Lymphoma

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Learning Objective

- Classification of lymphoma .
- How the child with each lymphoma present
- Investigations for diagnosis and differentiate from other disease.
- Treatment.
- Psychosocial and economic support which interfere with Immunity

Lymphoma can be classified into

1- Hodgkin`s lymphoma (HL)

2- Non – Hodgkin`s lymphoma (NHL)

Hodgkin's disease

- The true nature of Hodgkin`s disease may still be obscure → as a neoplasm of the lymphatic system → based on the presence of a malignant cell (Reed-Sternberg cells).

- (HL) is a malignant process involving the lymphoreticular system that accounts for 6% of childhood cancers. approximately 5% of cancers in children ≤14 yr old; it accounts for approximately 15% of cancers in adolescents (15-19 yr), making HL the mostcommon malignancy in this age-group.

- There is a bimodal age distribution, with peaks at 15-35 yr of age and again after 50 yr.

- Infectious agents may be involved, such as human herpesvirus 6, cytomegalovirus, and **Epstein-Barr virus**

- The Reed-Sternberg (RS) cell, a pathognomonic feature of HL, is a large cell (15-45 μm in diameter) with multiple or multilobulated nuclei. This cell type is considered the hallmark of HL

Etiology and epidemiology

- 30 -40% of childhood lymphomas.
- The incidence of which increases steadily throughout life.
- Male : Female ratio of 2.7.
- The true nature of Hodgkin`s disease may still be obscure → as a neoplasm of the lymphatic system → based on the presence of a putative malignant cell population (Reed-Sternberg cells).
- Infection → poliovirus , Epstein – Barr virus(EBV) [The Reed – Sternberg cells harbour the EBV genome]
- Socioeconomic → high socioeconomic small family → high risk for HD.
- Cong. immunodeficiencies : ataxia telangiectasia wiskott – Aldrich syndrome and Blooms syndrome .
- ↑ risk of developing the disease in parents and siblings of the same family → could indicate either environment or genetic influence

(WHO)/Revised European–American Classification of Lymphoid Neoplasms for Hodgkin Lymphoma :

- Nodular lymphocyte predominance
- Classical Hodgkin lymphoma
- Lymphocyte rich
- Mixed cellularity
- Nodular sclerosis
- Lymphocyte depletion

Clinical manifestations

1-Painless lymphadenopathy :nontender, firm, rubbery, cervical or supraclavicular is the most frequent presenting symptom in up 80% of children

2- Constitutional symptoms :-[No →A, one or more B]

- presence of unexplained fever
- Night sweats
- Unexplained lost of 10% or more of body weight in the 6 months before admission

3- 60% mostly asymptomatic

4- Splenomegaly, hepatomegaly and symptoms relating to lung or pleural involvement

5- Mediastinum involvement

Recommendations for diagnostic work- up of children with Hodgkin`s disease

1-Mandatory procedures

- Surgical biopsy reviewed by experienced pathologist
- History (special attention to fever, sweating wt loss)
- Physical examination with cytology or biopsy of doubtful nodes.
- CBC with blood film ,ESR , S.ferritin
- Chest X-ray (postero-anterior and lateral views).
- Lymphogram or CT scan in the younger child.

2- Procedures required under certain conditions

- Chest CT scan if mediastinal , hilar or pulmonary involvement is present
- Abdominal ultrasound or CT scan if lymphogram is equivocal or if the child has hepatomegaly or splenomegaly with normal lymphogram .
- Postnasal space X-ray if cervical nodes are involved .
- Bone marrow biopsy if systemic symptoms are associated with stage II-IV .
- Liver biopsy if hepatomegaly is homogenous.
- Radiolsotopie bone scan if stage IV.
- Pleural cytology if there is a pleural effusion.

3-Promising research procedures

- Positron emission tomography .
- Mediastinal magnetic resonance imaging .
- Interleukin -2 receptor and CD8 serum levels

Staging of Hodgkin lymphoma

Stage 1
Involvement of a single lymph node region (1) or a single extralymphatic organ or site
Stage 11
Involvement of two or more lymph node regions on the same side of the diaphragm or solitary involvement of an extralymphatic organ or site and one or more lymph node regions on the same side of diaphragm
Stage III
- Involvement of two or more lymph node regions on the same side of the diaphragm or solitary involvement of an extralymphatic organ or site and one or more lymph node regions on the same side of diaphragm
- Involvement of lymph node regions on both side of the diaphragm which may be accompanied by localized involvement of extralymphatic organ or site or by involvement of the spleen or both.

Stage IV
- Diffuse or disseminated involvement of one or more extralymphatic organs or tissues with or without associated lymph node enlargement

Treatment
- Radiotherapy.
- Chemotherapy: **COPP** (cyclophosphamide, vincristine [Oncovin], procarbazine, and prednisone) or **ABVD** (doxorubicin [Adriamycin], bleomycin, vinblastine, and dacarbazine), with the addition of prednisone,

Lugano Classification for Hodgkin Lymphoma*

STAGE	INVOLVEMENT	EXTRANODAL STATUS
I	One node or group of adjacent nodes	Single extranodal lesions without nodal involvement
II	Two or more nodal groups on the same side of the diaphragm	Stage I or II by nodal extent with limited contiguous extranodal involvement
II bulky	II as above with "bulky" disease	Not applicable
III	Nodes on both sides of the diaphragm; nodes above the diaphragm with spleen involvement	Not applicable
IV	Additional noncontiguous extralymphatic involvement	Not applicable

* The absence or presence of fever >38°C (100.4°F) for 3 consecutive days, drenching night sweats, or unexplained loss of >10% of body weight in the 6 mo preceding admission are to be denoted in all cases by the suffix letter A or B, respectively.

Non –Hodgkin`s lymphoma (NHL)

The classification system of choice worldwide is the world Health organization (WHO) and expansion of the Revised European – American lymphoma (REAL)

1) B cell type

- Precursor B- lymphoblastic
- Leukaemia / lymphoma
- Mature (peripheral) B-cell neoplasm
- Diffuse large B-cell lymphoma
- Follicular lymphoma
- Burkitt lymphoma
- [Mantle cell]

2) T-Cell and natural killer neoplasms

* Precursor T- lympoblastic
- Leukaemia / lymphoma
- Mature (peripheral) T-cell neoplasm

* Anaplastic large-cell lymphoma
- - T-NHL cell, primary systemic type
- - [Anaplastic large cell lymphoma
- - T-NHL cell, primary cutaneous type
- Mycosis fungoides

* [Peripheral T-cell, not otherwise characterized

Epidemiology

- In developed countries NHL represent 60-70% of all childhood lymphoma .
- Affecting children mainly between 7-10 years of age.
- The male: female value was 2.5
- Increased incidence in children with inherited or acquired immuno-deficiencies (AIDS) are clinically aggressive
- Sensitivity to Epstein- Barr Virus (EBV) and the occurrence of malignant lymphoma → Burkitt type

Clinical manifestations of NHL

In children are largely determined by disease site and extent

1- Abdomen is the most common primary site (30-45%).

- Intussusceptions leading to the discovery of a small excisable tumor.

large and rapidly growing abdominal distention, nausea, Vomiting, change in bowel habits

2- Mediastinum tumors (25-35%)

- are typically T-cell lymphoblastic lymphomas, but in rare cases they can be large B-cell or Burkitt lymphomas.
- Mediastinal compression or cervical or axillary lymphadenopathy
- Chest X-ray show localized thymic mass often associated with pleural or pericardial effusions
- Patients risk of developing respiratory distress, worsened or provoked by general anesthesia
- Superior vena cave syndrome (swelling of arms, neck and face)

3- Other sites

- The third most common site is Head & neck including waldeyer`s ring and the facial bones (10-20%), followed by the superficial lymph nodes (5-10%)
- **Bone marrow** involvement may cause anemia or thrombocytopenia
- **CNS involvement** → Headache, increased intracranial pressure or cranial nerve palsies.
- 5-10% includes tumors arise from less common sites such as bone, skin, thyroid, orbit, eyelid, kidney and epidural space.
- Bone lymphoma→ localized or generalized and associated with hypercalemia
- Kidney lymphoma → can be confused with nephroblastoma → tumor is bilateral, the infiltration multinodular or diffuse and renal failure is present
- Skin :subcutaneous lymphoma =children age < 2years

Diagnosis of NHL

- Physical examination
- Chest and nasopharyngeal X-ray .
- Abdominal ultrasound
- Bilateral bone marrow aspirations .
- CSF examination .
- Complete blood count and blood film morphology
- LDH, serum electrolytes, BUN, creatinine, uric acid levels.
- Bone scan and skeletal survey .
- Local CT scan (head and neck tumors)
- Magnetic resonance imaging (CNS disease)

- Abdominal CT scan
- Bone marrow biopsy in large-cell NHL

Staging of NHL

Stage I

- A single tumor (extranodal) or single anatomical area (nodal) with the exclusion of the mediastinum or abdomen .

Stage II

- Recected a single tumor (extranodal) with regional node involvement.
- Two or more nodal areas on the same side of the diaphragm.
- Two single (extranodal) tumours with or without regional node involvement on the same side of the diaphragm.
- A primary gastrointestinal tract tumor usually in the ileocecal area, with or without involvement of associated mesenteric nodes only.

Stage III

- Two single tumors (extranodal) on opposite sides of the diaphragm
- Two or more nodal areas above and below the diaphragm
- All the primary intrathoracic tumors (mediastinal, pleural, thymic)
- All extensive primary intra- abdominal disease, unresectable.
- All paraspinal or epidural tumors, regardless of other tumour site (s)

Stage IV

- Any of the above with initial CNS and / or bone marrow involvement.

Cytogenetics and molecular biology

In Burkitt lymphoma tumor cell are characterized by a translocation of

- T (8;14) (q24;q32) → the oncogene c-myc
- T (2;8) (p12;q24) and
- T (8;22) (q24;q11)
- in T-cell→ chromosomal abnormalities involve chromosome 14 or 7

Treatment OF NHL

- **Surgery** :: is used mainly for diagnosis
- **Radiotherapy** used only in special circumstances, such as CNS involvement in LBL or the presence of acute superior mediastinal syndrome or paraplegias
- **Chemotherapy:**multiagent systemic chemotherapy and/or immunotherapy with intrathecal medication

Prognosis of NHL

The prognosis is excellent for most forms of childhood and adolescent NHL . Patients with localized disease have a 90–100% survival rate, and those with advanced disease have 80–95% survival.