Pathology of hematopoietic system

Leukemias, lymphomas
Bone marrow

- Blood stem cell
  - Myeloid stem cell
    - Myeloblast
      - Red blood cells
      - Platelets
  - Lymphoid stem cell
    - Lymphoblast
      - White blood cells
Leukemia

- Neoplastic Proliferations of WBCs in Bone Marrow
  - Anemia, infection, bleeding

- Acute Leukemias
  - Blast (precursor) cells
  - Rapidly fatal if not treated

- Chronic Leukemias
  - More mature cells
  - Longer life expectancy
# Leukemia

<table>
<thead>
<tr>
<th>Lymphoid</th>
<th>Acute</th>
<th>Chronic</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALL</td>
<td>CLL</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Myeloid</th>
<th>Acute</th>
<th>Chronic</th>
</tr>
</thead>
<tbody>
<tr>
<td>AML</td>
<td>CML</td>
<td></td>
</tr>
</tbody>
</table>
Malignant proliferation of myeloid cells

- Myelodysplastic syndrome
- Chronic myeloproliferative diseases (myeloproliferative syndromes)
- Acute myelogenous leukemia
- Myelodysplastic/myeloproliferative overlap syndromes
Myeloproliferative syndromes

- disorders of the hematopoietic stem cell in the bone marrow which excess cells production = effective hematopoiesis

- They may evolve into, myelodysplastic syndrome and acute myeloid leukemia
Chronic myeloproliferative diseases

- **Philadelphia Chromosome "positive"**
  - Chronic myelogenous leukemia (CML)

- **Philadelphia Chromosome "negative"**
  - Polycythemia vera (PV)
  - Essential thrombocytosis (ET)
  - Primary myelofibrosis (MF)
Chronic Myelogenous Leukemia

- Up to 20% of leukemias
- Cause: unknown
  - radiation
  - benzene exposure
- t(9;22) (bcr-abl) (Philadelphia chromosome)
- Proliferation of more mature granulocytes
  - normal to increased platelet count
  - anemia
Chronic Myelogenous Leukemia (CML)

- Long chronic phase (matured neutrophils, blasts less than 10%, basophilia, eosinophioliia)
- Accelerated phase (10-20% blasts)
- Blast phase - blast crisis

- Hydroxyurea, interferons
- Bone marrow transplantation
Clinical features

- 5-6 decades
- Slight male predominance
- Fatigue, anorexia, weight loss
- Hepatosplenomegaly- abdominal dyscomfot
- Lymphadenomegaly
- Acute leukemia conversion – 80%
- Median survival 3-4y
Chronic Myelogenous Leukemia
Polycythemia vera

- Clonal hematopoietic stem cell disease with uncontrolled proliferation of RBCs
- JAK 2 mutation
- Extramedullary hematopoiesis = myeloid metaplasia – spleen, liver, lymph nodes
- Peak age – 40-60y
- Acute leukemic conversion- 10%
- Median survival 13y
Polycythemia vera

- Insidious onset, nonspecific symptoms
- Plethora
- Hematosplenomegaly
- Headache, dizziness, visual problems, angina pectoris, claudication, GIT ulcers (histamin from basophils),
- Thrombosis, infarcts, strokes
Primary (idiopathic) Myelofibrosis

- Benzen, radiation, idiopathic
- 60-70y
- Hepatosplenomegaly
- Acute leukemic conversion 10%
- Median survival 5 y
- JAK 2 mutation
- Marrow becomes fibrotic
  - extramedullary hematopoiesis
  - dry tap
Esential Thrombocytemia

- 50-70y
- Moderate hepatosplenomegaly
- Acute leukemic conversion - 5%
- Median survival – more than 10y
- JAK 2 mutation
- Thrombosis, hemorrhage
Myelodysplastic syndrome

- disorders of the hematopoietic stem cell in the bone marrow.
- In MDS, hematopoiesis (blood production) is disorderly and ineffective (The number and quality of blood-forming cells decline irreversibly, further impairing blood production)
New WHO classification 2008

- Refractory cytopenia with unilineage dysplasia (Refractory anemia, Refractory neutropenia, and Refractory thrombocytopenia)
- Refractory anemia with ring sideroblasts (RARS)
- Refractory cytopenia with multilineage dysplasia (RCMD) includes: the subset Refractory cytopenia with multilineage dysplasia and ring sideroblasts (RCMD-RS).
- Refractory anemia with excess blasts I and II. RAEB was divided into *RAEB-I (5-9% blasts) and RAEB-II (10-19%) blasts, which has a poorer prognosis than RAEB-I.
  - 5q- syndrome (typically seen in older women with normal or high platelet counts and isolated deletions of the long arm of chromosome 5 in bone marrow cells, was added to the classification).
  - Myelodysplasia unclassifiable (seen in those cases of megakaryocyte dysplasia with fibrosis and others)
  - Refractory cytopenia of childhood (dysplasia in childhood)
Acute Myelogenous Leukemia
1. AML with recurrent genetic abnormalities
   - AML with t(8;21)(q22;q22)
   - RUNX1-RUNX1T1
   - AML with inv(16)(p13.1q22) or t(16;16)(p13.1;p22); CBFB-MYH11
   - Acute promyelocytic leukemia with t(15;17)(q22;q12); PML-RARA
   - AML with t(9;11)(p22;q23)MLLT3-MLL
   - AML with t(6;9)(p23;q34); DEK-NUP214
   - AML with inv(3)(q21q26.2) or t(3.3)(q21;q26.2); RPN1-EVI1
   - AML (megakaryoblastic) with t(1;22)(p13;q13); RBM15-MKL1
   - Provisional AML with mutated NPM1
   - Provisional AML with mutated CEBPA

2. AML with myelodysplasia-related changes

3. Therapy-related myeloid neoplasms

4. Acute myeloid leukemia, NOS
   - AML with minimal differentiation
   - AML without maturation
   - AML with maturation
   - Acute myelomonocytic leukemia
   - Acute monoblastic and monocytic leukemia
   - Acute erythroid leukemia
   - Acute megakaryoblastic leukemia
   - Acute basophilic leukemia
   - Acute panmyelosis with myelofibrosis
   - Myeloid sarcoma
   - Myeloid proliferations related to Down syndrome
   - Transient abnormal myelopoiesis
   - Myeloid leukemia associated with Down syndrome
   - Blastic plasmacytoid dendritic cell neoplasm
Acute Myelogenous (myeloid) Leukemia

- Proliferation of myeloblasts
  - anemia, thrombocytopenia, increased WBC
- Myeloid, monocytic, RBC, or megakaryocytic
  - flow cytometry
  - myeloperoxidase +, TdT-
- Auer rod
- Over age of 20
Acute Myelogenous Leukemia

- Radiation, cytotoxic chemotherapy (alkylation agents), benzen
- In bone marrow –more than 20% of blasts
- Granulocytopenia, thrombocytopenia, anemia
- Opportunistic infection
- Bleeding
- 5y survival less than 30%
Lymphomas

- proliferations of lymphoid cells in lymph nodes or extranodal location (mucoses – BALT, MALT, glands, spleen, skin, brain, bone marrow)

- Hodgkin’s lymphoma
- Non-Hodgkin’s lymphoma
  - nodal
  - extranodal
    - B cell
    - T cell/NK
  - precursor cells
  - mature cells
Non-hodgkin’s lymphomas (NHL)
WHO classification B-cell neoplasias

B-cell neoplasias from precursor cells
Lymphoblastic leukemia /lymphoblastic lymphoma

**Mature (peripheral) B-cell neoplasias**
B-chronic lymphocytic leukemia/small cell lymphoma (CLL/SLL)
B-prolymphocytic leukemia
Lymphopsmosmocytic lymphoma
**SPLENIC MARGINAL ZONE B CELL LYMPHOMA**
Hairy cell leukemia
Plasma cell myeloma
Extranodal lymphoma B – cell marginal zone MALT type
Nodal B cell lymphoma – marginal zone
Follicular lymphoma
Mantle cell lymphoma
Difuse large B cell lymphoma
Burkitt’s lymphoma
Acute Lymphoblastic Leukemia (ALL)

B- lymphoblastic leukemia/lymphoma NOS
B- lymphoblastic leukemia/lymphoma with repetitive genetic abnormalities
  \( t(9;22)(q34;q11) \) – BCR/ABL
  \( t(v;11q23) \) – MLL
  \( t(1;19)(q23;p13) \) – E2A/PBX1
  \( t(12;21)(p12;q22) \) – ETV/CBF-alfa
hyperdiploidní typ ALL
hypodiploidní typ ALL

T-acute lymphoblastic leukemia from precursor cells
Acute Lymphoblastic Leukemia (ALL)

- B- or T-cell precursors (lymphoblasts)
  - flow cytometry
  - Most common (80%) leukemia of childhood !!!!!!

- anemia, thrombocytopenia, increased WBC
- lymphadenopathy/splenomegaly

- Good prognosis: Age 4-6y, hyperploidity, t(12,21)(p13,q22) (TEL/AML1)

- Poor outcome:<4, >10y, hypoploid, t(9,22) (BRC/ABL)
B LYMPHOBLASTIC LEUKEMIA /LYMPHOMA

**Morphology**

Lymphoblasts

**Immunology**

<table>
<thead>
<tr>
<th>Marker</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>TdT</td>
<td>+/−</td>
</tr>
<tr>
<td>CD10 (CALLA)</td>
<td>+/−</td>
</tr>
<tr>
<td>Cytoplasmic µ</td>
<td>−/+/−</td>
</tr>
<tr>
<td>CD19, 79a</td>
<td>−/+/−</td>
</tr>
</tbody>
</table>

**Genetics**

No consistent abnormality.

**Clinical**

Children >> adults.

Aggressive disease but frequently curable.

**Official name:** “Precursor B lymphoblastic leukemia/lymphoma”
Acute Lymphoblastic Leukemia
Chronic Lymphocytic Leukemia (CLL/SLL)

- Proliferation of small mature B-lymphocytes
  - flow cytometry (monoclonal Kappa or lambda)
- Lymphadenopathy
- Lymphocytosis
- May be anemia, thrombocytopenia
- Hypogamaglobulinemia - infections
- May have Ab production and AIHA
- 50% 6-year survival (but loso 20-30y)
- Richter syndrome – transformation to DLBCL
Age: CLL is most common in older adults, is rare in young adults, and hardly ever develops in children. About 90% of people diagnosed with CLL are older than 50.

Gender. Men develop CLL more often than women.

Ethnicity. B-cell CLL is more common in people of Russian and European descent, and hardly ever develops in people from China, Japan, or Southeast Asian countries. The reason(s) for this geographic difference is not known.

Clin sy:
- Swelling of lymph nodes in the neck, under the arms, or in the groin. This is a common symptom that people with CLL usually notice first.
- Discomfort or fullness in the upper left part of the abdomen, caused when the spleen increases in size
- Fever and infection
- Abnormal bleeding
- Shortness of breath
- Weight loss
Chronic Lymphocytic Leukemia
IMMUNOCYTOMA / LYMPHOPLASMACYTIC LYMPHOMA (Waldenstrem macroglobulinemia)

Morphology
Plasmocytoid lymphocytes, plasma cells (+/- Dutcher bodies), lymphocytes.

Immunology
- Surface IgM: +
- Cytoplasmatic Ig: +
- CD5, CD10: -
- CD19, 20, 22, 79a: +

Genetics
No specific abnormalities.

Clinical
Adults. Indolent course.

Often associated with a serum IgM paraprotein.
**SPLENIC MARGINAL ZONE B CELL LYMPHOMA**

<table>
<thead>
<tr>
<th><strong>Morphology</strong></th>
<th>Small centrocyte-like, cells “monocytoid B cells”, lymphocytes, plasma cells.</th>
</tr>
</thead>
</table>
| **Immunology** | Surface Ig +  
|              | CD5, 10 -  
|              | CD19, 20, 22, 79a +  
|              | CD23 - |
| **Genetics**  | No specific abnormalities. |
| **Clinical**  | Splenomegaly. |
|               | ? Always leukemic. |
|               | Provisional in REAL scheme.  
|               | Corresponds to “splenic lymphoma with villous lymphocytes” |
Hairy cell leukemia

- Rare chronic
- Middle aged men
- Pancytopenia
- Splenomegaly
- fried egg appearance
**HAIRY CELL LEUKEMIA**

<table>
<thead>
<tr>
<th><strong>Morphology</strong></th>
<th>Small lymphoid cells with bean shaped nuclei and pale cytoplasm.</th>
</tr>
</thead>
</table>
| **Immunology** | Surface Ig +  
CD5, 10, 23 -  
CD11c, 25 +  
CD19, 20, 22, 79a +  
CD103 , DBA44 + |
| **Genetics**   | No specific abnormalities.                                       |
| **Clinical**   | Adults, often with splenomegaly and pancytopenia.  
Indolent course. |
# MARGINAL ZONE B CELL LYMPHOMA EXTRANODAL (MALT-TYPE)

**Morphology**
- Small centrocyte-like cells “monocytoid B cells”, lymphocytes, plasma cells.

**Immunology**
- Surface Ig +
- CD5, 10 -
- CD19, 20, 22, 79a +
- CD23 -

**Genetics**
- \(t(11;18)\) in many cases
- Trisom 3

**Clinical**
- Indolent course, often localized. May transform to large cell lymphoma.

The R.E.A.L. scheme includes nodal marginal zone lymphoma (“monocytoid B cell lymphoma”) as a provisional antity.
# PLASMA CELL MYELOMA

<table>
<thead>
<tr>
<th>Morphology</th>
<th>Plasma cells.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immunology</td>
<td>Surface Ig</td>
</tr>
<tr>
<td></td>
<td>Cytoplasmatic Ig</td>
</tr>
<tr>
<td></td>
<td>EMA</td>
</tr>
<tr>
<td></td>
<td>CD19, 20, 22</td>
</tr>
<tr>
<td></td>
<td>CD79a</td>
</tr>
<tr>
<td></td>
<td>CD 138</td>
</tr>
<tr>
<td>Genetics</td>
<td>t(11;14) in a few cases.</td>
</tr>
<tr>
<td>Clinical</td>
<td>Adults. Lytic bone lesions, less commonly soft tissue tumor. Relapse after plateau phase.</td>
</tr>
<tr>
<td></td>
<td>Usually associated with a serum paraprotein and/or urinary light chain excretion</td>
</tr>
</tbody>
</table>
PLASMA CELL MYELOMA

- Neoplasm of plasma cells
  - monoclonal protein in serum (SPEP)
  - Proteinuria (Bence-Jones) (UPEP)
- Lytic lesions in bones
  - fractures
- Anemia, increased globulin
  - Rouleaux formation
- Renal failure/ amyloidosis
PLASMA CELL MYELOMA
FOLLICLE CENTER LYMPHOMA

**Morphology**
Mixture of germinal center blasts and cleaved cells (centroblasts and centrocytes).

**Immunology**
- Surface Ig: +
- CD5: -
- CD10: +/-
- CD19, 20, 22, 79a: +
- BCL-2: +

**Genetics**
t(14;18) & BCL-2 rearrangements in majority of cases.

**Clinical**
Adults. Indolent course (median survival 7-9 yrs).

Equivalent to "centroblastic/centrocytic" and "follicular centroblastic" lymphomas in Kiel scheme.
GRADING OF FOLLICULAR LYMPHOMA

<table>
<thead>
<tr>
<th>Grade</th>
<th>Working Formulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>“Small cleaved cell”</td>
</tr>
<tr>
<td>II</td>
<td>“Mixed small cleaved and large cell”</td>
</tr>
<tr>
<td>III</td>
<td>“Large cell”</td>
</tr>
</tbody>
</table>
# MANTLE CELL LYMPHOMA

**Morphology**
Small irregularly shaped centrocyte-like cells.

**Immunology**
- Surface Ig ($\lambda$>$\kappa$) +
- CD5
- CD10 -/+ 
- CD19, 20, 22, 79a + 
- CD23 - 
- Cyclin D1 +

**Genetics**
t(11;14).


*BCL-1* rearrangement.

**Clinical**
Adults. Men, Moderately aggressive course (median survival 3-4 yrs).

Equivalent to “centrocytic lymphoma” in Kiel scheme
**DIFFUSE LARGE B CELL LYMPHOMA**

<table>
<thead>
<tr>
<th><strong>Morphology</strong></th>
<th>Monomorphous large cells with prominent nucleoli and basophilic cytoplasm.</th>
</tr>
</thead>
</table>
| **Immunology** | Surface Ig +/-  
Cytoplasmatic Ig +/-  
CD5, CD10 +/-  
CD19, 20, 22, 79a + |
| **Genetics**   | t(14;18) in approx 30%.  
*BCL-6* rearranged (40%) and/or mutated (75%). |
| **Clinical**   | Children or adults. Aggressive course, but may be curable. |

Combines “centroblastic” and “immunoblastic” categories from Kiel scheme.
## BURKITT’S LYMPHOMA

<table>
<thead>
<tr>
<th><strong>Morphology</strong></th>
<th>Medium sized cells, basophilic cytoplasm. “Starry sky” appearance. High mitotic rate.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Immunology</strong></td>
<td>Surface IgM + CD5, 23 - CD10 + CD19, 20, 22, 79a + Ki 67 &gt;85% of cells</td>
</tr>
<tr>
<td><strong>Genetics</strong></td>
<td>t(2;8), t(8;14) or t(8;22). Rearrangement of c-MYC</td>
</tr>
<tr>
<td><strong>Clinical</strong></td>
<td>Children &gt;&gt; adults. Aggressive but curable in children.</td>
</tr>
</tbody>
</table>

“Burkitt-like” lymphoma is a provisional entity in the REAL scheme
WHO classification T- A NK-cell neoplasias

T-cell precursor neoplasis
T lymphoblastic leukemia /lymphoma

MAture T and NK-cell neoplasias
T-prolymphocytic leukemia
T CELL LARGE GRANULAR LYMPHOCYTIC LEUKAEMIA
Aggressive NK-cell neoplasias
T-cell leukemia/lymphoma of adults dospělých (HTLV-1+)
Extranodal NK/T-cell lymphoma- nasal type
ENTEROPATHY- ASSOCIATED T-CELL LYMPHOMA
Hepatosplenic T-cell lymphoma
SUBCUTANEOUS PANNICULITIS-LIKE T-CELL LYMPHOMA
Mycosis fungoides/Sézaryho syndrom
CUTANEOUS ANAPLASTIC LARGE CELL T-CELL LYMPHOMA CD30
POSITIVE
Peripheral T-cell lymphoma NOS
Angioimmunoblastic T-cell lymphoma
Anaplastic large cell lymphoma lymfoma ALK pozitive
Anaplastic large cell lymphoma ALK negative
# T LYMPHOBLASTIC LEUKEMIA/LYMPHOMA

<table>
<thead>
<tr>
<th><strong>Morphology</strong></th>
<th>Lymphoblasts, identical cytologically to B lymphoblasts.</th>
</tr>
</thead>
</table>
| **Immunology**  | TdT +  
                CD1a +/-  
                CD3 +/-  
                CD7 +  
                CD4±8 +  |
| **Genetics**    | *SCL/TAL-1* rearrangement in approx 25%  |
| **Clinical**    | Frequently involves mediastinum. Adolescents and young adults. Highly aggressive but potentially curable.  

**Official name:**  
“Precursor T lymphoblastic lymphoma/leukemia”
T CELL PROLYMPHOCYTIC LEUKAEMIA

Morphology  Small lymphoid cells, with some nuclear irregularity.

Immunology  CD2, 3, 5, 7  +
CD4        +
CD8        -/+  

Genetics  Inv 14(q11;32) in some cases. Trisomy 8q

Clinical  Adults. Often leukemic.
          More aggressive than B cell chronic lymphocytic leukemia.

Includes T cell prolymphocytic leukemia.
**Morphology**
Small to medium lymphoid cells with eccentric round or oval nuclei. Azurophilic cytoplasmatic granules.

**Immunology**
- CD2: +
- CD3, 8: +/-
- CD16: +
- CD56, 57: -/+  

**Genetics**
No specific abnormalities.

**Clinical**
Adults, usually leukemic. Neutropenia ± anemia. Indolent course.

Two types.
T cell: CD3+, CD56-, CD57+/-.
NK cell: CD3-, CD56+, CD57+/-.
ENTEROPATHY-ASSOCIATED T-CELL LYMPHOMA

Morphology
Neoplastic cells range from small lymphocytes to large bizarre cells.

Immunology
- CD3, 7 +
- CD8 +/-
- CD103 +
- TIA-1 +

Genetics
No specific abnormalities.

Clinical
- Adults. Aggressive course, often with intestinal perforation.
- May be associated with celiac disease
ADULT T CELL LEUKAEMIA /LYMPHOMA

Morphology
Pleomorphic infiltrate of small and large lymphoid cells.

Immunology
CD2, 3, 4, 5, 25 +
CD7 -

Genetics
Integrated HTLV-1 genome.

Clinical
Adults. Commonest in Japan and Caribbean. Hypercalcemia, leukaemia, bone lysis common. May be aggressive or indolent.
# MYCOSIS FUNGOIDES

<table>
<thead>
<tr>
<th>Clinical</th>
<th>Adults. Patches, plaques &amp; tumours. Preferential location: buttocks, other sun-protected areas (early phases).</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphology</td>
<td>Small pleomorphic (cerebriform) cells. During the course of the disease large cell transformation may occur indicating a worse prognosis (immunoblasts, large cell anaplastic, large cell pleomorphic)</td>
</tr>
<tr>
<td>Immunology</td>
<td>CD2, 3, 4, 5 + CD</td>
</tr>
<tr>
<td>Genetics</td>
<td>No specific abnormalities. Monoclonal rearrangement of the TCR may be absent in early phases.</td>
</tr>
<tr>
<td>Treatment guidelines</td>
<td>Early phase: PUVA, interferon-2a, retinoids (alone or in combination); topical chemotherapy. Advanced disease chemotherapy; extracorporeal photopheresis; radiotherapy.</td>
</tr>
</tbody>
</table>
EARLY MYCOSIS FUNGOIDES

Epidermotropism of solitary lymphocytes aligned along basal layer of epidermis

Psoriasiform pattern
Plaques of mycosis fungoides are characterised by a dense, band-like infiltrate within the upper dermis.
MYCOSIS FUNGOIDES PLAQUE STAGE

Intraepidermal collections of lymphocytes (so-called Pautrier’s “microabscesses”)

Cytomorphologically small pleomorphic (cerebriform) cells predominate
# Sézary’s Syndrome

<table>
<thead>
<tr>
<th><strong>Clinical</strong></th>
<th>Elderly adults. Pruritic erythroderma, generalised lymphadenopathy &amp; circulating Sézary cells. Usually aggressive course.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Morphology</strong></td>
<td>Small pleomorphic (cerebriform) cells. During the course of the disease there may be appearance of tumours with large cell morphology immunoblats, large cell anaplastic, large cell pleomorphic).</td>
</tr>
<tr>
<td><strong>Immunology</strong></td>
<td>CD2, 3, 4, 5 + CD8 –</td>
</tr>
<tr>
<td><strong>Genetics</strong></td>
<td>No specific abnormalities. Monoclonal rearrangement of the TCR may be absent in early phases.</td>
</tr>
<tr>
<td><strong>Treatment guidelines</strong></td>
<td>PUVA, interferon-2a, retinoids (alone or in combination); extracorporeal photopheresis; radiotherapy; chlorambucil combined with prednisone (Winkelmann scheme); systemic chemotherapy.</td>
</tr>
</tbody>
</table>
Sézary’s Syndrome

Erythroderma: note enlarged inguinal lymph nodes

Hyperkeratosis of the palms
Sézary’s Syndrome

Sézary cells in the peripheral blood

Dense band-like infiltrate of lymphocytes in the skin
CUTANEOUS ANAPLASTIC LARGE CELL T-CELL LYMPHOMA  CD30 POSITIVE

<table>
<thead>
<tr>
<th>Clinical</th>
<th>Adults &amp; younger patients. Solitary or regionally localised tumours, often ulcerated. Generally favourable prognosis.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphology</td>
<td>Nodular infiltrates characterised by cohesive sheets of large, CD30 positive cells. Cytomorphology. Usually large anaplastic cells; large pleomorphic cells or immunoblasts.</td>
</tr>
<tr>
<td>Immunology</td>
<td>CD2, 3, 4, 5 +</td>
</tr>
<tr>
<td></td>
<td>CD30 +</td>
</tr>
<tr>
<td></td>
<td>CD8 –</td>
</tr>
<tr>
<td></td>
<td>CD15, EMA –</td>
</tr>
<tr>
<td>Genetics</td>
<td>Usually absence of t(2;5). Monoclonal rearrangement of the TCR detected in the majority of cases.</td>
</tr>
<tr>
<td>Treatment guidelines</td>
<td>Solitary or localised lesions: radiotherapy (with or without previous surgical excision); Generalised lesions: systemic chemotherapy.</td>
</tr>
</tbody>
</table>
CUTANEOUS ANAPLASTIC LARGE CELL T-CELL LYMPHOMA

Infiltrate of anaplastic cells admixed with small lymphocytes & other inflammatory cells.

CD30 + anaplastic lymphocytes

Anaplastic cells, many bi- or multi-nucleated
ANAPLASTIC LARGE CELL LYMPHOMA
Definition and Cytogenetics

(agrresive, but curable, good prognosis, often extranodal

The (2;5) translocation

Initially thought to be associated with true histiocytic malignancy but then linked to anaplastic large cell lymphoma.
Occasionally there is evidence of haemophagocytosis, characterised by large macrophages engulfing neoplastic lymphocytes or other blood cells.
**PERIPHERAL T CELL LYMPHOMA, UNSPECIFIED**

<table>
<thead>
<tr>
<th><strong>Morphology</strong></th>
<th>Atypical lymphocytes of varying sizes. Variable reactive background elements, e.g. macrophages, vessels, etc.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Immunology</strong></td>
<td>CD3 +/- Variable expression of other T cell markers.</td>
</tr>
<tr>
<td><strong>Genetics</strong></td>
<td>No specific abnormalities.</td>
</tr>
<tr>
<td><strong>Clinical</strong></td>
<td>Adults. Aggressive course, but potentially curable.</td>
</tr>
</tbody>
</table>

“Unspecified” reflects suspicion that subtypes (currently unidentifiable) exist.
# ANGIOIMMUNOBLASTIC T CELL LYMPHOMA

<table>
<thead>
<tr>
<th><strong>Morphology</strong></th>
<th>Architecture effaced, arborizing high endothelial venules, no secondary follicles. Mixed infiltrate of lymphocytes, blasts and atypical clear cells.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Immunology</strong></td>
<td>T cell phenotype. Large follicular dendritic cell clusters around proliferating venules.</td>
</tr>
<tr>
<td><strong>Genetics</strong></td>
<td>No specific abnormalities.</td>
</tr>
<tr>
<td><strong>Clinical</strong></td>
<td>Systemic disease with lymphadenopathy, fever, weight loss, and skin rash. Polyclonal hypergamma-globulinemia. Aggressive course.</td>
</tr>
</tbody>
</table>
5- y survival > 70%:

- Follicular lymphoma
- MALT lymphoma
- Anaplastic large cell lymphoma

5- y survival 50-70%:

- Nodal B cell lymphoma – marginal zone
- Lymphoplasmocytic lymphoma
- SLL/CLL

5- y survival 30-50%:

- large B cell lymphoma
- Burkitt lymphoma
- Burkitt-like lymphoma

The worst prognosis:

- T lymphoblastic lymphoma
- Peripheral T cell lymphoma
- Mantle cell lymphoma
HODGKIN´s lymphoma/HODGKIN´s disease

EBV infection, genetic changes, immune alteration
2-3 decades, 5 decade

1) Nodular lymphocyte predominant Hodgkin lymphoma
2) Classical Hodgkin lymphoma
Nodular Sclerosis (the most common)
Mixed Cellularity (the highest association with EBV, common in HIV)
Lymphocyte rich
Lymphocyte Depleted
Nodular lymphocyte predominant Hodgkin lymphoma

- B cell antigen
- Lack CD15, CD30
- Popcorn cells
- Indolent type
- Men under 35y
- Cervical, axillary and inguinal LN
- Mediastinum rare
- B sings and symptoms in 20%
- 5y survival in 80%

Classical Hodgkin lymphoma

- LN cervical, anterior mediastinum
- B signs in 40% (low fever, cyclical, night sweats, weight loss, pruritus, alcoholic pain)
- HRS cells
HODGKIN’S DISEASE

Lymphocyte Predominance

Low power

High power
HODGKIN’S DISEASE
Lymphocyte Predominance

B cell marker on reactive and neoplastic cells

T cell marker on reactive cells
HODGKIN’S DISEASE: “CLASSICAL” SUBTYPES

Nodular Sclerosis

Low power
Lacunar cells
Reed-Sternberg cells
HODGKIN’S DISEASE: “CLASSICAL” SUBTYPES

Mixed Cellularity

Low power

B cells

High power

“Mummified cells” Reed-Sternberg cells