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LYMPHOMA
Lymphoma

3rd most common cancer in children
Incidence of 15 per million children
Two broad categories

1- Hodgkin disease
2- Non- Hodgkin disease
Hodgkin disease:

* Malignant process of lymphoreticular system
* 6% of childhood cancer
* 5% of cancer in \( \leq 14 \) yr
* 15% in person 15-19 yr
* Rare \( < 10 \) yr
Epidemiology:
* Bimodal incidence
* Early peak middle to late 20s
* Second peak after 50 yr
* Sex Male : Female
  4: 1 for 3-7 yr
  3: 1 for 7-9 yr
  1-3: 1 for > 10 yr
* 100 folds risk for unaffected monozygotic twin of affected twin
* Associated with specific HLA antigen
* Infectious agents
  - Human herpes virus 6
  - CMV
  - Epstein – Barr virus
* Immunodeficiency
Etiology:
Reed –Sternberg cell
Hallmark of disease
Large (15-45 μm) multiple / multilobulated nuclei
Colonial in origin
Arises from germinal center B cells
Rye Classification System

1- Lymphocyte predominant

2- Mixed cellularity

3- Nodular sclerosis

4- Lymphocyte depletion
Lymphocyte Predominant

10-15% of patients
More common in male
Younger patients
Localized disease

Mixed cellularity

30% of patients
< 10 yr of age
Advanced disease
Extranodal extension
Lymphocyte depletion

- Rare in children
- Common with HIV

Nodular sclerosis

- Most common
- 40% of younger patients
- 70% of adolescents
REAL Classification
( Revised European – American Classification of Lymphoid Neoplasms )
* Nodular lymphocyte predominance
* Classical Hodgkin lymphoma
* Lymphocyte rich
* Mix cellularity
* Nodular sclerosis
* Lymphocyte depletion
* Anaplastic large cell lymphoma
Hodgkin like
Lymphocyte predominant Hodgkin Lymphoma
Lymphocyte predominant Hodgkin Lymphoma
Nodular Sclerosis
Mixed Cellularity
Reed-Sternberg Cell
Clinical Manifestations

* Lymphadenopathy cervical / supraclavicular
* Painless, non tender, firm and rubbery
* Hepatosplenomegaly
* Cough, dyspnea, hypoxia
* Pleural or pericardial effusion
* Hepatocellular dysfunction
* B.M infiltration
  ( Anemia, neutropenia, thrombocytopenia)
* Disease below diaphragm is rare (only 3%)
Mediastinal Mass in Hodgkin Disease
Systemic Symptoms (B symptoms)

* Important in staging
* Unexplained fever > 39°C
* Weight loss > 10% in 3m
* Drenching night sweats

Immune System abnormalities

* Anergy to delayed-hypersensitivity skin test
* Abnormal cellular immune response
* Decreased CD4:CD8 ratio
* Reduce natural killer cell cytotoxicity
DIAGNOSIS

- Excisional Biopsy
  - Light Microscopy
  - Immunocytochemistry
  - Molecular Studies
- Chest X – Ray
  - Mediastinal Mass
- CT Scan
  - Chest
  - Abdomen
  - Pelvis
- Blood CP & ESR
- LFT’s
- Bone Marrow Aspiration
- Serum Copper & Ferritin
- Bone Scan
- Gallium 67 Scan / FDG/PET
Ann Arbor Staging Classification for Hodgkin Disease

- **Stage I**
  Involvement of a single lymph node (1) or of a single extra lymphatic site or organ (1_f)

- **Stage II**
  Involvement of two or more lymph node regions on the same side of the diaphragm (II) or localized involvement of an extra lymphatic site or organ and one or more lymph node regions on the same side of the diaphragm (II_f)

- **Stage III**
  Involvement of lymph node regions on both sides of the diaphragm (III) which may be accompanied by the involvement of spleen (III_S) or by localized involvement of an extra lymphatic site or organ (III_f) or both (III_sf)

- **Stage IV**
  Diffuse or disseminated involvement of one or more extra lymphatic organs or tissues with or without associated lymph node involvement.

- **The absence or presence of fever > 38C for three consecutive days, drenching night sweats, or unexplained loss of > 10% body weight in the 6 months preceding admission** are to be denoted in all cases by the suffix letters A & B respectively.
TREATMENT

- Treatment depends on:
  - Stage of the disease
  - Age at diagnosis
  - Presence / absence of B symptoms
  - Presence of hilar lymphadenopathy
  - Presence of bulky nodal disease

- Current Treatment Regimen
  - Combined chemotherapy with or without low dose involved field radiation therapy
Chemotherapy Regimens

- **MOPP**
  (Mechlorethamine, Vincristine, Procarbazine, Prednisolone)

- **COPP**
  (Cyclophosphamide, Vincristine, Procarbazine, Prednisolone)

- **ABVD**
  (Adriamycin, Bleomycin, Vinblastine, Dacarbazine)

- **BEACOPP** (For advanced stage disease)
  (Bleomycin, Etoposide, Doxorubicin, Cyclophosphamide, Vincristine, Procarbazine, Prednisolone)
P00R PROGNOSTIC FACTORS

- Tumor Bulk
- Advanced stage at diagnosis
- Presence of B symptoms
LONG TERM COMPLICATIONS

- Secondary malignancy
  - Acute Myelogenous Leukemia
  - Non Hodgkin lymphoma
  - Carcinomas of breast, lungs & thyroid

- Short stature
- Hypothyroidism
- Sterility
- Dental caries
- Sub clinical pulmonary dysfunction
- Ischemic heart disease
PROGNOSIS

Early Stage Disease
- 5 year survival ....95%

Advanced Stage Disease
- 5 year survival ....90%

Relapses common within first 3 years from diagnosis

Relapses treated with Autologous Stem Cell Transplantation
NON-HODGKIN LYMPHOMA
EPIDEMIOLOGY

- 60% of all lymphomas in children
- 8-10% of all malignancies in children between 5-19 yrs of age

Secondary causes of NHL include:

- Inherited / acquired immune deficiencies
- Viruses
  - HIV
  - EBV
- Genetic Syndromes
  - Ataxia Telangiectasia
  - Bloom syndrome
PATHOLOGICAL SUB TYPES OF NHL

- Burkitt Lymphoma
  40% of NHL
  B Cell Origin

- Lymphoblastic Lymphoma
  30% of NHL
  80% T Cell Origin & 20% B Cell Origin

- Diffuse Large B Cell Lymphoma
  20% of NHL
  B Cell Origin

- Anaplastic Large Cell Lymphoma
  10% of NHL
  70% T Cell Origin
Burkitt Lymphoma
Diffuse Large B Cell Lymphoma
T lymphoblastic Lymphoma
Anaplastic Large Cell Lymphoma
CLINICAL MANIFESTATIONS

- **Burkitt Lymphoma**
  - Abdominal Tumor
  - Head & Neck Disease
  - Involvement of bone marrow & CNS

- **Lymphoblastic Lymphoma**
  - Intrathoracic / mediastinal supradiaphragmatic mass
  - Involvement of bone marrow & CNS

- **Diffuse Large B Cell Lymphoma**
  - Abdominal Mass
  - Mediastinal Mass

- **Anaplastic Large Cell Lymphoma**
  - Primary cutaneous manifestation
  - Systemic disease (fever, weight loss)
  - Dissemination to liver, spleen, lung, mediastinum & skin
Other clinical features include:
- Lymphadenopathy
- Superior vena cava syndrome
- Dyspnea
- Abdominal Mass
- Intestinal obstruction / intussusception
- Ascites
- Nasal Stuffiness
- Earache
- Tonsil enlargement
- Localised bone involvement
- Acute paraplegia secondary to CNS / spinal cord compression
- Tumor Lysis Syndrome
Burkitt Lymphoma
Burkitt Lymphoma
## Staging system for childhood Non-Hodgkin lymphoma

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
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<tbody>
<tr>
<td>I</td>
<td>A single tumor (extranodal) or single anatomic area (nodal) with the exclusion of mediastinum or abdomen</td>
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<tr>
<td>II</td>
<td>A single tumor (extranodal) with regional node involvement two or more nodes areas on the same side of diaphragm Two single (extranodal) tumors with or without the regional node involvement on same side of diaphragm A primary gastrointestinal tract tumor usually in the ileocecal area, with or without involvement of associated mesenteric nodes, which may must be grossly (&gt; 90%) resected</td>
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| III   | Two single tumors (extranodal) on opposite side of the diaphragm  
      | Two more nodal areas above and below the diaphragm  
      | Any primary intrathoracic tumor (mediastinal, pleural, or thymic)  
      | Any extensive primary intra-abdominal disease |
| IV    | Any of the above, with initial involvement of central nervous system or bone marrow at time of diagnosis |
DIFFERENTIAL DIAGNOSIS

- Hodgkin Disease
- Leukemia
- Germ Cell Tumor
- Wilms Tumor
- Neuroblastoma
- Rhabdomyosarcoma
- Reactive lymphadenitis
LABORATORY FINDINGS

- Tissue biopsy for:
  - Flow cytometry
  - Karyotyping

- Complete Blood Count

- Serum Electrolytes, Calcium, Phosphorus, Uric acid

- LFT’s & RFT’s

- Bone Marrow Aspiration & Biopsy

- CSF Examination

- Chest X Ray

- CT Scan
  - Head & Neck
  - Chest
  - Abdomen & Pelvis

- PET Scan & Bone Scan
TREATMENT

- Systemic Chemotherapy
- Intrathecal chemotherapy
- Radiotherapy indicated in:
  - CNS Disease
  - SVC Syndrome
  - Paraplegia
Chemotherapy Regimens

- COPAD
  (Cyclophosphamide, Vincristinr, Prednisolone, Doxorubicin)

- COMP
  (Cyclophosphamide, Vincristine, Methotrexate, 6 Mercaptopurine, Prednisolone)
Duration of Treatment

- Burkitt Lymphoma & Diffuse Large B Cell Lymphoma .......... 6 weeks to 6 months
- Lymphoblastic Lymphoma ...... 24 months
Supportive Treatment

- G-CSF prophylaxis for fever & neutropenia
- Antibiotic prophylaxis
- Blood & platelet transfusions
- Allopurinol
- Parenteral nutrition
COMPLICATIONS

- Infections
- Mucositis
- Pancytopenia
- Electrolyte imbalance
- Poor nutrition
- Growth retardation
- Cardiac Toxicity
- Gonadal Toxicity with Infertility
- Secondary malignancies
PROGNOSIS

- Localized disease
  90 – 100% survival

- Advanced Disease
  60-95% survival
THANK YOU