Lymphoid Neoplasms

Definitions and Classifications

One confusing aspect of the lymphoid neoplasms concerns the use of the terms *lymphocytic leukemia* and *lymphoma*. *Leukemia* is used for neoplasms that present with widespread involvement of the bone marrow and (usually, but not always) the peripheral blood. *Lymphoma* is used for proliferations that arise as discrete tissue masses. Originally these terms were attached to what were considered distinct entities, but with time and increased understanding these divisions have blurred. Many entities called "lymphoma" occasionally have leukemic presentations, and evolution to "leukemia" is not unusual during the progression of incurable "lymphomas." Conversely, tumors identical to "leukemias" sometimes arise as soft-tissue masses without detectable bone marrow disease. Hence, when applied to particular neoplasms, the terms *leukemia* and *lymphoma* merely reflect the usual tissue distribution of each disease at presentation.

Within the large group of lymphomas, *Hodgkin lymphoma* is segregated from all other forms, which constitute the *non-Hodgkin lymphomas (NHLs)*. Hodgkin lymphoma has distinctive pathologic features and is treated in a unique fashion. Another special group of B cell tumors, which differs from most lymphomas, is the *plasma cell neoplasms*. These most often arise in the bone marrow and only infrequently involve lymph nodes or the peripheral blood. Taken together, the diverse lymphoid neoplasms constitute a complex, clinically important group of cancers, with about 100,000 new cases being diagnosed each year in the United States.

The clinical presentation of the various lymphoid neoplasms is most often determined by the anatomic distribution of disease. Two thirds of NHLs and virtually all Hodgkin lymphomas present as enlarged nontender lymph nodes (often > 2 cm). The remaining one third of NHLs present with symptoms related to the involvement of extranodal sites (e.g., skin, stomach, or brain). The lymphocytic leukemias most often come to attention because of signs and symptoms related to the suppression of normal hematopoiesis by tumor cells in the bone marrow. Finally, the most common plasma cell neoplasm, multiple myeloma, causes bony destruction of the skeleton and often presents with pain due to pathologic fractures. Other symptoms related to lymphoid tumors are frequently caused by proteins secreted from the tumor cells or from immune cells that are responding to the tumor. Specific examples include the plasma cell tumors, in which much of the pathophysiology is related to the secretion of whole antibodies or Ig fragments; Hodgkin lymphoma, which is often associated with fever related to the release of cytokines from inflammatory cells responding to the tumor cells; and peripheral T-cell lymphomas, tumors of functional T cells that often release a number of inflammatory cytokines and chemokines.

Historically, few areas of pathology evoked as much controversy as the classification of lymphoid neoplasms, but consensus has been reached through use of objective molecular diagnostic tools. The current World Health Organization (WHO) classification scheme (Table 13-4) uses morphologic, immunophenotypic, genotypic, and clinical features to sort the lymphoid neoplasms into five broad categories, which are separated according to the cell of origin:

1. Precursor B-cell neoplasms (neoplasms of immature B cells)
2. Peripheral B-cell neoplasms (neoplasms of mature B cells)
3. Precursor T-cell neoplasms (neoplasms of immature T cells)
4. Peripheral T-cell and NK-cell neoplasms (neoplasms of mature T cells and NK cells)
5. Hodgkin lymphoma (neoplasms of Reed-Sternberg cells and variants)

Before discussing the specific entities of the WHO classification, some important principles relevant to the lymphoid neoplasms should be emphasized.

- Lymphoid neoplasia can be suspected from the clinical features, but histologic examination of lymph nodes or other involved tissues is required for diagnosis.

Table 13-4 World Health Organization Classification of Lymphoid Neoplasms

I. Precursor B-Cell Neoplasms
B-cell acute lymphoblastic leukemia/lymphoma (B-ALL)
II. Peripheral B-Cell Neoplasms
Chronic lymphocytic leukemia/small lymphocytic lymphoma
B-cell prolymphocytic leukemia
Lymphoplasmacytic lymphoma
Splenic and nodal marginal zone lymphomas
Extranodal marginal zone lymphoma
Mantle cell lymphoma
Follicular lymphoma
Marginal zone lymphoma
Hairy cell leukemia
Plasmacytoma/plasma cell myeloma
Diffuse large B-cell lymphoma
Burkitt lymphoma
III. Precursor T-Cell Neoplasms
T-cell acute lymphoblastic leukemia/lymphoma (T-ALL)
IV. Peripheral T-Cell and NK-Cell Neoplasms
T-cell prolymphocytic leukemia
Large granular lymphocytic leukemia
Mycosis fungoides/Sézary syndrome
Peripheral T-cell lymphoma, unspecified
Anaplastic large-cell lymphoma
Angioimmunoblastic T-cell lymphoma
Enteropathy-associated T-cell lymphoma
Panniculitis-like T-cell lymphoma
Hepatosplenic γδT-cell lymphoma
Adult T-cell leukemia/lymphoma
Extranodal NK/T-cell lymphoma
NK-cell leukemia
V. Hodgkin Lymphoma
Classical subtypes
Nodular sclerosis
Mixed cellularity
Lymphocyte-rich
Lymphocyte depletion
Lymphocyte predominance

NK, Natural killer.