

Thursday, April 26, 2007

11:00 A.M – 1:00 P.M

LYMPHOMA

MICROSCOPIC LABORATORY

Lymphatic Diseases

Slides to be reviewed:

#31: Hodgkin's lymphoma, nodular sclerosing type

#32: Non-Hodgkin's lymphoma (mantle zone lymphoma)

#33: Multiple myeloma

#34: Reactive lymph node

#35: Chronic lymphocytic leukaemia in spleen

#36: Extramedullary hematopoiesis (EMH) (Spleen)

#31: Hodgkin's lymphoma, nodular sclerosing type

Cervical lymph node from a 25-year-old man with night sweats, weight loss and lymphadenopathy. The nodal architecture is completely effaced by broad bands of fibrous tissue separating nodular areas of increased cellularity. These nodules show a polymorphic cell population, which includes numerous lacunar cells, Reed-Sternberg cells, histiocytes and eosinophils. Large areas of necrosis are also identified.

1. What subtypes of Hodgkin's disease are there?

Nodular sclerosis, mixed cellularity, lymphocyte predominant, lymphocyte depleted (rare).

2. What is the cell of origin in Hodgkin's disease?

In the lymphocyte predominant variant, this is a B cell neoplasm (CD15 and CD30 positive). In other forms, the origin is more enigmatic, though many show immunoglobulin gene rearrangements that suggest B cell origin too.

3. What clinical characteristics are useful in distinguishing Hodgkin's lymphoma from non-Hodgkin's lymphoma?

Hodgkin's is more often localized to a single axial group of nodes (cervical, mediastinal, para-aortic) and shows orderly spread by contiguity. Extranodal involvement is uncommon, in contrast to NHL.

4. What is the single most important histopathologic diagnostic criterion for Hodgkin's lymphoma?

The presence of the Reed-Sternberg cell (or variants).

#32: Non-Hodgkin's lymphoma (mantle cell lymphoma)

This lymph node was obtained from a 71-year-old man, with weight loss and diffuse lymphadenopathy. Note the abnormal nodal architecture, with broadly expansile nodular

masses of monotonous small to intermediate sized lymphocytes demonstrating nucleoli, nuclear cleavage or non-cleavage and mitotic activity. This neoplasm derived from the follicular mantle zone and represents a small cell lymphoma whose nuclear shape is intermediate between that of a small lymphocytic and that of a small, cleaved cell lymphoma.

1. Describe an overall classification of the non-Hodgkin's lymphomas and where "mantle cell lymphoma" would be placed.

Review the REAL Classification, indicating that mantle cell lymphoma would fall in the Peripheral B-cell Neoplasm group.

2. What are the methods for specifically identifying this a mantle cell lymphoma?

The cells show t (11;14) and have the unique immunophenotype of CD5+, CD19+, CD20+, CD22+, CD24+, Leu 8+, HLA-DR+. (The students have no need to know this array of immunomarkers, however). Immunoglobulin heavy and light chain genes are rearranged in most cases.

3. There are a number of classification systems for non-Hodgkin's lymphoma. Describe what the most recent system aims to do, and how it is organized.

Review the categories of the REAL classification, including I. Precursor B-cell neoplasms; II: Precursor T-cell Neoplasms; III: Peripheral B-cell neoplasms; and IV: Peripheral T-cell and Natural Killer Cell Neoplasms (See the large Robbins, pg. 652).

#33: Multiple myeloma

A 52-year-old succumbed after a four month history of bone fractures and pain, widespread lytic lesions on skeletal X-rays, and bone marrow biopsy confirming multiple myeloma. On low power, note the ragged appearance of the bony trabeculae, whose edges are eroded by the neoplastic cell population. Find the areas that on low power appear hypercellular; in these foci, although many normal hematopoietic elements are preserved

(including red cell precursors and megakaryocytes) there is a prominent increase in the numbers of plasma cells and plasmacytoid forms. Recall the “cartwheel” or “clockface” appearance of the plasma cell nucleus and the perinuclear clear Golgi zone as helpful features to identify the plasma cells.

1. To confirm the presence of multiple myeloma clinically, apart from bone marrow biopsy and X-rays, what tests are particularly important?

Serum protein electrophoresis (SPEP) looking for monoclonal (M) spike, and urine electrophoresis (UEP) looking for Bence-Jones protein.

2. What diagnostic test can the pathologist perform to be certain that this is a monoclonal plasma cell neoplasm rather than a polyclonal reactive plasmacytosis of the bone marrow?

Immunostaining for kappa and lambda light chains, and looking for homogeneity vs. heterogeneity (the latter favoring polyclonal plasma cells).

3. State the conditions which fall in the category of “Plasma Cell Dyscrasias.”

Multiple myeloma, Waldenstrom’s macroglobulinemia, cryoglobulemia, light and heavy chain disease, monoclonal gammopathy of undetermined significance; amyloidosis.

#34: Reactive Lymph Node

A patient with breast carcinoma underwent lumpectomy and lymph node resection, and this sample was examined by the pathologist (no tumor was found in the lymph node). Note the focal follicular hyperplasia present, while other follicles show germinal centre atrophy with prominent follicular mantles. The paracortical areas are widened and contain numerous histiocytes, which impart a “mottled” appearance to these areas. Marked sinus histiocytosis is also noted.

1. What are the basic features which differentiate a reactive lymph node from lymphoma?

Overall preservation of nodal architecture, heterogeneity of lymphoid cells both are features of reactive nodes.

2. How would the pathology laboratory handle a fresh specimen of lymph node to workup a possible lymphoma OR metastatic carcinoma?

To workup lymphoma, fresh specimen analyzed by FLOW CYTOMETRY, IMMUNOSTAINS, GENE REARRANGEMENT STUDIES

To workup possible metastatic Ca, CYTOKERATIN IMMUNOSTAIN

#35: Chronic lymphocytic leukaemia in spleen

This 60-year-old man was known for many years to have CLL, presenting originally with fatigue and weight loss and a total peripheral blood WBC count of 100,000. He later developed hypersplenism, requiring splenectomy. Note the diffuse involvement of the white and red splenic pulp by a population of monomorphous, small lymphocytes with clumped chromatin, inconspicuous nucleoli and scanty cytoplasm. No plasmacytic or immunoblastic differentiation is noted. The lymphoid infiltration obscures and invades the splenic architecture such that distinction between red and white pulp is difficult.

1. What is the difference between chronic lymphocytic leukaemia and small lymphocytic lymphoma?

None: they are morphologically, phenotypically, and genotypically indistinguishable, differing only in the degree of peripheral blood lymphocytosis. They are B cell neoplasms.

2. What are the distinctive chromosomal changes associated with this disease?

Trisomy 12, deletions of 13q12-14 and deletions of 11q (each of which is seen in 20-30% of cases).

3. What is the usual clinical course? What may eventually happen to these patients?

Course is variable, with overall median survival of 4-6 yrs. Patients who present with minimal tumor burden may survive for 10 years or more. CLL and SLL may transform to more aggressive lymphoid neoplasms: prolymphocytic transformation in 15-30% of patients, or transformation to diffuse large B-cell lymphoma in about 10% of patients.

#36: Extramedullary hematopoiesis (EMH) (Spleen)

A 63-year-old woman with widely disseminated breast cancer was admitted for acute gastrointestinal haemorrhage. She was found to have an extremely low platelet count (30,000) and a bone marrow biopsy showed extensive marrow replacement by breast carcinoma. At autopsy several weeks later, there was a marked splenomegaly (1500g., with normal <150).

1. State three conditions in which EMH of the spleen may be seen.

NEOPLASTIC hematologic disorders (leukemia, lymphoma, myeloma) which involve the bone marrow; CHRONIC ANEMIAS; CHRONIC HEMATOPOIETIC

DISORDERS (Thrombotic thrombocytopenic purpura/hemolytic uremic syndrome).

2. What abnormalities in the complete blood count (CBC) might be present in this patient?

Neutropenia and/or anemia are other possible CBC changes that may accompany extensive bone marrow replacement by carcinoma.