infrequent. After *H. pylori* eradication, symptoms generally improve quickly, but molecular evidence of persistent disease may be present for 12–18 months. Additional therapy is not indicated unless progressive disease is documented. Patients with more extensive disease or progressive disease are most often treated with single-agent chemotherapy such as chlorambucil. Combination regimens that include rituximab are also highly effective. Coexistent diffuse large B-cell lymphoma must be treated with combination chemotherapy (see below). The additional acquired mutations that mediate the histologic progression also convey *Helicobacter* independence to the growth.

Mantle Cell Lymphoma Mantle cell lymphoma makes up ~6% of all non-Hodgkin's lymphomas. This lymphoma was previously placed in a number of other subtypes. Its existence was confirmed by the recognition that these lymphomas have a characteristic chromosomal translocation, t(11;14), between the immunoglobulin heavy chain gene on chromosome 14 and the *bcl-1* gene on chromosome 11, and regularly overexpress the BCL-1 protein, also known as cyclin D1. Table 134-10 shows the clinical characteristics of mantle cell lymphoma.

The diagnosis of mantle cell lymphoma can be made accurately by an expert hematopathologist. As with all subtypes of lymphoma, an adequate biopsy is important. The differential diagnosis of mantle cell lymphoma includes other small cell B-cell lymphomas. In particular, mantle cell lymphoma and small lymphocytic lymphoma share a characteristic expression of CD5. Mantle cell lymphoma usually has a slightly indented nucleus.

The most common presentation of mantle cell lymphoma is with palpable lymphadenopathy, frequently accompanied by systemic symptoms. The median age is 63 years, and men are affected four times as commonly as women. Approximately 70% of patients will be stage IV at the time of diagnosis, with frequent bone marrow and peripheral blood involvement. Of the extranodal organs that can be involved, gastrointestinal involvement is particularly important to recognize. Patients who present with lymphomatosis polyposis in the large intestine usually have mantle cell lymphoma. Table 134-11 outlines the evaluation of patients with mantle cell lymphoma. Patients who present with gastrointestinal tract involvement often have Waldeyer's ring involvement, and vice versa. The 5-year survival for all patients with mantle cell lymphoma is ~25%, with only occasional patients who present with a high IPI score surviving 5 years and ~50% of patients with a low IPI score surviving 5 years.

TREATMENT MANTLE CELL LYMPHOMA

Current therapies for mantle cell lymphoma are evolving. Patients with localized disease might be treated with combination chemotherapy followed by radiotherapy; however, these patients are exceedingly rare. For the usual presentation with disseminated disease, standard lymphoma treatments have been unsatisfactory, with the minority of patients achieving complete remission. Aggressive combination chemotherapy regimens followed by autologous or allogeneic bone marrow transplantation are frequently offered to younger patients. For the occasional elderly, asymptomatic patient, observation followed by single-agent chemotherapy might be the most practical approach. An intensive combination chemotherapy regimen originally used in the treatment of acute leukemia, HyperC-VAD (cyclophosphamide, vincristine, doxorubicin, dexamethasone, cytarabine, and methotrexate), in combination with rituximab, seems to be associated with better response rates, particularly in younger patients. Alternating two regimens, HyperC-VAD with rituximab added (R-HyperC-VAD) and rituximab plus high-dose methotrexate and cytarabine, can achieve complete responses in >80% of patients and an 8-year survival of 56%, comparable to regimens using high-dose therapy and autologous hematopoietic stem cell transplantation. Bendamustine plus rituximab has been found to induce complete responses in about 31% of patients, but the responses are generally not long lasting. Bortezomib and temsirolimus are single agents that induce transient partial responses in a minority of patients and are being added to primary combinations.

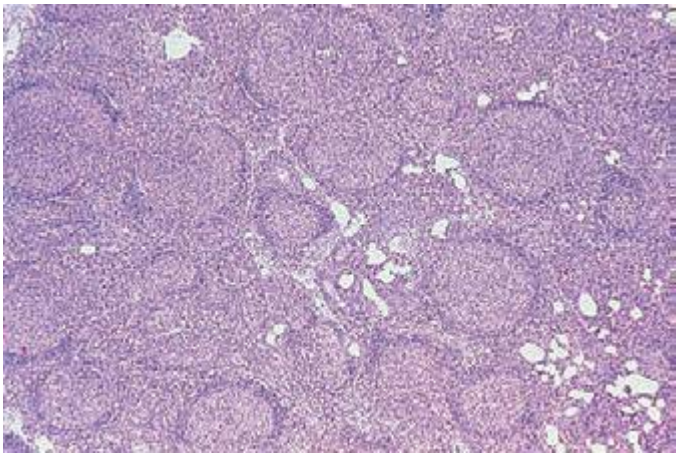

FIGURE 134-7 Follicular lymphoma. The normal nodal architecture is effaced by nodular expansions of tumor cells. Nodules vary in size and contain predominantly small lymphocytes with cleaved nuclei along with variable numbers of larger cells with vesicular chromatin and prominent nucleoli.

Follicular Lymphoma Follicular lymphomas make up 22% of non-Hodgkin's lymphomas worldwide and at least 30% of non-Hodgkin's lymphomas diagnosed in the United States. This type of lymphoma can be diagnosed accurately on morphologic findings alone and has been the diagnosis in the majority of patients in therapeutic trials for "low-grade" lymphoma in the past. The clinical characteristics of follicular lymphoma are presented in Table 134-10.

Evaluation of an adequate biopsy by an expert hematopathologist is sufficient to make a diagnosis of follicular lymphoma. The tumor is composed of small cleaved and large cells in varying proportions organized in a follicular pattern of growth (Fig. 134-7). Confirmation of B-cell immunophenotype and the existence of the t(14;18) and abnormal expression of BCL-2 protein are confirmatory. The major differential diagnosis is between lymphoma and reactive follicular hyperplasia. The coexistence of diffuse large B-cell lymphoma must be considered. Patients with follicular lymphoma are often subclassified into those with predominantly small cells, those with a mixture of small and large cells, and those with predominantly large cells. Although this distinction cannot be made simply or very accurately, these subdivisions do have prognostic significance. Patients with follicular lymphoma with predominantly large cells have a higher proliferative fraction, progress more rapidly, and have a shorter overall survival with simple chemotherapy regimens.

The most common presentation for follicular lymphoma is with new, painless lymphadenopathy. Multiple sites of lymphoid involvement are typical, and unusual sites such as epitrochlear nodes are sometimes seen. However, essentially any organ can be involved, and extranodal presentations do occur. Most patients do not have fevers, sweats, or weight loss, and an IPI score of 0 or 1 is found in ~50% of patients. Fewer than 10% of patients have a high (i.e., 4 or 5) IPI score. The staging evaluation for patients with follicular lymphoma should include the studies shown in Table 134-11.

TREATMENT FOLLICULAR LYMPHOMA

Follicular lymphoma is one of the malignancies most responsive to chemotherapy and radiotherapy. In addition, tumors in as many as 25% of the patients undergo spontaneous regression—usually transient—without therapy. In an asymptomatic patient, no initial treatment and watchful waiting can be an appropriate management strategy and is particularly likely to be adopted for older patients