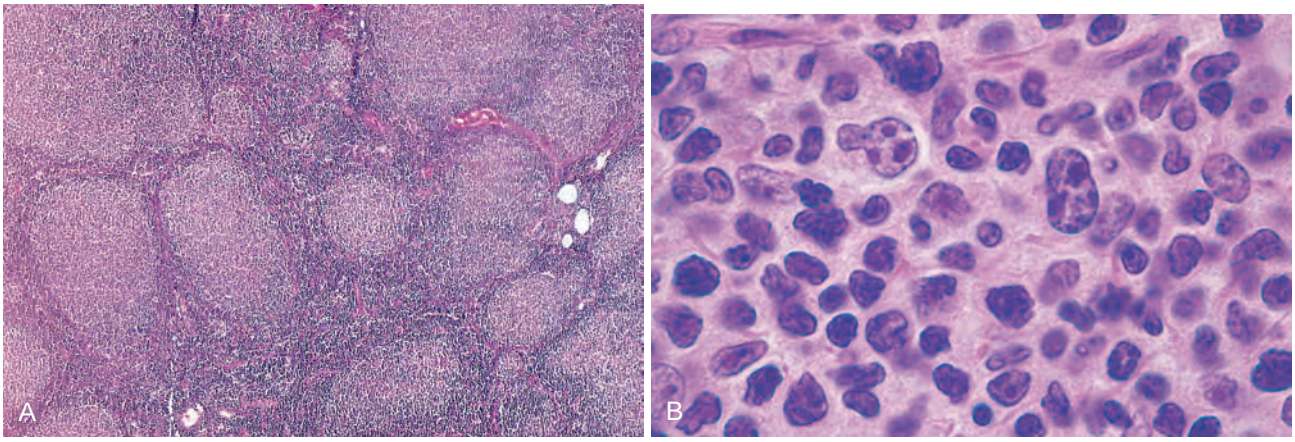

Figure 13-10 Follicular lymphoma (lymph node). **A,** Nodular aggregates of lymphoma cells are present throughout lymph node. **B,** At high magnification, small lymphoid cells with condensed chromatin and irregular or cleaved nuclear outlines (centrocytes) are mixed with a population of larger cells with nucleoli (centroblasts). (**A,** Courtesy Dr. Robert W. McKenna, Department of Pathology, University of Texas Southwestern Medical School, Dallas, Texas.)

methyltransferase that regulates gene expression, suggesting that epigenetic abnormalities have an important role in this neoplasm; however, the functional significance of *MLL2* mutations has yet to be deciphered.

Particularly early in the disease, follicular lymphoma cells growing in lymph nodes are found within a network of reactive follicular dendritic cells admixed with macrophages and T cells. Expression profiling studies have shown that differences in the genes expressed by these reactive cells are predictive of outcome, implying that the response of follicular lymphoma cells to therapy is influenced by the surrounding microenvironment.

MORPHOLOGY

In most cases, a predominantly nodular or nodular and diffuse growth pattern is observed in involved lymph nodes (Fig. 13-10*A*). Two principal cell types are present in varying proportions: (1) small cells with irregular or cleaved nuclear contours and scant cytoplasm, referred to as **centrocytes** (small cleaved cells); and (2) larger cells with open nuclear chromatin, several nucleoli, and modest amounts of cytoplasm, referred to as **centroblasts** (Fig. 13-10*B*). In most follicular lymphomas, small cleaved cells are in the majority. Peripheral blood involvement sufficient to produce lymphocytosis (usually less than 20,000 cells/mm^3) is seen in about 10% of cases. Bone marrow involvement occurs in 85% of cases and characteristically takes the form of paratrabecular lymphoid aggregates. The splenic white pulp (Fig. 13-11) and hepatic portal triads are also frequently involved.

Immunophenotype. The neoplastic cells closely resemble normal germinal center B cells, expressing CD19, CD20, CD10, surface Ig, and BCL6. Unlike CLL/SLL and mantle cell lymphoma, CD5 is not expressed. BCL2 is expressed in more than 90% of cases, in distinction to normal follicular center B cells, which are BCL2-negative (Fig. 13-12).

Clinical Features. Follicular lymphoma tends to present with painless, generalized lymphadenopathy. Involvement of extranodal sites, such as the gastrointestinal tract, central nervous system, or testis, is relatively uncommon. Although incurable, it usually follows an indolent waxing and waning course. Survival (median, 7 to 9 years) is not improved by aggressive therapy; hence, the usual approach is to palliate patients with low-dose chemotherapy or immunotherapy (e.g., anti-CD20 antibody) when they become symptomatic.

Histologic transformation occurs in 30% to 50% of follicular lymphomas, most commonly to diffuse large B-cell lymphoma. Less commonly, tumors resembling Burkitt lymphoma emerge that are associated with chromosomal translocations involving *MYC*. Like normal germinal center B cells, follicular lymphomas have ongoing somatic hypermutation, which may promote transformation by causing point mutations or chromosomal aberrations. The median survival is less than 1 year after transformation.

Diffuse Large B-Cell Lymphoma

Diffuse large B-cell lymphoma (DLBCL) is the most common form of NHL. Each year in the United States there are about 25,000 new cases. There is a slight male

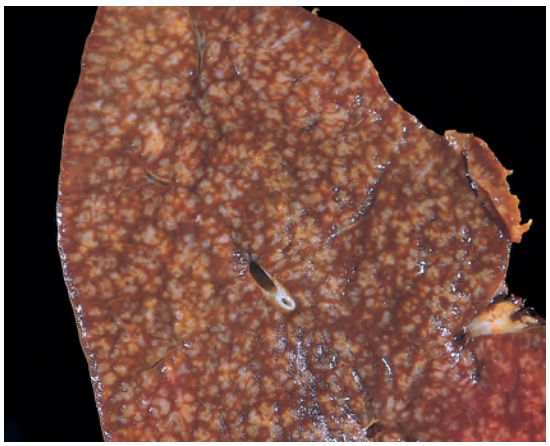

Figure 13-11 Follicular lymphoma (spleen). Prominent nodules represent white pulp follicles expanded by follicular lymphoma cells. Other indolent B-cell lymphomas (small lymphocytic lymphoma, mantle cell lymphoma, marginal zone lymphoma) can produce an identical pattern of involvement. (Courtesy Dr. Jeffrey Jorgenson, Department of Hematopathology, MD Anderson Cancer Center, Houston, Texas.)