Heme-Lymph Lab: Lymphoma/Myeloma

Objectives

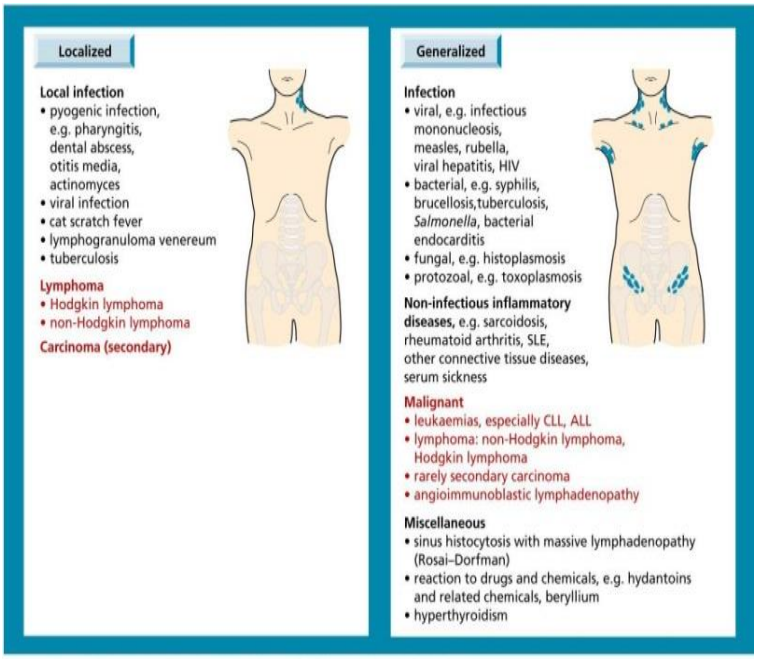
Laboratory Instructors:

1. Assist students during self study

Students:

1. Review the introductory material
2. Study the case histories provided for Hematology MD Lab 3
3. Examine the pathological material related to each case using virtual microscopy
4. Answer the questions related to each case

Lymphadenopathy: Differential Diagnosis



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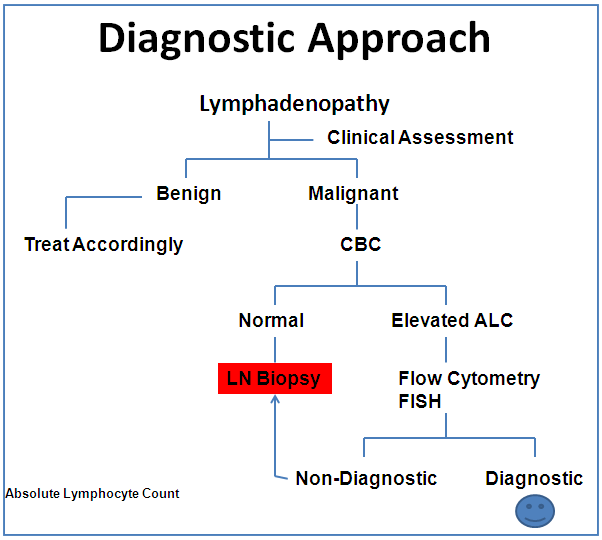

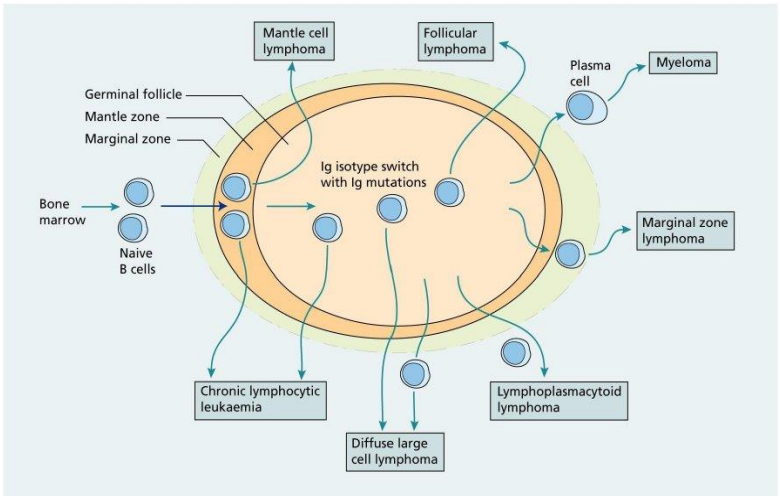

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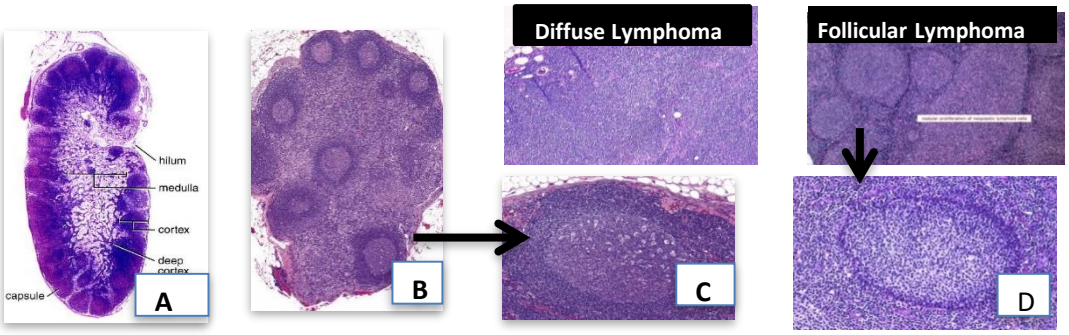
Left: Proposed cellular origin of B-lymphoid malignancies. The cellular origin of different lymphoid malignancies can be inferred from immunoglobulin gene rearrangement status and membrane phenotype. Mantle cell lymphoma and a proportion of B-cell chronic lymphocytic lymphoma (B-CLL) cases have unmutated immunoglobulin genes whereas marginal zone lymphoma, diffuse large cell lymphoma, follicle cell lymphoma, lymphoplasmacytoid lymphoma and some B-CLL cases have mutated immunoglobulin genes

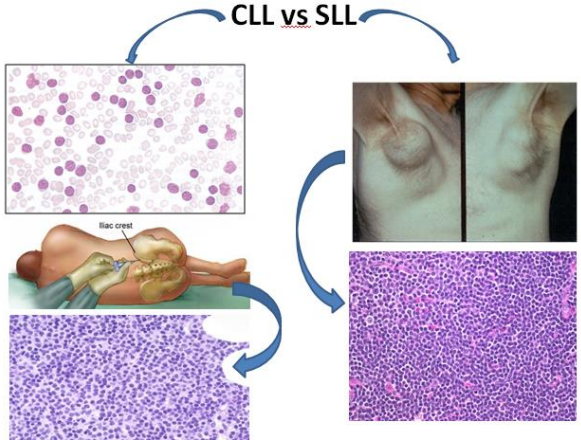
Lymph Node Biopsy: Benign vs Malignant



Above: In benign reactive LN hyperplasia (B), the normal architecture of LN (A) is preserved but all or some components are expanded. In the example shown in B, note the expanded follicles and paracortical areas. In lymphoma, there is replacement (effacement) of normal LN architecture by diffuse or follicular pattern of growth. Lymphoid follicles of hyperplasia contain tingible body macrophages (C) in contradistinction to FL follicles (D).

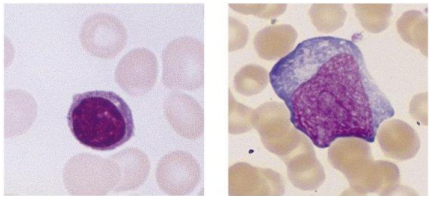
Leukemia vs Lymphoma

1. **Leukemia = Blood and BM presentation**
   - **Abnormal CBC**
   - **Circulating malignant cells**
   - **Bone marrow involvement (≥ 20%)**
2. **Lymphoma = LN/soft tissue presentation**
   - **Lymphadenopathy**
3. **Leukemia/Lymphoma : 1 + 2**
   Examples: CLL/SLL; T-ALL/LBL

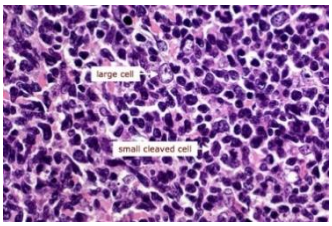


Above: Chronic lymphocytic leukemia (CLL) and small lymphocytic lymphoma (SLL) are different presentations of the same disease. In CLL (left panel), the disease involves blood (top left) and bone marrow (left bottom). In SLL, the malignant transformation is believed to take place in LNs (leading to lymphadenopathy, top right). With time, the picture between the 2 presentations blurs. Histologically, cytologically, phenotypically, and genetically the 2 presentations are identical. There is diffuse infiltration of LN (SLL, bottom right) or BM (CLL, bottom left) by small mature-looking lymphocytes.

Lymphoma: Histology vs Cytology

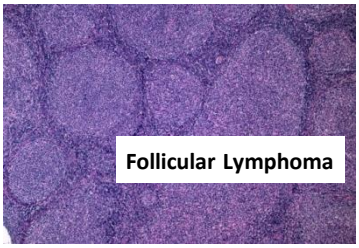


Cytology = Individual cells on a smear
Left: small lymphocyte; Right: Large (activated) lymphocyte or a blast. Cytology shows more detailed individual cell morphology

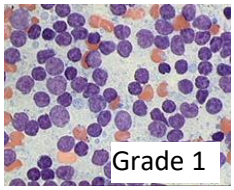


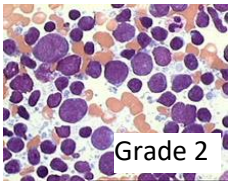
Histology = Tissue section
Large cells: vesicular nuclei, open chromatin; Small cells: compact nuclei. Histology preserves tissue architecture needed to assess pattern of growth, fibrosis…etc.

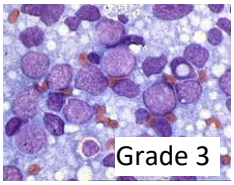
Follicular NHL



Designation as FOLLICULAR or DIFFUSE NHL is determined by low power projection of LN section. Shown to the left is a follicular lymphoma. In diffuse lymphoma, LN is replaced by sheets of lymphoma cells.

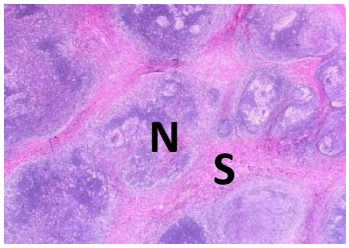


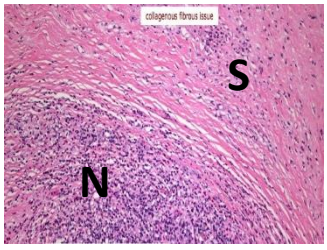


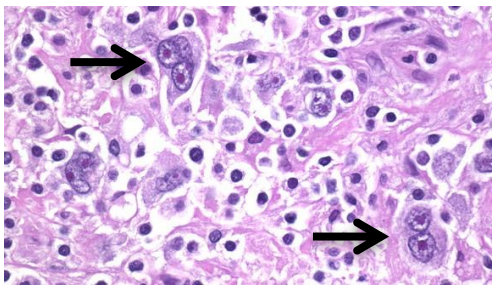


Within follicular lymphoma, there are 3 histologic 'grades' based on cell size (high power projection): grade 1, predominantly small cleaved cells; grade 2, mixture of small and large cells; grade 3, predominantly large cells. Grades 1-2 have an indolent clinical course and are considered 'low' grade lymphomas whereas grade 3 has a more aggressive clinical course.

Nodular Sclerosis Hodgkin Lymphoma (NSHL)

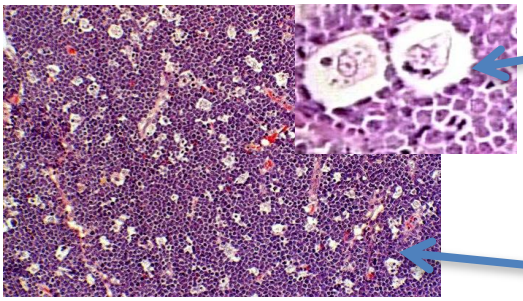






Not to be confused with follicular lymphoma, in NSHL the irregularly shaped nodules (N) result from bands of collagen fibers (S) that run throughout the LN which is characteristic of this most common subtype of HL. Diagnosis of HL requires the demonstration of Reed-Sternberg cells (arrows, above right)

Lymphoma: Morphology of Interest

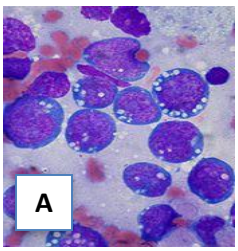


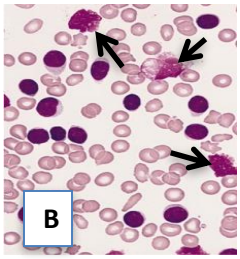
The **'stars'** are normal macrophages engulfing debris of dead lymphoma cells

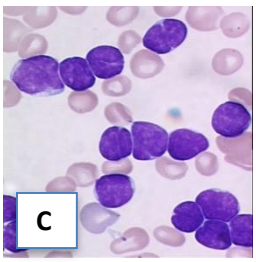
Starry Sky appearance

Characteristic, but not specific for Burkitt lymphoma. It indicates high proliferation rate seen in high grade NHL.

The **'sky'** is the lymphoma cells looking blue by H & E stain



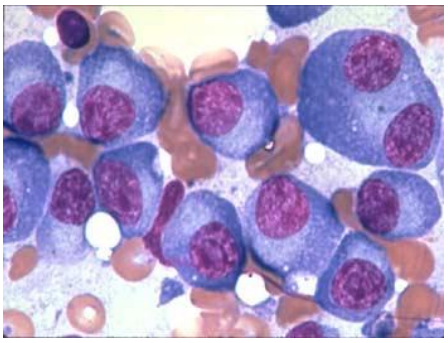


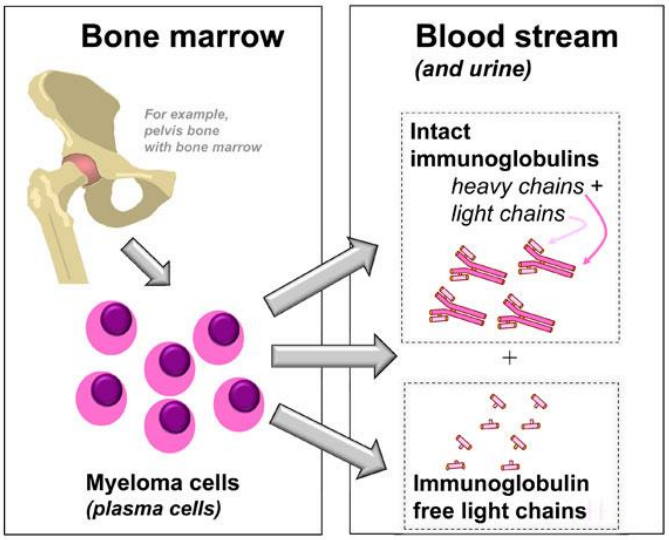


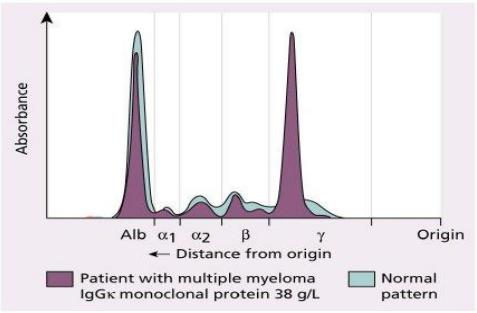
A. intermediate size cells with open chromatin of the nuclei and deep blue cytoplasm with vacuoles typical of Burkitt lymphoma **B**: typical cells of CLL- small lymphocytes, clumped (compact) chromatin of round or oval nuclei and scant amount of cytoplasm. These cells are indistinguishable morphologically from normal small lymphocytes. Smudge cells (arrows) are nuclei of ruptured CLL cells during preparation of smear. **C**: Small cleaved cells typical of follicular lymphoma grade 1. Cleaved refers to deep clefts in the nuclei of these cells

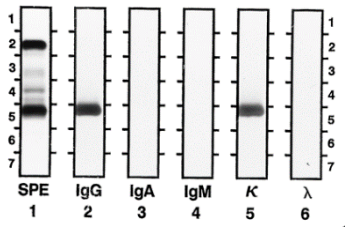
Plasma Cell Myeloma

Characteristic morphological features of plasma cells (Right), round nucleus (sometimes cart wheel arrangement of chromatin), eccentric nuclei, deep blue cytoplasm except around the nucleus (perinuclear halo) an area rich in golgi. Multiple myeloma results from clonal expansion of malignant plasma cells.









Clonal myeloma cells produce monoclonal Ig (above) which can be detected in blood or urine. Myeloma cells may produce more light chains than heavy chains. Uncoupled (free) light chain can be detected in serum as Free Light Chains (FLC) or in the urine as Bence-Jones protein. The monoclonal protein (M-spike, paraprotein) can be detected by serum protein electrophoresis (SPEP)(top right) and specific Ig isotype determined by immunoelectrophoresis (IEP) or immunofixation (lower right)

'C' in CRAB refers to hyperCalcemia. This results from plasma cell-induced osteoclast activation, bone resorption and release of calcium into the blood. Bone resorption takes place around plasma cell tumors within BM resulting in thinning of cortical bone and giving the characteristic 'punched out' lytic lesions on bone X-ray (Left humorous X-ray) . It can also leads to fracture or collapse of vertebral bodies (X-ray and MRI of spine). Renal disease in multiple myeloma is multifactorial but is predominantly due to filtration of light chains through the glomeruli due to their low molecular weight. Anemia is also multifactorial including decreased RBC production secondary to BM involvement, decreased erythropoietin production secondary to renal dysfunction and side effect of anti-myeloma therapy.