LEUKAEMIA and LYMPHOMA

Dr Mubarak Abdelrahman
Assistant Professor Jazan University
OBJECTIVES

• Identify etiology and epidemiology for leukemia and lymphoma.

• Discuss common types of leukemia.

• Distinguish between Hodgkin and non-Hodgkin lymphomas.

• Identify prognosis of leukemia and lymphoma.

• Interpret results of CBC, BM and radiology.

• Discuss treatment of leukemia and lymphoma.
Leukemia

Definition:

• Leukemia is a group of malignant diseases in which genetic abnormalities in a hematopoietic cell give rise to unregulated clonal proliferation of cells.
• The result is a disruption of normal marrow function or marrow failure.
ETIOLOGY

- **Unknown** and is probably multi-factorial.
- **Genetics and environmental factors:**
  - CML a translocation bet. chromosome 9 and 22.
  - Increased risk in Down, Wiskott-Aldrich, ...
- **Environmental factors** e.g. ionizing radiation.
EPIDEMIOLOGY

• About 31% of childhood malignancy.
• **Acute lymphoblastic leukemia (ALL):** 75-80%
• **Acute myeloid leukemia (AML):** 15-20%.
• **Chronic myeloid leukemia (CML):** less than 5%.
• **Chronic lymphocytic leukemia (CLL):** not found in childhood.
Classification of Acute Lymphoblastic Leukemia

**ACUTE LYMPHOBLASTIC LEUKEMIA (ALL):**

**ALL-L1** morphology Precursor B-cell ALL

**ALL-L2** Precursor T-cell ALL.

**ALL B cell-L3** morphology (i.e., Burkitt's leukemia).
Classification of Acute Myeloid Leukemia

• ACUTE MYELOID LEUKEMIA (AML): (WHO)
• FAB (French-American-British) classification: AML (M0-M7).
Clinical presentation

• **General**: fever, malaise, anorexia, ..
• **Bone marrow infiltration**: anemia, neutropenia and thrombocytopenia.
• **Reticulo-endothelial infiltration**: hepatosplenomegaly and lymphadenopathy.
• **Other organ infiltration**: CNS, testes also bone, skin, gingiva
DIFFERENTIAL DIAGNOSIS

• Infection: Epstein-Barr virus, mycobacteria.
• Noninfectious: Aplastic anemia, JRA, SLE, ITP, ..
• Malignant diagnoses: lymphoma, neuroblastoma,..
• Proliferation and accumulation of histiocytes e.g. Langerhans cell histiocytosis
LABORATORY AND IMAGING STUDIES

• **CBC:** low Hb and low plts are common.
• The WBC count (low, normal or high).
• **The diagnosis** is by finding of **immature blast cells** (blast morphology) on the peripheral blood smear or bone marrow aspirate (25%).
• **Definitive diagnosis and typing** requires the evaluation of cell surface markers (**immunophenotype**) by flow cytometry.
Cytogenetic analysis: Certain types have specific chromosomal abnormalities.

A lumbar puncture to evaluate the possibility of CNS involvement.

A chest x-ray to exclude an anterior mediastinal mass, which is commonly seen in T-cell ALL.

Electrolytes, calcium, phosphorus, uric acid, and renal and hepatic function should be monitored in all patients.
Anterior mediastinal mass
Treatment of ALL

Before starting treatment:

• Treat anemia, thrombocytopenia and infection.
• Hydration and allopurinol to protect renal function against tumour lysis syndrome.
Treatment of ALL

Induction of remission:

• Eradication of the leukemic blasts and restoration of normal marrow function.
• Four weeks of 3-4 agents chemotherapy.
• Current induction achieve remission rates of 95%.
Treatment of ALL

Consolidate remission:
Blocks of intensive chemotherapy, but increased toxicity.

CNS prophylaxis:
Intrathecal chemotherapy to prevent CNS relapse.
Treatment of ALL

**Continuing maintenance therapy:**

Chemotherapy of modest intensity is continued up to 3 years from diagnosis.

Co-trimoxazole is given routinely to prevent *Pneumocystis carinii* pneumonia.
Treatment of AML

The treatment of AML different from ALL because:

• Non-myelosuppressive drugs (vincristine) not effective.
• The low-dose continuation therapy not helpful in AML.
• Induction is the most effective (two courses of drugs, 1 to 2 weeks apart) regardless of blood counts.
• Most experts recommend a stem cell transplantation in the first remission, except in Down syndrome and those with favorable cytogenetics.
General Prognostic Factors in ALL

Based on:

*Age, initial WBC count, genetic characteristics, and response to induction therapy.*

<table>
<thead>
<tr>
<th>Factor</th>
<th>Favorable (Lower Risk)</th>
<th>Unfavorable (higher risk)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1-9.99 years</td>
<td>&lt;1 or ≥10 years</td>
</tr>
<tr>
<td>Gender</td>
<td>Females</td>
<td>Males</td>
</tr>
<tr>
<td>Initial WBC count</td>
<td>&lt;50,000/mm³</td>
<td>≥50,000/mm³</td>
</tr>
<tr>
<td>CNS or testicular disease at diagnosis</td>
<td>Absent</td>
<td>Present</td>
</tr>
<tr>
<td>Cytogenetic</td>
<td>t(12;21)</td>
<td>t(4;11), t(9;22)</td>
</tr>
<tr>
<td>Response to therapy</td>
<td>Rapid</td>
<td>Slow</td>
</tr>
</tbody>
</table>
PROGNOSIS

• The overall cure rate for:

1- ALL 80%.

• Relapse occurs most commonly in the bone marrow, also in CNS, testes, ...

2- AML 50%.

• The prognosis for relapsed AML is poor.
Pediatric Lymphomas
Cervical adenopathy
LYMPHOMA

HODGKINS
(40%)

LARGE CELL LYMPHOMA
(<15%)

IMMUNOBLASTIC
(50%)

NON-HODGKINS
(60%)

LYMPHOBLASTIC LYMPHOMA
(30-40%)

ANAPLASTIC
(50%)

BURKITT’S LYMPHOMA
(40-50%)
NON-HODGKINS (NHL)

Incidence/Etiology:

- 6% childhood cancer
  60% of childhood lymphomas
- Peak age of 5-15; M:F ratio of 2.5:1
- Increased with
  - SCIDS, HIV, EBV
  - post t-cell depleted BMT
  - post solid organ transplant
- Geographic, viral, genetic & immunologic factors
Clinical Presentations

◆ Abdomen: (35%): pain, distention, jaundice, GI problems, mass.
◆ Head/neck (13%): lymphadenopathy, jaw swelling, single enlarged tonsil, nasal obstruction, rhinorrhea,
◆ Mediastinum (26%): SVC syndrome.
◆ CNS (rare): Headache, Vom., irritability, papilledema.

+ Fever, malaise, night sweats, wt. loss,
**Unfavorable:**
- Incomplete remission in first 2 months of treatment.
- Large tumor burden (LDH >1000).
- Stages III and IV: CNS or BM involvement.
- Relapse.

**More favorable:** Stage I or II, head/neck, peripheral nodes, GI tract.
NHL Treatment

◆ Surgery; for diagnostic or second look.
◆ Radiation Therapy: emergency airway obstruction or CNS complication or local control of residual mass.
◆ Chemotherapy: Combination chemo is usual, with overall cure rates 60-80+%; high risk of tumor lysis and hyperuricemia.
◆ Relapse: Re-induction, followed by BMT
Hodgkin’s Disease

◆ Immune system malignancy, involving B or T lymphocytes.
◆ Reed-Sternberg cells.
◆ Spread: slow, predictable, with extension to contiguous lymph nodes.
◆ Infiltration to non-lymphoid organs is rare.
Hodgkin’s disease with Reed Sternberg cell
Incidence and Etiology

◆ Hodgkin’s 5% of childhood cancers
◆ Bimodal peaks, at 15-35 and >50; rare < 5
◆ M:F ratio of 3:1
◆ Increased in immunologic disorders, HIV, EBV
Types of Hodgkin’s Lymphoma

◆ **Nodular sclerosing:** 40-60%, lower cervical, supraclavicular, mediastinal nodes.

◆ **Mixed cellularity:** 15-30%; advanced disease with extranodal involvement.

◆ **Lymphocyte predominance:** 5-15%, presents as localized disease.

◆ **Lymphocyte depletion:** <5%, widespread disease
Clinical Presentation

- Painless lymph node swelling; supraclavicular and cervical nodes (90%).
  Palpable non-tender, firm, mobile, rubbery nodes.
- Mediastinal adenopathy (60%); SVC
  Bulky: when mass is > 1/3 thorax diameter

**B symptoms:** Fever of >38°C for 3 days, drenching night sweats, 10% weight loss within 6 months.
Hodgkin’s Ann Arbor Staging

I  Single lymph node region
II  Two+ node regions on same side of diaphragm
III Nodes on both sides of diaphragm, or localized extra-lymphatic spread
IV  Diffuse or disseminated involvement of one+ extra-lymphatic organs or tissues
Prognosis

FAVORABLE:
<10, F, favorable subtypes (LP and NS) and Stage I non-bulky disease

UNFAVORABLE:
Persistently elevated ESR;
LD histopathology;
bulky disease--largest dimension >10cm;
B symptoms;
Treatment and Prognosis

- Dependent on age, stage, and tumor burden
- Radiotherapy (RT) alone, Chemotherapy (CTX) alone.

**RT:** varies from involved field for localized disease to extended field to total nodal irradiation.

- Most often multimodal therapy, with low-dose involved field RT and multi-agent CTX.
- Combined modality 70-90% cure.