Hematopathology II
Chronic Leukemias and Lymphomas

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Hematopoietic neoplasms

Acute
Lymphoid
Acute lymphoblastic leukemia
Myeloid
Acute myeloid leukemia

Chronic
Lymphoid
Chronic leukemias
Myeloid
Myeloproliferative disorders

Plasma cell disorders
Lymphomas

Chronic Leukemias

1) Chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL)
2) Hairy cell leukemia
3) Adult T-cell leukemia/lymphoma
Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma

- Can involve blood/bone marrow and lymph nodes, but cells are the same
- CLL is the most common leukemia of adults in the Western world (21,000 new cases/year in the USA)
- B-cell neoplasm that typically express CD20, CD5 (pan T-cell marker) and CD23
- Trisomy 12, 11q-, 13q- and deletion of 17p (p53)

Clinical features of CLL/SLL

- Most patients are elderly (median age: 60). They tend to have immune dysfunction and hypogammaglobulinemia
- Some patients may have autoimmune hemolytic anemia
- Some patients transform to a higher grade process: Prolymphocytic leukemia or diffuse large cell lymphoma (Richter syndrome or transformation)
- Recent studies indicate that prognosis is based on the presence of mutations of the immunoglobulin heavy chain (IGH) gene. Those with IGH mutations have a favorable outcome

CLL/SLL

- Two cell types: Predominantly small round lymphocytes (6-12 um), condensed chromatin and scant cytoplasm and fewer larger cells (prolymphocytes / paraimmunoblasts)
- Peripheral blood shows typical small lymphocytes with scant cytoplasm some smear may show disrupted tumor cells (smudge cells)
**Hairy Cell Leukemia**

- Cells have cytoplasmic projections (hair like)
- Usually middle aged men presenting with pancytopenia, monocytopenia, splenomegaly (most common), hepatomegaly, infections
- Bone marrow is always involved; spleen involvement shows primarily red-pulp infiltration
- Cytochemical staining shows tartrate resistant acid phosphatase (TRAP)
- Excellent prognosis, response to gentle chemotherapy
# Adult T-cell Leukemia/Lymphoma

- Very rare in the U.S., but seen frequently in southern Japan, West Africa, and Caribbean
- Patients usually have skin lesions, hepatosplenomegaly, lymphocytosis and hypercalcemia
- A tumor of CD4 positive T-cells that is seen in adults infected with HTLV-1
- Typical floret-like lymphocytes (CD4+) in the peripheral blood
- Usually fatal, but rarely tumor involves only skin and follows indolent course

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**Hematopoietic neoplasms**

- Acute
  - Lymphoid: Acute lymphoblastic leukemia
  - Myeloid: Acute myeloid leukemia
- Chronic
  - Lymphoid
  - Myeloid: Myeloproliferative disorders
  - Chronic leukemias
  - Plasma cell disorders
  - Lymphomas
Lymphomas

Non-Hodgkin

- Follicular lymphoma
- Mantle cell lymphoma
- Burkitt lymphoma
- Diffuse large B-cell lymphoma

Hodgkin

B-cell

T-cell

Etiology of lymphoma

- Chromosomal abnormalities
- Immune deficiencies: AIDS, Post-transplant, rheumatoid arthritis, SLE, Sjogren’s syndrome
- Viruses: HTLV-I, EBV, HHV-8, Hepatitis C
- Bacteria: Helicobacter pylori in gastric MALT (mucosa associated lymphoid tissue) lymphoma
- Iatrogenic (radiation)

Geographical variations

Endemic Burkitt lymphoma – Africa
MALT lymphoma – Mediterranean
Peripheral T-cell lymphoma – Asia
How to make a diagnosis of lymphoma?

We usually need a lymph node or a tissue biopsy to make the diagnosis of lymphoma:
- Histology
- Immunophenotype (immunohistochemistry, flow cytometry)
  - B-cell: 85%
  - T-cell: 15%
- Cytogenetic Abnormalities
- Molecular (all lymphomas derive from a single cell: monoclonal)

Distinct expression of markers (antigens)

Markers help determine lineage of a hematopoietic neoplasm

B cell markers: CD19, CD20
T cell markers: CD2, CD3, CD4, CD5, CD7, CD8
Myeloid markers: CD13, CD33, Myeloperoxidase

Follicular Lymphoma

- Constitutes 40% of adult NHLs
- Painless lymphadenopathy (generalized)
- Overall median survival is 7-9 yrs.
- Recent therapy using anti-CD20 antibody is effective
- May transform to DLCL in 30% to 50% of cases (survival <1 yr)
Follicular Lymphoma

- Two types of cells are seen: Small cells with cleaved or irregular nuclei (centrocytes) and larger cells with open nuclear chromatin and several nucleoli (centroblasts)

- Immunophenotype CD19, CD20, CD10 positive

- Genotypic findings: t(14;18) [BCL2/IGH fusion] causing BCL2 over-amplification (anti-apoptotic)

Benign reactive lymph node

Benign reactive follicle
Follicular Lymphoma
(BCL2 expression)

Mantle cell lymphoma

• Approximately 4% of NHLs, mainly seen in older males
• Composed of small cells with irregular nuclei
• Immunophenotype CD19, CD20, CD5 positive
• t(11;14) [Cyclin D1–IGH fusion]
  Causing Cyclin D1 over-amplification (increased proliferation)
• Moderately aggressive, median survival 3-5 years

Mantle cell lymphoma

Cyclin D1 overexpression

John Lazarchick, ASH Image Bank 2011; 2011-4158
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Burkitt Lymphoma

- Children or young adults; aggressive disease
- Most tumors present at extranodal sites
  - Mandible (endemic-African), abdomen (non-endemic)
- Tumor cells are round, smaller than DLCL but larger than CLL
- Increased number of histiocytes surrounded by clear space gives an impression of “starry sky pattern”

Burkitt Lymphoma

- B-cell neoplasm (positive for CD20, CD19); also expresses CD10 (germinal center cell origin)
- African (endemic): latently infected with EBV (almost all cases)
- Sporadic (non-endemic)
- HIV-associated: 25% of HIV-associated BL are EBV positive
- MYC is located on chromosome 8 and translocated to immunoglobulin heavy chain locus \( IGH(t(8;14)), \) or light chain loci

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Important lymphoma translocations to know

- Follicular lymphoma: t(14;18) [BCL2/IGH fusion]
  - causing BCL2 over-amplification (anti-apoptotic)

- Mantle cell lymphoma: t(11;14) [Cyclin D1/IGH fusion]
  - causing Cyclin D1 over-amplification (increased proliferation)

- Burkitt lymphoma: t(8;14) [MYC/IGH fusion]
  - causing MYC over-amplification (increased proliferation)

Thanks!

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