Patholog

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Lympho-Reticular System

First and Second Lectures

Two main parts:

1. Primary lymphoid organs : Bone Marrow + Thymus.
2. Secondary lymphoid organs : Lymph Nodes, Spleen, Tonsils and Mucosa- associated lymphoid tissue MALT (in many organs such as GIT, respiratory, urinary and reproductive tracts).

Lymph Node Histology : Is Dynamic

- Lymph Node ; normally, is Bean-like, small and not palpable

  Less than (5 mm) in size.
- Cortex : Lymphoid follicles of B-lymphocytes
- Para cortex : T-lymphocytes and post – capillary venules.
- Medulla : Sinuses and medullary cords which are containing :

  (B-lymphocytes, plasma cells and macrophages).

  Over 600 Lymph Nodes in the Body

Diseases of Lymph Nodes

All diseases of lymph Nodes are presented with lymph node enlargement which is called Lymphadenopathy (LAP) and includes two groups :

1. Reactive and Inflammatory Diseases (LAP).
2. Neoplastic Diseases (LAP). (Lymph node is larger than 1cm in size)

Reactive and Inflammatory LAP

1. Acute Non-Specific Lymphadenitis:

- ✓ Acute bacterial infection *by* *Strepto – pyogenus* and *Staph – aureus*
- ✓ Lymph node is enlarged, painful and tender.
- ✓ Abscess formation such as inflammation of cervical lymph nodes in Acute Tonsillitis and Pharyngitis, especially in children.
- ✓ Return to normal after infection subsides.

2. Chronic Non-specific Lymphadenitis :

- Common in axillary and inguinal lymph nodes.
- Lymph node is Painless and Not – Tender.
- Two morphological patterns by M/E :
  - Follicular Hyperplasia.
  - Sinus Hyperplasia (Sinus Histiocytosis).
  - Mixed Follicular and Sinus Hyperplasia.

Follicular Hyperplasia (B-cell Hyperplasia)

- ☒ L.N. is enlarged with numerous follicles have prominent germinal centers which are called (Secondary Follicles).
- ☒ It is not specific disease and has many causes : Examples
  - Regional L.N. draining chronic lesions (IBD and Peptic ulcer).
  - Rheumatoid arthritis.
  - HIV-infection.

Sinus Hyperplasia (Sinus Histiocytosis)

- Dilatation and distention of sinuses by large numbers of Histiocytes and Macrophages. It has many causes (non-specific) such as :
- Regional L.N. draining chronic infection (Foot Infection + Inguinal LAP).
- Malignancy (Breast Carcinoma + Axillary LAP).
- Whipple Disease.

3. Granulomatous Inflammation (Granulomatous Lymphadenitis):

One of the common cause of LAP

a. Infection: common cause

TB (commonest), Atypical Mycobacterial Infection, Leprosy, Syphilis, Toxoplasmosis, Leishmaniasis, Brucellosis, Fungal Infection, Tularemia, Chlamydial Infection, Cat – Scratch Disease and Mesenteric Lymphadenitis by (*Yersinia pseudotuberculosis*) .

b. Unknown Etiology: Sarcoidosis and Crohn Disease.

c. Malignancy: Lymph Nodes are draining areas of carcinomas and lymphomas (Hodgkin Lymphomas and Non-Hodgkin lymphomas).

Neoplastic LAP

1. Metastatic (Secondary) Tumors
2. Malignant Lymphoma : Two Types
    a. Hodgkin Lymphoma (HL)
    b. Non-Hodgkin Lymphoma (NHL)

1. Metastatic Tumors

- Most common tumors of lymph nodes are Metastatic Tumors. Lymph nodes are most common sites of metastasis for :
    - All carcinoma (Except Basal Cell Carcinoma).
    - Some Sarcoma.
    - Malignant Melanoma.

2. Malignant Lymphoma (ML)

- Most common Primary Tumor of Lymphoreticular System is Malignant Lymphoma with formation of Tissue Masses.
- Bone marrow involvement can be either at the beginning or as evolution of lymphoma to leukemia.

- All Lymphomas are Malignant.
- Some are High- grade and fatal.
- Others are low-grade with long survival.
- Most arise from lymphocytes, mainly occurs in Lymph Nodes but can occur in Spleen, BM, Thymus, Tonsils, Pharynx, GIT, Skin and CNS (Nodal or Extra nodal sites of involvement) .

Classification of Lymphomas

Two major types :

1. Hodgkin Lymphoma (HL)
2. Non-Hodgkin Lymphoma (NHL)

Hodgkin Lymphoma

☒ It is first type of ML described by Thomas Hodgkin (1832) then Sternberg (1898) and Reed (1902) who described characteristic neoplastic giant cell of HL, which is called Reed- Sternberg Cell (RS-Cell).

☒ HL 25-30% of ML Male > Female.

☒ Bimodal age distribution (Peak 15-40 years) and (Peak 50-70 years).

☒ Definition: Type of lymphoma in which Typical or Classical Reed - Sternberg Cells (RS-Cells) are present in a characteristic background of Reactive Inflammatory Cells of various types, accompanied by variable degree of Fibrosis depending on the subtypes of HL.

☒ Causes: Unknown, EB- virus, HIV and Genetic factors.

Clinical Features :

❖ Painless, Not Tender and Firm-Rubbery Enlarged L.N. (LAP).

❖ Commonly involves Cervical lymph nodes, followed by Axillary, Inguinal and Mediastinal lymph nodes.

❖ Extra nodal HL is very rare (Commonly Nodal HL).

- Sometime symptoms (B – Symptoms in advanced disease).
  - Fever > 38°c, Weight loss > 10 % in 6 months.
  - Night sweating, Anemia (Pallor) and Pruritus.
- Spleen ➔ frequent involved and enlarged (Splenomegaly)
- Liver and Bone Marrow may be involved.

Diagnosis of Hodgkin Lymphoma

- ✓ Microscopical examination of enlarged lymph node (L.N. Biopsy).
- ✓ L.N. architecture is completely destroyed by two essential features :
  1. Classical (Typical) Reed- Sternberg Cells.
  2. Inflammatory Reactive Background of Lymphocytes, Eosinophils, Plasma cells, Neutrophils and Macrophages.
  3. Fibrosis.
- ✓ Granuloma sometime present in lymph nodes or other organs.

Classical (Typical) Reed – Sternberg Cells (RS-Cells) :

- Large (giant) cell (20 – 50 µm).
- Binucleate cell (Two nuclei) or bilobed nucleus.
- Thick nuclear membrane.
- Nucleus is vesicular.
- Large central round eosinophilic nucleolus surrounding by clear -halo.
- Mirror –image nuclei or owl – eye appearance .
- Cytoplasm is abundant and pinkish.
- B-cell in origin, CD15 positive and CD30 positive.

Variants of Reed – Sternberg Cells (RS-Cells):

- ☒ Hodgkin cells: Mononuclear Reed-Sternberg cells (single nucleus).
- ☒ Lacunar cells: Single multi-lobated nucleus and shrinkage cytoplasm lying within clear space or lacuna.
- ☒ Popcorn cells: Lymphocytic -Histiocytic cells, folded nucleus (L&H cell).

Classification of Hodgkin Lymphoma

WHO classification in 2008 / Updated 2016 – 2017

Histological subtypes depend on:

- ❖ Inflammatory Background.
- ❖ Reed-Sternberg cell variants.
- ❖ Fibrosis.

Classification of Hodgkin Lymphomas (HL):

1. Classical / Classic Hodgkin Lymphoma :
   - Nodular Sclerosis Subtype / Classic HL
   - Mixed Cellularity Subtype / Classic HL
   - Lymphocyte – Rich Subtype / Classic HL
   - Lymphocyte – Depletion Subtype / Classic HL
2. Non- Classical Hodgkin Lymphoma :
   - Nodular Lymphocyte-Predominant HL

1. Classical /Classic Hodgkin Lymphoma

A. Nodular Sclerosis Subtype HL :

- ✓ Commonest subtype in west (65 -75% of HL).
- ✓ Adolescents and Young Adult, Male = Female.
- ✓ Lower cervical, Supraclavicular and Mediastinal LAP.

- ✓ M/E :
    - Wide bands of fibrosis divide lymph node into Nodules.
    - Many Lacunar cells.
    - Classical RS- cells are present.
- ✓ Prognosis is Excellent.

B. Mixed cellularity Subtype HL :

- ✓ 20 – 25 % of HL in western countries.
- ✓ Commonest subtype in 3rd world including Iraq.
- ✓ More common in male.
- ✓ Commonly related to EBV and HIV.
- ✓ M/E :
    - Numerous Classical RS – cells and Hodgkin cells.
    - Mixed inflammatory background of eosinophils, plasma cells, lymphocytes and macrophages.
- ✓ Intermediate to good prognosis.

C. Lymphocyte – Rich Classical Subtype HL :

- ✓ 5% of HL.
- ✓ M/E :
    - Lymphocyte predominant background.
    - Few Classical RS – cells are present.
- ✓ Relapse is very rare.
- ✓ Prognosis is very good to excellent.

D. Lymphocyte-Depletion Subtype HL :

- ✓ Least subtype (1% of HL).
- ✓ Old male, related to EBV.
- ✓ Affect abdominal and pelvic lymph nodes.
- ✓ M/E :
    - Numerous Atypical RS-cells with Fibrosis.
    - Few Lymphocytes.
    - Diffuse Fibrosis (Not Band- like Fibrosis)
- ✓ Prognosis is very poor and advanced stage (Stage III-IV).

2. Non- Classical Hodgkin Lymphoma

Nodular Lymphocyte-Predominant HL :

- ✓ 5 % of HL.
- ✓ Young male.
- ✓ Commonly cervical or axillary LAP.
- ✓ M/E :
    - Nodular growth pattern but without Fibrosis.
    - Small Lymphocytes and Histiocytes (L & H cells).
    - Numerous Popcorn cells are present.
    - No Classic RS -cells.
- ✓ Prognosis is Excellent.
- ✓ Majority of the patients are at stage-I.
- ✓ Frequent relapses.