PATHOLOGY OF HEMATOLYMPHOID SYSTEM NON-NEOPLASTIC WBC DISORDERS

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WHITE BLOOD CELL DISORDERS

reactive, in response to a primary disease (infection)
neoplastic, leukemia

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

reduction in no. of granulocytes

if severe,

NEUTROPENIA/ AGRANULOCYTOSIS

no — mostly neutrophils

- Patients become susceptible to infections (namely bacterial and fungal)
- If neutrophil count drops below 500 cells/uL → spontaneous infection by microflora (higher risk for infections)
- Decreased production: aplastic anemia, myelophthisic anemia, myelodysplastic syndrome, advanced megaloblastic anemia, chemotherapy, drugs (anti-epileptic, anti-hyperthyroidism) (suppress granulocytopoiesis)
- Increased destruction: immune mediated (SLE, ABs against WBCs), splenomegaly (leads to sequestration and rapid removal of neutrophils), overwhelming bacterial, fungal or rickettsial infections (causing marrow hypercellularity)

Pathogenesis

increased peripheral utilization

commonest ← مرتين حسب

REACTIVE LEUKOCYTOSIS

inflammatory states, microbial or non-microbial

- Neutrophilia: infections, inflammation (necrosis)
  - acute bacterial (pyogenic) → sterile
  - → MI, burns
- Lymphocytosis: vial infections, Bordetella pertussis infection, chronic infections (TB, brucellosis)
  - infectious mononucleosis, EBV
  - accompanies monocytosis in chronic immunologic stimulation like TB and Brucellosis
- Monocytosis: chronic infections, rheumatologic diseases, inflammatory bowel disease
  - non-specific, in acute and chronic (more common)
  - TB, malaria
  - autoimmune
  - (ulcerative colitis, chron's)
- Eosinophilia: asthma, allergic diseases, drug sensitivity, parasitic infections, Hodgkin lymphoma
  - specific
  - worms, helminths
- Basophilia: rare, seen in myeloproliferative neoplasms (CML + Polycythemia vera)

Benign, normal response to an antigen

REACTIVE LYMPHADENITIS

- Antigenic stimulation in lymph nodes
  - Infections or non-microbial inflammatory stimuli
- Causes lymph node enlargement (lymphadenopathy)
  - Any immune response against foreign antigens
  - palpable
- Can be localized or generalized
  - neck, axilla...

ACUTE NON-SPECIFIC LYMPHADENITIS

gradual

by streching of nerves around it / chronic is painless

either a group of nodes draining a specific region, or generalized systemic infections

- Swollen, enlarged and painful lymph nodes
- Overlying skin is red and may develop a sinus tract

tract of inflammatory cells from LNs to skin

- The germinal centers in the lymph node are enlarged, infiltrated by neutrophils. With severe infection, liquefactive necrosis develop and may enlarge to form an abscess.

Inflamed nodes in acute nonspecific lymphadenitis are swollen, gray-red, and engorged. Histologically, there are **large germinal centers** containing numerous mitotic figures. When the cause is a pyogenic organism, a neutrophilic infiltrate is seen around the follicles and within the lymphoid sinuses. With severe infections, the centers of follicles can undergo necrosis, leading to the formation of an abscess.

digestion of cellular structures by neutrophilic enzymes

pus

collection of Pus

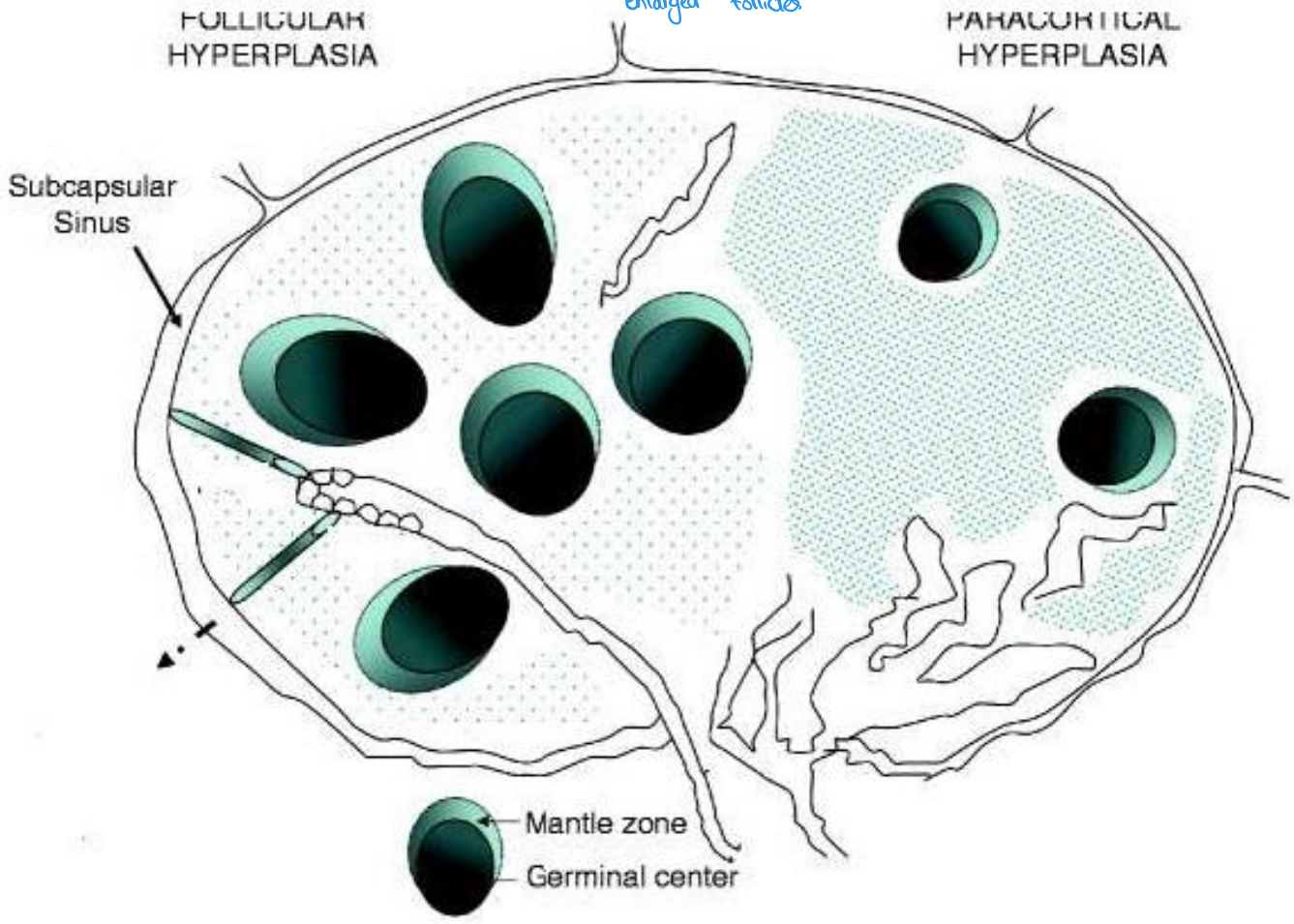
CAT-SCRATCH DISEASE

- Bartonella henselae Bacterium, Extracellular
- Transmitted from cats (bite, scratch, infected saliva)
- Most commonly in children
- Causes acute lymphadenitis in neck/axilla area → self-limited; Painful
- Symptoms appear after two weeks of infection — incubation period
- Bacteria causes liquefactive necrosis and necrotizing granulomas in lymph nodes — like in TB
- Mostly self-limited in 2-4 months, rarely can disseminate into visceral organs

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 — creating germinal centers; infect T cells, but proliferation of B cells
- Paracortical hyperplasia: proliferation of T-lymphocytes, seen in viral infections (example EBV), after vaccination and drug reaction — in the paracortex, effacing the B cells follicles; in blood ↑ eosinophilia, LNs ↑ T cell proliferation
- Sinus histiocytosis: proliferation of macrophages in lymph node sinuses, seen in adjacent cancer — lymph nodes draining cancer; an immune reponse to tumor antigens; not a metastasis

follicular hyperplasia
⇓
enlarged follicles



Phagocytosis of RBCs → Anemia

Inflammation (proliferation of lymphocytes and histiocytes)

HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS

- HLH is uncommon disease (life threatining)
- 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 (severely)
- Activated macrophages release TNF and IL-6 that causes systemic symptoms of inflammation (systemic inflammatory response syndrome "SIRS") (fever, tachypnea, tachycardia, hypotention and leukocytosis)

HLH-TYPES

- 1) Infants and young children
- Homozygous defects in gene PRF1 that encodes perforin
- An essential enzyme in cytotoxic T-lymphocytes and natural killer cells

becomes less effecient → longer engagment with infected cells

HLH-TYPES

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

must be exposed to EBV to develop HLH

HLH-TYPES

without an 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

HLH-TYPES

not an infection

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

SYMPTOMS

- Fever, splenomegaly and pancytopenia
- High ferritin (inflammatory marker)
- High triglyceridemia
- High serum IL-2
- Low level of blood cytotoxic T-cells and natural killer cells
- BM: numerous macrophages engulfing RBCs, platelets and granulocytes