PATHOLOGY OF HEMATOLYMPHOID SYSTEM NON-NEOPLASTIC WBC DISORDERS

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WHITE BLOOD CELL DISORDERS

- Disorders include deficiency (leukopenia) and proliferation (leukocytosis)
- Leukocytosis: increased number of WBC in peripheral blood (any cause). If benign, it is called reactive leukocytosis (benigns, chronics)
- Leukemia: increased number of WBC in peripheral blood secondary to neoplastic disease (↳ secondary to a stimulus as a reaction / Idiopathic)
- Leukocytosis is more common than leukopenia
- Reactive leukocytosis is more common than leukemia

RBCs disorders: Anemia more common than polycythemia

NEUTROPENIA/ AGRANULOCYTOSIS

Low Neutrophil Count
more serious than Neutrophilia

- Patients become susceptible to infections (namely bacterial and fungal)
- If neutrophil count drops below 500 cells/uL → spontaneous infection by the normal bacteria in the body.
- Decreased production: aplastic anemia, myelophthisic anemia, myelodysplastic syndrome, advanced megaloblastic anemia, chemotherapy, drugs (anti-epileptic, anti-hyperthyroidism)
  ↳ patients with these medicines should routinely check their WBC count.
- Increased destruction: immune mediated, splenomegaly, overwhelming bacterial, fungal or rickettsial infections
  ↳ systemic lupus erthymatosis
  ↳ The organism destroy the neutrophils

→ In case of hemolitic anemia when it's sever it will lead to destruction of leukocytes.

REACTIVE LEUKOCYTOSIS

Neutrophilia leads to leukocytosis / it's has the greatest ratio in WBCs

- Neutrophilia: infections, inflammation (necrosis) — 1st Most common cause of leukocytosis
- Lymphocytosis: vial infections, Bordetella pertussis infection, chronic infections (TB, brucellosis) — 2nd — In Children more common than neutrophilia.
- Monocytosis: chronic infections, rheumatologic diseases, inflammatory bowel disease — 3rd — non-specific → Acute / chronic → more common — ant inflamations
- Eosinophilia: asthma, allergic diseases, drug sensitivity, parasitic infections, Hodgkin lymphoma (neoplastic) — specific diseases vs general — worms
- Basophilia: rare, seen in myeloproliferative neoplasms — like P.Vera.

REACTIVE LYMPHADENITIS

↳ benign
↳ Antigenic

- Antigenic stimulation in lymph nodes
- Causes lymph node enlargement (lymphadenopathy)
- Can be localized or generalized

↳ in certain area of lymph nodes

↳ Can either be benign or malegnant

ACUTE NON-SPECIFIC LYMPHADENITIS

↳ usually follows an acute infection

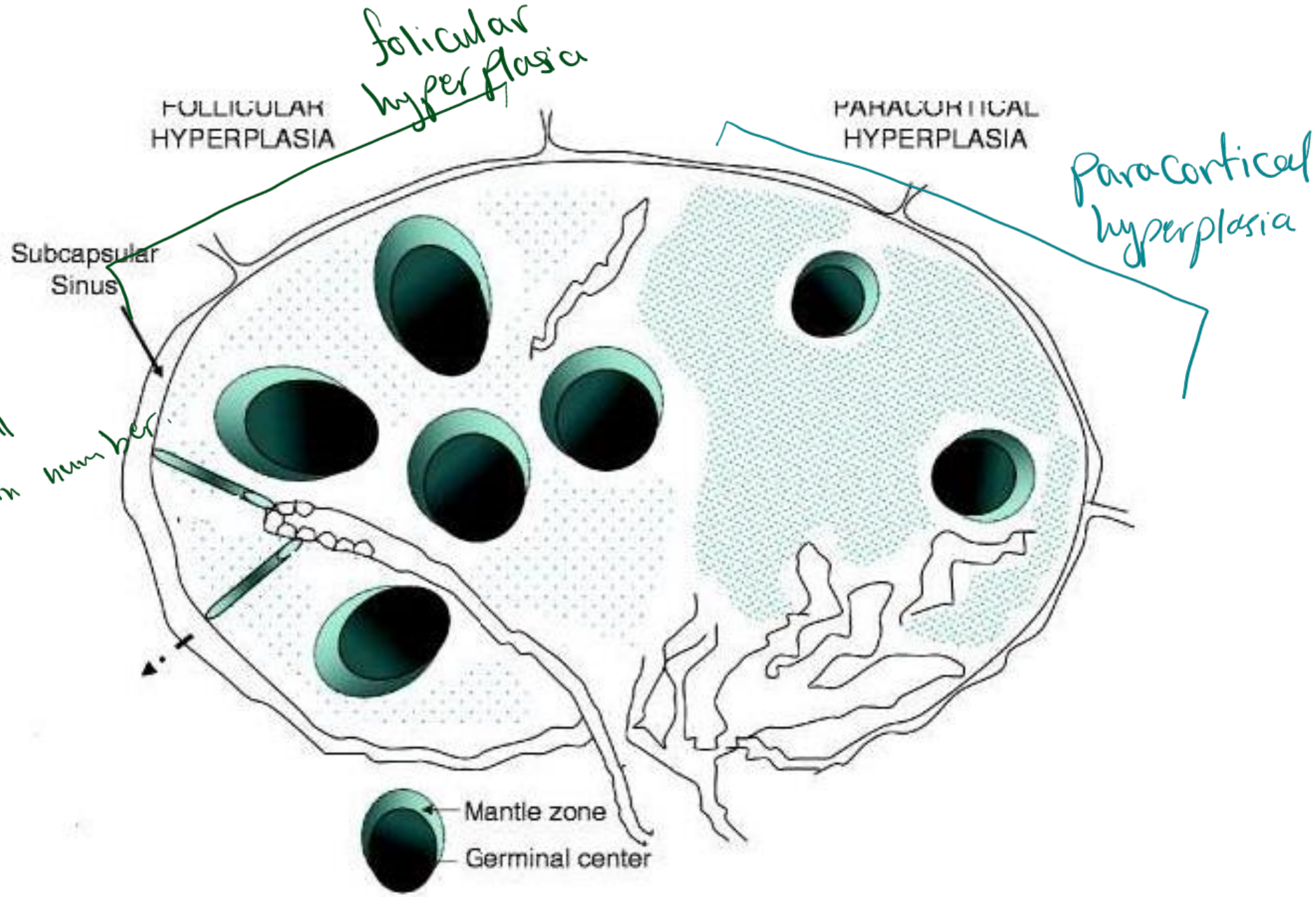
- Swollen, enlarged and painful lymph nodes
  - ↳ Rapid enlargment → stretch the nerves around the lymph nodes → Painful
  - In chronic cases stretching occure gradually so it's painless.
- Overlying skin is red and may develop a sinus tract
  - ↳ In very sever cases
  - ↳ tract of inflamatory cells from the lymph node to skin.
- The germinal centers in the lymph node are enlarged, and crowded infiltrated by neutrophils. With severe infection, liquefactive necrosis develop and may enlarge to form an abscess.
  - ↳ not common in lymph nodes
  - → liquid like tissue due to necrosis.
  - ↳ Histological term
  - ↳ Medical term
  - ↳ formation of a mass of tissue.

CHRONIC NON-SPECIFIC LYMPHADENITIS

- Chronic enlargement of lymph node, painless → Benign
- Follicular hyperplasia: chronic proliferation of B-lymphocytes, seen in rheumatologic diseases, toxoplasmosis and HIV infection → Affects CD-4
- Paracortical hyperplasia: proliferation of T-lymphocytes, seen in viral infections (example EBV), after vaccination and drug reaction + peripheral blood eosinophilia.
- Sinus histiocytosis: proliferation of macrophages in lymph node sinuses, seen in adjacent cancer

3 types
most common
least common

☆ Breast carcinoma → larg lymph nodes in the axilla.
↳ does not indicate metastasis.



follicular hyperplasia

paracortical hyperplasia

* lymphatic follicles will increase in number

CAT-SCRATCH DISEASE

- Bartonella henselae
- Transmitted from cats (bite, scratch, infected saliva) — special young cats
- Most commonly in children and young adults
- Causes acute lymphadenitis in neck/axilla area — painful
- Symptoms appear after two weeks of infection — incubation period
- Bacteria causes liquefactive necrosis and necrotizing granulomas in lymph nodes — seen in TB infection but not specific, can also be seen in fungal infections and in Cat Scratch Disease.
- Mostly self-limited in 2-4 months, rarely can disseminate into visceral organs — mild, can be treated by antibiotics

The special about Cat scratch disease

Visceral infection → more sever

HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS

↳ Phagocytosis of RBCs → Anemia along with lymphohistocytosis

- HLH is uncommon disease Life threatening
- Viral infection or other inflammatory agents activate macrophages (histiocytes) throughout body to engulf normal blood cells and their precursors in bone marrow
- Patients have defective genes related to the function of cytotoxic T-cells and natural killer cells, thus they are engaged with their target (virus-infected cells) for a long period and release excess interferon-γ that activates macrophages
- Activated macrophages release TNF and IL-6 that causes systemic symptoms of inflammation (systemic inflammatory response syndrome "SIRS")

So they take longer time to kill the cells they engage with. → Sever Inflamation and response in the body.

HLH-TYPES

- 1) Infants and young children who are born with a
- Homozygous defects in gene PRF1 that encodes perforin
- An essential enzyme in cytotoxic T-lymphocytes and natural killer cells , perforates the cell membrane of the infected cell.

HLH-TYPES

- 2) Adolescents and adults
- X-linked lymphoproliferative disorder (males)
  most common in males
- Defective Signaling lymphocyte activation molecule (SLAM)-associated protein
- Inefficient killing of EBV-infected B-lymphocyte

HLH-TYPES

no infection

- 3) May be associated with systemic inflammatory disorders such as rheumatologic diseases
- Patients have heterozygous genetic defects in genes required for cytotoxic T-cells

↳ unknown exactly what genes are they

HLH-TYPES

- 4) T-cell lymphomas
- Malignant T-cells produce aberrant cytokines leading to dysregulation of normal cytotoxic T-cells

→ Not functioning well → more engagment and activation of macrophages

SYMPTOMS

Rapid Symptoms

- Fever, splenomegaly and pancytopenia
  - due to inflammation
  - And hepatomegaly
- High ferritin
  - as an inflammatory marker
- High triglyceridemia
  - unknown exactly how but thought to be secondary to liver dysfunction : hepatomegaly → Abnormal metabolism of lipids → more secreation of triglycerides in blood.
- High serum IL-2
- Low level of blood cytotoxic T-cells and natural killer cells
- Diagnosis → BM: numerous macrophages engulfing RBCs, platelets and granulocytes