the result of the soluble exotoxin. When the organism reaches the nodes, the multiple microscopic abscesses are formed in the cortex. Eosinophils are prominent part of the reaction and give a green colour to the pus. These foci rapidly coalesce and the central mass caseates to form a structure less mass which contains fragments of nuclear material and discrete clumps of bacteria.

The abscesses are rapidly encapsulated, and when this occurs the acute reaction in the surrounding tissues subsides but the abscesses continue to enlarge. With enlargement, there is progressive necrosis and reformation of the capsule which gives the lesion a very characteristic structure of concentric lamellations. Spread from lymph nodes produces lesion in the lungs and these may consist of extensive bronchopneumonia and overlying pleuritis.

The pulmonary lesions consist of extensive bronchopneumonia. When abscesses rupture into bronchi in which there are soft caseopurulent foci, or there may be discrete nodules of varying size and number. In cases of bronchopneumonia, there is a pleuritis, often adhesion. When the adhesions are few and localized adjacent to the nodules, the remaining pleural cavity may be normal. When the adhesions are more diffuse, there is a large amount of serous fluid in the cavities and a thin layer of fibrin on the pleura. The nodular lesions in the lung are similar to those in lymph nodes and have a narrow zone of bronchopneumonia outside the capsule. With time, the pulmonary nodules become sharply circumscribed, encapsulated sub pleural abscesses. The pulmonary lesions are associated with characteristic lesions in bronchial lymph nodes which may be much enlarged. Dissemination of the infection from the lungs to other viscera is uncommon.

Metastases are occasionally observed in the renal cortex as discrete abscesses or descending pyelonephritis. Other viscera chiefly the liver and spleen, may contain solitary abscess of the typical form.

Sequelae

Caseous lymphadenitis is rarely fatal, and in deed it seldom cause debilitation. It economic important is due to regulation concerning the sale of carcass that show evidence of the disease. When fatalities occur, they are cause primarily by large pleuropneumonia and abscesses. resulting in pleuritis, often adhesions are found and localized adjacent to the nodules, the remaining pleural cavity may be normal. Dissemination of the infection from the lungs to other viscera is uncommon.

ANTHRAX

Aetiology: *Bacillus anthracis*, a large gram +ve, spore-forming organism which is highly pathogenic for most herbivorous animals and human, whereas carnivorous animals, bird and reptiles are resistant. In ruminants the disease is usually brief and septicaemic; however, in dogs and pigs, localization in the throat the intestine occurs.

Pathogenesis:

There is an initial lymphangitis and lymphadenitis, which develops into septicaemia, spread to the blood is via the lymphatics as well as lymphovenous

connections within the lymph nodes, and numerous bacilli spread in the lymph from node to node during the filtering mechanism. The bacilli which enter the blood are taken up in other part of the lymphoreticular system, especially the spleen to establish secondary centers of infection and proliferation.

Note: There is notably little response on the part of the susceptible animal to the local establishment of anthrax infection

Pathology of Bovine anthrax

The infection is usually septicaemic and sudden death is the first indication of its presence in a herd.

The carcass of cattle that died of this disease putrefies quickly and becomes very rapidly distended with putrefactive gases, and blood exudates from natural orifices. These changes are not diagnostic.

The anatomic pathology in cattle is characterized by severe splenomegaly, multiple haemorrhage and oedematous effusion in connective tissue. A very large and soft spleen is the most significant lesion and very rarely it is absent. In anthrax, sometimes the enlarged spleen ruptures spontaneously, and when it is incised, the pulp exudes very thick black-red blood which brightens in colour on exposure to air. Smear and histological sections of the affected spleen will reveal large numbers of bacilli if carcass is fresh.

In some cases in which the organism gain entry through the oesophagus there is haemorrhagic lymphagitis of the glands of the throat and oedema of the connective tissue of these regions.

Pathology of ovine Anthrax

Sheep are more susceptible than cattle. Local lesions do not occur except in the unusual instances of percutaneous infection in which the lesion may take the form of a spreading oedema from the outset or initially appear as hard circumscribed nodes. The disease takes the same course as in cattle except that it is more rapid. Splenomegaly is not so prominent in sheep because of the greater level of collagen in the splenic capsule of sheep. The parenchyma is however dark soft and oedematous. Effusion does not occur in sheep.

Horse – Anthrax lasts for several days and is characterized by large swelling which occurs in the ventral part of the abdomen, thorax, and peri-anal region and about the external genital. Septicaemia rarely occurs in Horse. The lesion is localized to the throat and intestine. When septicaemia occurs anatomic pathological changes are the same as that of the cattle.

Streptococcal Adenitis in swine (Jowl abscess)

This is a cervical adenitis caused by *Streptococcus porcinus*. Like in strangles in horse, the deep infection follows colonization of the oral cavity likely the tonsils. The disease has become less common with introduction of better hygiene.

Pathogenesis and Pathology

Transmission occurs through direct contact with infected animals, which can shed organisms for months. Invasion of the nasopharynx is followed by fever and leukocytosis which resolve by lymph node enlargement in 2 weeks. The mandibular lymph nodes are most often involved followed by retropharyngeal and

parotial nodes. It is rarely a fatal disease. Abscesses are usually multiple and measures 1 – 10m indiameter. The pus typically greenish in colour and creamy in consistency and without odour.

In the dog, the disease is similar to what is seen in pigs.

3 Histoplasmosis

The disease is a diffuse disease of the monocyte-macrophage system caused by *Histoplasma capsulatum*. *H. capsulatum* fungus and the parasit phase is yeastlike. It is largely noncontagious disease of humans, dogs, cats, swine, cattle, horses and wild animals.

Pathogenesis: The organism is inhaled and results in a mild-self-limiting infection with hypertrophy of tracheobronchial lymph nodes in asymptomatic dog and cats. Disseminated histoplasmosis in dogs and cats results in gastrointestinal or liver disease of long duration. Disseminated histoplasmosis is characterized by neutrophilia and monocytosis in some animals. Nonregenerative anaemia is common because of chronic inflammation.

Dogs dying of this disease are emaciated. The large bowel is thickened with mucosal corrugations caused by infiltration of the submucosa and lamina propria with macrophages, lymphocytes and plasma cells.

Pathology: The pulmonary lesions of histoplasmosis may be in form of grayish, rounded nodules of 1-2cm in diameter and with a distinct tendency to become confluent, or there may be a diffuse increase in the consistency of the lungs.

The lymph nodes are markedly enlarged but are discrete and without adhesions. There may be no indication of normal architecture on the cut surface, with the uniformity resembling lymphoma. The spleen is enlarged, sometimes to several times its normal size, gray and firm. The liver is uniformly enlarged.

Histologically: There are coalescing granulomas with histiocytosis, and cortical replacement by the reaction. In the spleen there is marked sinus expansion and filling by fixed cells of stromal origin and by colonization with macrophages, many of which contain the invested organisms. In the liver, the infiltrating cells collect in miliary foci in the portal triads and sinusoids, causing extensive displacement and atrophy of the liver parenchyma.

4 Lymphosarcoma

Lymphosarcoma is a significant disease in domestic animals with species variations in aetiology, tumour distribution, clinical and necropsy findings. Animals with lymphosarcoma may or may not be leukaemic i.e have neoplastic cells in bone marrow and blood. In dogs, lymphosarcoma, occurs predominantly in middle-aged animals. It occurs as alimentary, cutaneous, and mediastinal forms, with the multicentric form most common. In all forms of the disease, dogs are anorexic and lethargic, eventually becoming cachectic. The multicentric form leads to generalized enlargement of lymph nodes, with or without hepatic and splenic enlargement and infiltration of bone marrow. Dogs with the mediastinal form are dyspnoic and have reduced exercise tolerance. In the alimentary form, vomiting, diarrhea and blood in the stool are observed. Nodules, plaques and ulcers are present in the skin if

dogs with the cutaneous form of lymphosarcoma. Occasionally, dogs are presented because of polyuria & polydipsia. These dogs have hypercalcaemia, and frequently azotaemia as a result of hypercalcaemic nephropathy. Mild to moderate non-regenerative anaemia is observed and the anaemia may be microcytic and hypochromic because bleeding tumours of the intestines have depleted the iron stores.

Cytology

Aspirates of enlarged lymph nodes show a preponderance of large lymphocytes of uniform morphology. These cells are usually fragile, and as a result the aspirate may contain numerous naked nuclei and free cytoplasmic fragments. The nuclei in intact cells are large with a mantle of scant coarse cytoplasm. Nuclear chromatin is finely stippled and rectangular and triangular nucleoli are common

Necropsy finding in canine lymphosarcoma varies with the form of the disease. When lymph nodes are enlarged, they are white-gray and bulge when incised. Similar lesion is frequently present in the spleen and liver.

5. MYELOPROLIFERATIVE DISORDERS

The myeloproliferative disorders refer to neoplastic transformation of one or more of the descendants of the myeloid stem cell. These disorders may result in release of abnormal cells into peripheral circulation or may pancytopenia because of the interference with haemopoiesis. Frequently there is combination of abnormal haemopoiesis and leukaemia. Neoplasm of one myeloid cell line cause impaired differentiation within that population and may interfere with differentiation and maturation of other cell lines.

LEUKAEMIAS

Leukaemias arise when normal bone marrow cells acquire somatic mutations that confer a selective growth advantage on the mutated cells. Leukaemic cell proliferation may be driven by cytokines such as IL-1 and tumor necrosis factor. The tumor cells may produce their own growth factors or induce production of growth factors by neighboring cells. The leukaemias have been classified as acute or chronic based on clinical course and degree of differentiation of the neoplastic cells. The acute myeloid leukaemias, because of poor differentiated cells in the blood and bone marrow, are difficult to classify and to differentiate from lymphocytic leukaemias.

Acute Leukaemias

a. **Acute Myelogenous Leukaemias (M1 and M2).** They are sub classified into acute myeloblastic leukaemias without maturation (M1) and with maturation (M2) The latter have a greater number of cells with a few cytoplasmic granules typical of immature promyelocytes. Affected dogs and cats are usually in good condition. Affected dogs and cats are usually in good condition. Some may show evidence of bleeding such as epistaxis

b. **Promyelocytic Leukaemias (M3)** is a rare neoplasm of dogs and cats.

c. **Myelomonocytic leukaemias (M4)** is a concurrent leukaemia of neutrophil and monocyte precursors

d. **Monocytic Leukaemia (M5)** occurs infrequently in dogs, cats, horses and cattle. Affected

Animals have recent weight loss, anorexia, and depression.

2. Malignant Histiocytosis

Malignant histiocytosis is a disease of dogs and cats characterized by neoplastic proliferation of macrophages in many organs including the skin (see Chapter 11). Dogs with malignant histiocytosis may have anorexia, weight loss, lethargy, and anaemia.

Generalized lymph node enlargement is common.

3. Erythrocytic Sarcoma

Erythrocytic sarcoma (M6) (erythremic myelosis) in cats is characterized by lethargy, pallor, and a variety of hematologic abnormalities including a severe, nonregenerative anemia with hematocrits as low as 0.06 L/L (6%).

4. Megakaryoblastic Leukemia

Megakaryoblastic leukemia (M7) is a rare disease of dogs and cats. There is usually a rapid clinical course with variable degree of pancytopenia.

5. Plasma Cell Sarcoma

Plasma Cell Sarcoma (Plasma cell myeloma)

Plasma cell sarcoma is not common but does occur in dogs and cats. There are two basic disease mechanisms in animals with plasma cell sarcoma; one is caused by neoplastic cell proliferation the others is the result of protein released from the neoplastic plasma cells. Although plasma cell neoplasm has been described in other tissues, most reside in the bone marrow where they interfere with haemopoiesis and erode endosteum of the bone by focal osteolysis. Although the lymph nodes and the lamina propria of the gut are the richest sources of normal plasma cells, they are not the sites where plasma cell sarcomas occur. The bone marrow microenvironment possesses distinct mechanism for capturing genetically abnormal pre-B-lymphocytes via stromal adhesive proteins and nurturing their differentiation into a population of plasma cells no longer capable of division or travel.

Cytokines produced by the neoplastic plasma cells and others by bone marrow stromal cells favour preferential proliferation of the neoplastic cells. IL-6 produced by bone stromal cells, is particularly important in the recruitment of abnormal pre-B-lymphocytes and co-ordination of the cytokines which is responsible for their maturation. It also promotes longevity of the tumour cells by delaying apoptosis. It abnormally plays a central role in co-ordinating the cytokines responsible for osteoblastic activity and in this promotes localized bone resorption and to accommodate the expanding tumour.

Laboratory Features of plasma cell sarcoma includes

(a) Hyperglobulinemia: This is a consistent finding; only small number myelomas are nonsecretory. A monoclonal, marrow based globulin spike is found in the β or δ regions of the electrophoretic-gram.

(b) Anaemia due to myelophthisis, dilution of erythrocyte mass by increased plasma volume resulting from increased plasma osmotic pressure, and shortened erythrocytes life span caused by coating of erythrocytes with protein and subsequent phagocytosis.

(c) Thrombocytopenia and leucopenia as a sequel of myelophthisis.

(d) Platelet dysfunction caused by binding with abnormal immunoglobulin.

(e) Hypercalcaemia resulting from tumour releases of osteoclast activating factor (tumour necrosis factor) and bone resorption, and paraprotein (Abnormal Ig)-Binding of ionized calcium, causing PTH secretion to replenish the ionized calcium.

(f) Azotaemia: - due to increased BUN.

(g) Hyperviscosity of plasma due to polymerization of some IgA and rare IgG forms to form high molecular weight complexes.

At necropsy, plasma cell sarcomas appear as soft gelatinous pink to red masses in bone marrow spaces including those of the vertebrae. Neoplasms may erode bone and extend into the surrounding soft tissue.

Microscopically, the tumours are composed of sheets of atypical to well differentiated plasma cells