

Malignant Lymphomas and Plasma Cell Myeloma

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Overview

- definitions -
 - lymphoma
 - lymphoproliferative disorder
 - plasma cell myeloma
- pathogenesis - “translocations”
- classification
 - Hodgkin’s and non-Hodgkin’s lymphomas

Essential Points about Lymphomas

- they are all “malignant”
- derived from B or T cells
- usually arise in lymph nodes, but can form in any organ
- differ from leukemias -
 - tumor cells not in peripheral blood
 - disease not usually centered in marrow

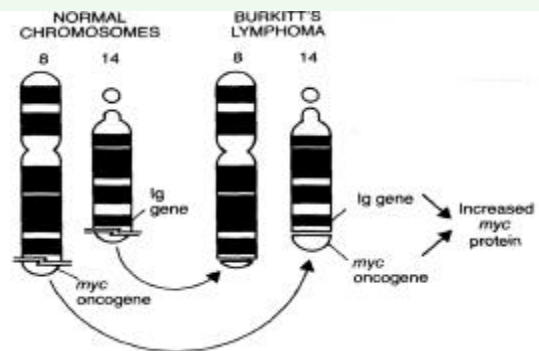
Pathogenesis of Lymphomas

- mutation in a single precursor cell - **monoclonal** expansion
- **chromosomal translocations** are most frequent mutation
- translocations arise during normal process of “**gene rearrangement**”

Pathogenesis of Lymphomas - 2

- translocations are characteristic of specific lymphomas
 - e.g.. t(14;18) in follicular lymphomas
 - t(8;14) in Burkitt’s lymphoma
- clone of cells is “**immortalized**”
- further mutations often occur leading to “**tumor progression**”

Chromosomal Translocations



General Clinical Features of Lymphomas

- usually present as enlarged lymph nodes (lymphadenopathy)
- may have other symptoms such as:
 - weight loss
 - fevers
 - night sweats

Classification of Lymphomas

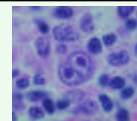
- important because lymphomas differ dramatically in their:
 - pattern of spread
 - growth rate
 - response to treatment and prognosis
- Two broad categories of lymphoma:
 - Hodgkin's lymphoma (disease) (~40%)
 - Non-Hodgkin's lymphomas (~60%)

Hodgkin's Lymphoma

- histologic subtypes in Hodgkin's not as important to treatment as is Stage
- **Classic** Hodgkin's lymphoma
 - nodular sclerosis (commonest overall)
 - mixed cellularity
- **Nodular lymphocyte predominant** form

Hodgkin's Lymphoma

- defined by the presence of tumor cells called "**Reed-Sternberg cells**"
- predictable pattern of spread allows for use of radiotherapy
- Staging very important
- usually curable

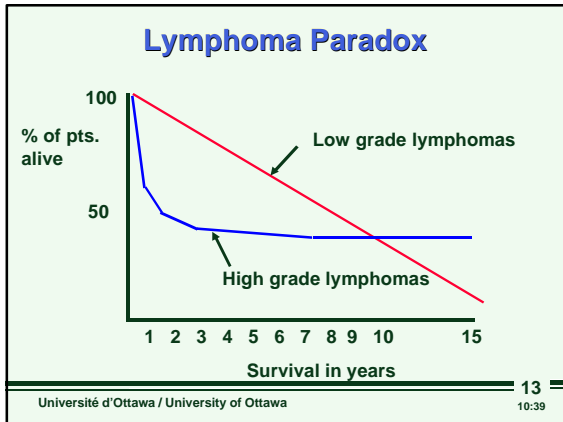


Non-Hodgkin's Lymphomas

- Histologic sub-type correlates with behavior and treatment
- classification scheme changing (again!!!)
- **Working Formulation** in texts now
- **W.H.O.** scheme will replace it

Classification of Non-Hodgkin's Lymphomas

- B-cell (~90%) versus T-cell (the rest)
- B-cell types can be thought of as:
 - **Low grade** (slow growing, but poorly responsive to treatment)
 - **Aggressive** or Intermediate grade (faster growing, potential for cure)
 - **High grade** (very lethal if untreated, behave and treated like acute leukemias)



Low Grade NHL's

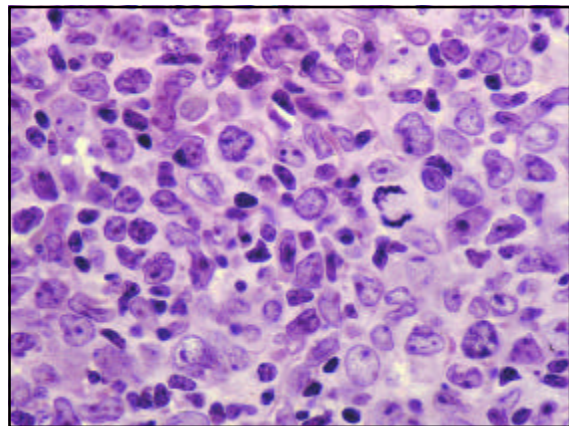
- include lymphomas of **small lymphocytes** (similar to CLL)
- also includes the **"follicular"** lymphomas

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Aggressive NHL's

- most common form
- wide age range
- include diffuse large B-cell lymphoma & most T-cell lymphomas
- treated with systemic chemotherapy with intent to cure

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High Grade NHL's

- include lymphoblastic and Burkitt's lymphomas
- very high mitotic rate correlates with rapid growth, response to treatment and relapse

"Starry-sky" pattern

Burkitt's

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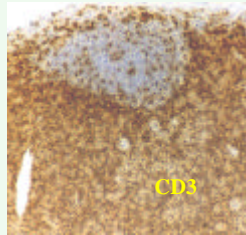
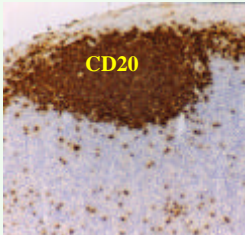
Tissue needed for diagnosis

- Open biopsy :
 - architectural and cytologic features
 - fresh tissue available for immunophenotyping and genetic studies
- Fine needle aspiration:
 - often adequate if node is inaccessible surgically or patient not surgically fit

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Normal Immunophenotypes

B cells: CD19, CD20, CD22, Kappa/lambda
T cells: CD3, CD5, CD4 or CD8



Immunophenotyping in Diagnosis

- B and T cells have specific surface markers, e.g. CD3 = T, CD20 = B
- B-cell monoclonality can be proven by showing “light chain restriction”



Plasma Cell Myeloma

- monoclonal tumor of plasma cells
 - often secrete monoclonal immunoglobulin (“M” protein) in serum
- bone marrow based
 - replaces marrow >> pancytopenia
 - dissolves bone >> “pathologic” fracture

Clinical Features of Myeloma

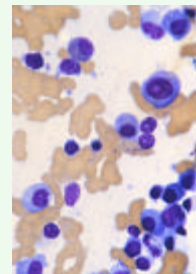
- age - usually > 50 years
- bone pain - back and ribs esp..
- infections - pneumonia, pyelonephritis (kidney)
- renal failure - many causes
- fatigue - anemia and hypercalcemia

Diagnosis of Myeloma

- typical x-ray findings:
 - multiple lytic “punched out” lesions in vertebrae, skull, ribs, pelvis
- serum or urine monoclonal “spike”
- +/- free light chains in urine (Bence-Jones protein)

Diagnosis of Plasma cell myeloma

- > 10% plasma cells in marrow, especially if growing in sheets



Staging & Prognosis in Myeloma

- high tumor cell burden predicted by:
 - Hb < 85
 - serum Calcium > 3 mmol/L
 - multiple lytic bony lesions
 - high M protein level (e.g.. IgG > 70 gm/L)
- Prognosis - low burden ~ 60 months
high burden ~ 15 months