Non-Hodgkin Lymphoma

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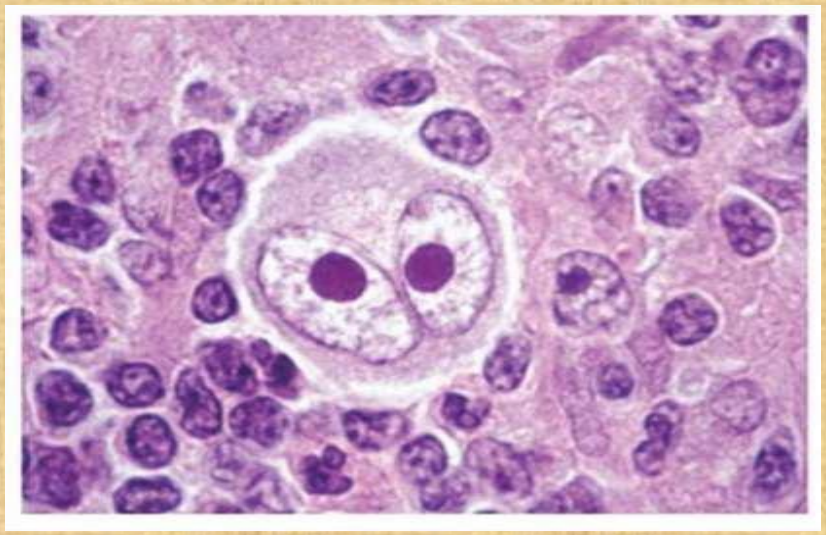
Introduction

- lymphoma → primary malignant tumor of lymphoid tissue (nodal & extranodal)
- Types →



Reed-Sternberg cell

- If present → Hodgkin lymphoma
- If absent → Non-Hodgkin lymphoma

Introduction

- ***Cells of origin*** → lymphoid cells of B cell origin (80%) or Tcell origin (20%)

- ***Epidemiology***
  - The incidence of NHL is 5-15/ 100000 per year
  - 3rd most frequently diagnosed cancer in males and 4th in females
  - The median age of presentation is 55 – 75 years
  - There is a slight male predominance.

Aetiology

NHLs may result from chromosomal translocations, infections, environmental factors, immunodeficiency states, and chronic inflammation.

- ***Chromosomal translocations***

Chromosomal translocations and molecular rearrangements play an important role in the pathogenesis of many lymphomas

Example: The **t (14:18)** translocation is the most common chromosomal abnormality associated with NHL. This translocation occurs in 85% of follicular lymphomas and 28% of higher-grade NHLs.

Aetiology

- ***Infections***
  - Epstein-Barr virus (EBV) which is associated with Burkitt lymphoma and T-cell lymphomas in immunocompromised patients.
  - Also, Herpesvirus, Hepatitis C virus (HCV), HIV and human T cell lymphotropic virus are associated with NHL.
  - Helicobacter pylori → gastric MALT lymphoma.
- ***Environmental factors***
  - Chemicals (eg, pesticides, herbicides, solvents, organic chemicals, hair dye)
  - Chemotherapy
  - Irradiation exposure

Aetiology

- ***Immunodeficiency states***
  - Congenital and acquired immunodeficiency states
  - Induced immunodeficiency states eg, immunosuppressive therapy, HIV, chemotherapy post-organ transplantation
  - Celiac disease has been associated with increased risk of malignant lymphomas
- ***Chronic inflammation***
  - autoimmune disorders, such as Sjogren syndrome and Hashimoto thyroiditis promotes the development of MALT lymphoma.

Classification

Mature B cell lymphomas	Mature T-cell and natural killer (NK) cell lymphomas
• *Diffuse large B cell (37%)* • *Follicular (29%)* • *MALT lymphoma (9%)* • *CLL/SLL (12%)* • *Mantle cell lymphoma (7%)* • *Burkitt lymphoma (0.8%)*	• *Primary T cell lymphoma NOS (29%)* • *Angioimmunoplastic lymphoma (18%)* • *Extranodal T cell or NK lymphoma (10%)* • *Adult T-cell lymphoma or leukemia* • *Anaplastic large cell lymphoma* • *Primary cutaneous lymphoma*

Clinical Features

Peripheral lymphadenopathy

- H/O of Multiple body swellings at anatomical sites of L.Ns
- Criteria → painless, progressive lymph node enlargement in most of cases
- pain at sites of nodal disease, precipitated by drinking alcohol, occurs in fewer than 10% of patients
- Unlike HL, NHL is often widely disseminated or multicentric at presentation
- NHL is more likely to be advanced stage at presentation

Clinical Features

- **B symptoms**

- More common than in Hodgkin lymphoma

- Their presence indicate advanced stage and poor prognosis.

1 Fever(>38^C)

-May first present as fever of unknown origin.

-Fever persists for days to weeks followed by afebrile intervals and then recurrence. This pattern is called Pel-Ebstein fever.

2 Recurrent drenching night sweats

3 Unexplained significant Weight loss (>10% in 6 months or less)

Clinical Features

Extranodal involvement

- More common than in Hodgkin lymphoma
- In more than one third of patients especially in high grade NHL
- May be present at the initial presentation
- The most common extranodal sites →

  GIT, GU, CNS, lung, bone marrow, thyroid, and skin

Clinical Features

Compression symptoms

- GI lymphoma → GIT obstruction & perforation
- CNS lymphoma → neurological manifestations
- Vertebral metastases → spinal cord compression
- Large bulky mediastinal tumor → SVC syndrome →
  - Dyspnea is the most common symptom
  - Dysphagia, hoarseness of voice, Cough, Chest pain
  - Facial & arm swelling, congested neck veins
  - Patients with cerebral edema may have headaches, confusion, or possibly coma,

Diagnosis

- History Taking :-

- Swellings (peripheral lymphadenopathy)
- B symptoms
- Previous infection
- Immune deficiencies
- Exposure to toxins
- Familial

Diagnosis

- Examination :-

  - Lymph nodes enlargement

    (size, number, location, consistency, fixed or not, tender or not, skin overlying)

    → large, hard, fixed, amalgamated

  - Hepatosplenomegaly
  - Skin involvement → erythema nodosum
  - Pulmonary findings
  - Neurological signs

Diagnosis

- Laboratory investigations :-

1 CBC with differential count and blood film

- Normal/ NNA/ Lymphopenia/ Lymphocytosis/ Eosinophilia

2 ESR

Usually raised / Indicator of disease activity

3 Liver Biochemistry

- Often abnormal with or without liver involvement

- Cholestatic Jaundice in LN of porta hepatis inv**olvement**

Diagnosis

- Laboratory investigations :-

4 Serum LDH

Raised level is adverse prognostic factor

5 Serum uric acid

Normal or raised (Tumor lysis syndrome)

6 Serum calcium

Raised (high osteoclastic activity)

Diagnosis

- Laboratory investigations :-

6 Renal function and Electrolytes

7 Virology: HIV, hepatitis B and C

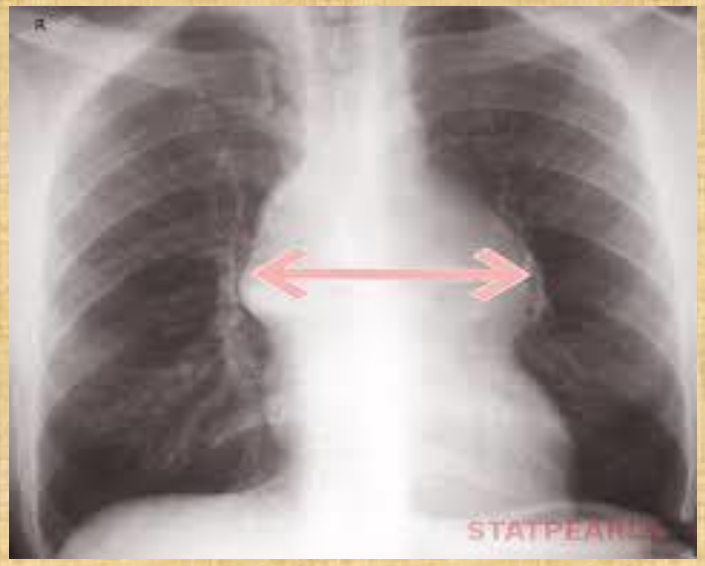
- HIV predisposes to NHL

- when potentially immunosuppressive therapy is to be recommended.

Diagnosis

- Imaging :-

1 Chest X-ray for mediastinal widening



2 CT scan of chest, abdomen, pelvis ± neck

It is the investigation of choice for staging

Diagnosis

3 PET scan a functional imaging technique

It is the investigation of choice for →

- detecting disease activity during and after treatment,

- detect relapse

- accurate staging of the patient and

- to establish sites of extranodal disease

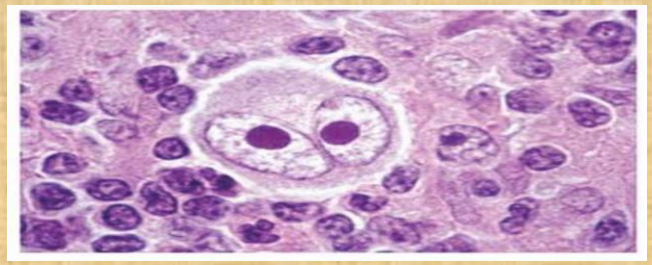
4 Cardiac evaluation (ECG, Echo)

Diagnosis

- Histopathological diagnosis :-

Lymph node or extranodal disease biopsy, is required for a definitive diagnosis (the gold standard investigation)

- Absence of →



- Immunophenotyping

CD30 → in anaplastic large cell lymphoma

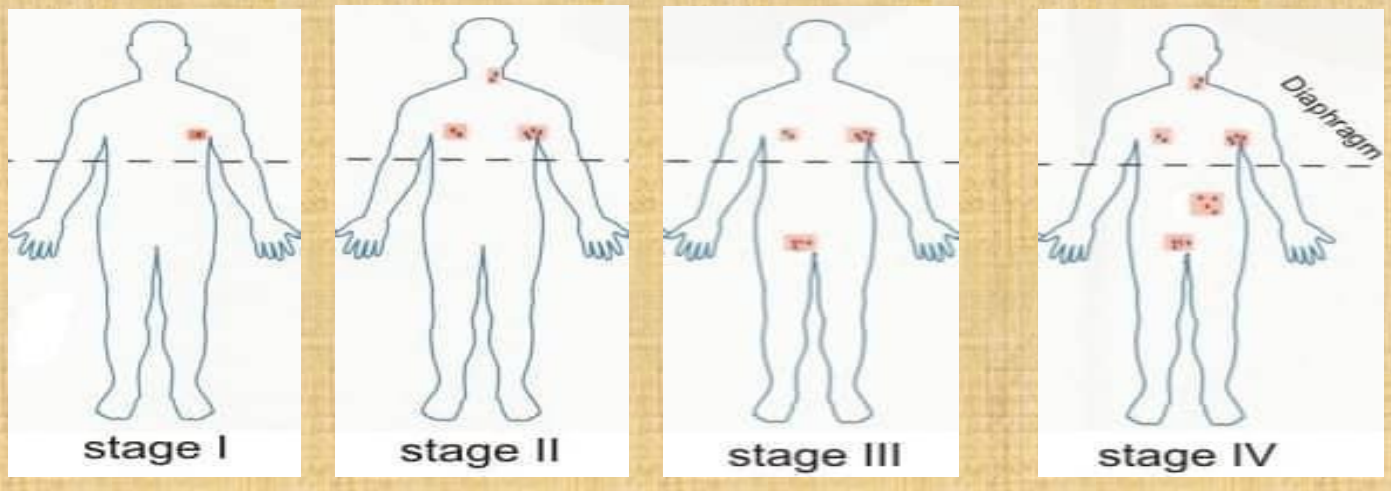
- BM examination :-

BMA & BMB are routinely recommended mainly for staging rather than for diagnosis

Staging (Ann Arbor staging system)

Stage	Description
I	Single LN region or extranodal lymphatic structure (spleen, thymus)
II	Two or more LN regions on the same side of diaphragm
III	Involves LN regions on both sides of diaphragm +\- involvement of spleen
IV	Diffuse involvement of one or more of exranodal tissues (liver, bone marrow or lung) +\- LN involvement

- *A and B for each stage according to absence or presence of B symptoms*



Grading

	High grade NHL (85%)	Low grade NHL (15%)
Onset	Rapidly growing	Slowly growing
B symptoms	Common	Uncommon
Extra-nodal involvement	Common Affecting GIT, GU, CNS, lung, skin, thyroid	Uncommon
BM Infiltration	Uncommon	Common

Treatment

❑ Low grade NHL:-

- Asymptomatic patients → just watchful waiting & observation

Indications of treatment:

1- Marked systemic symptoms

2- Compression syndromes

3- Bone marrow infiltration

Treatment

- **Options of therapy:-**

1. Radiotherapy → for stage I.
2. Chemotherapy → Oral chlorambucil, cyclophosphamide
3. Chemotherapy in combination with Rituximab (Monoclonal antibody therapy) → for stage III & IV
4. BM transplantation in patients with relapsed disease

Treatment

❑ High grade NHL:-

- Chemotherapy, commonly CHOP regimen in combination with Rituximab (**R-CHOP**) → first line treatment

✓ CHOP → Cyclophosphmide,
Doxorubicin (Hydroxydaunorubicin),
vincristine (Oncovin) ,
Prednisolone

- BM transplantation in patients with relapsed or refractory disease

Splenomegaly

Massive :-

- Beyond umbilicus, crosses mid-line
- >8 cm below left costal margin and/or >1000gm weight

Moderate :-

- Between costal margin & umbilicus
- 4-8 cm below left costal margin

Mild :-

- Just palpable (1-3cm) below left costal margin

Splenomegaly

I. ***Increased function***

✓ *Removal of defective RBCs*

- Spherocytosis
- Thalassemia
- Sickle cell anemia

✓ *Extramedullary hematopoiesis*

- marrow infiltration by myelofibrosis, leukemias, lymphomas, metastases
- marrow damage by radiation, toxins

Splenomegaly

I. ***Increased function***

✓ *Immune hyperplasia*

➢ *Response to infection (viral, bacterial, parasitic)*

- Viral → infectious mononucleosis, AIDS, viral hepatitis
- Bacterial → TB, typhoid fever, brucellosis, leptospirosis

  subacute bacterial endocarditis, bacterial sepsis,

  splenic abscess
- Parasitic → malaria Bilhaziasis

  leishmaniasis

Splenomegaly

I. ***Increased function***

- ✓ *Immune hyperplasia*

➢ *Disordered immunoregulation*

- rheumatoid arthritis, including cases of Felty's syndrome
- systemic lupus erythematosus
- serum sickness
- autoimmune hemolytic anemia
- sarcoidosis

Splenomegaly

II ***Abnormal blood flow***

a) ***Organ Failure*** → liver cirrhosis & portal hypertension

b) ***Vascular***

- hepatic vein obstruction
- portal vein obstruction
- Budd–Chiari syndrome
- splenic vein obstruction

c) ***Infections***

- hepatic schistosomiasis

Splenomegaly

III Infiltration

a) Benign and malignant "infiltrations

- Benign → Myeloproliferative neoplasms (PV, ET, PMF), Hemangioma, lymphangioma, splenic cysts, hamartomas, eosinophilic granuloma

- Malignant → Leukemias (acute, chronic, lymphoid, and myeloid)

  Lymphomas (Hodgkin's and non-Hodgkin's)

  Metastatic tumors (commonly melanoma)

b) Metabolic diseases

- Gaucher disease
- Niemann–Pick disease
- Amyloidosis

Massive Splenomegaly

- Bilharziasis (Egyptian splenomegaly)
- Thalassemia major
- Myeloproliferative neoplasms
  - Polycythemia vera (PV)
  - Essential thrombocytosis (ET)
  - Primary myelofibrosis (PMF)
  - Chronic myeloid leukemia (CML)
- Non-Hodgkin lymphoma
- Hairy cell leukemia
- Chronic malaria (tropical splenomegaly)
- kala-azar (visceral leishmaniasis)
- Sarcoidosis & storage diseases

Thank You