be expected to achieve a complete remission, and 50–70% of complete responders will be cured. The chances for a favorable response to treatment are predicted by the IPI. In fact, the IPI was developed based on the outcome of patients with diffuse large B-cell lymphoma treated with CHOP-like regimens. For the 35% of patients with a low IPI score of 0–1, the 5-year survival is >70%, whereas for the 20% of patients with a high IPI score of 4–5, the 5-year survival is ~20%. The addition of rituximab to CHOP has improved each of those numbers by ~15%. A number of other factors, including molecular features of the tumor, levels of circulating cytokines and soluble receptors, and other surrogate markers, have been shown to influence prognosis. However, they have not been validated as rigorously as the IPI and have not been uniformly applied clinically.

Because a number of patients with diffuse large B-cell lymphoma are either initially refractory to therapy or relapse after apparently effective chemotherapy, 30–40% of patients will be candidates for salvage treatment at some point. Alternative combination chemotherapy regimens can induce complete remission in as many as 50% of these patients, but long-term disease-free survival is seen in ≤10%. Autologous bone marrow transplantation is superior to salvage chemotherapy at usual doses and leads to long-term disease-free survival in ~40% of patients whose lymphomas remain chemotherapy-sensitive after relapse.

Burkitt's Lymphoma/Leukemia Burkitt's lymphoma/leukemia is a rare disease in adults in the United States, making up <1% of non-Hodgkin's lymphomas, but it makes up ~30% of childhood non-Hodgkin's lymphoma. Burkitt's leukemia, or L3 ALL, makes up a small proportion of childhood and adult acute leukemias. Table 134-10 shows the clinical features of Burkitt's lymphoma.

Burkitt's lymphoma can be diagnosed morphologically by an expert hematopathologist with a high degree of accuracy. The cells are homogeneous in size and shape (Fig. 134-9). Demonstration of a very high proliferative fraction and the presence of the t(8;14) or one of its variants, t(2;8) (*c-myc* and the λ light chain gene) or t(8;22) (*c-myc* and the κ light chain gene), can be confirmatory. Burkitt's cell leukemia is recognized by the typical monotonous mass of medium-sized cells with round nuclei, multiple nucleoli, and basophilic cytoplasm with cytoplasmic vacuoles. Demonstration of surface expression of immunoglobulin and one of the above-noted cytogenetic abnormalities is confirmatory.

Three distinct clinical forms of Burkitt's lymphoma are recognized: endemic, sporadic, and immunodeficiency-associated. Endemic and sporadic Burkitt's lymphomas occur frequently in children in Africa, and the sporadic form occurs in Western countries.

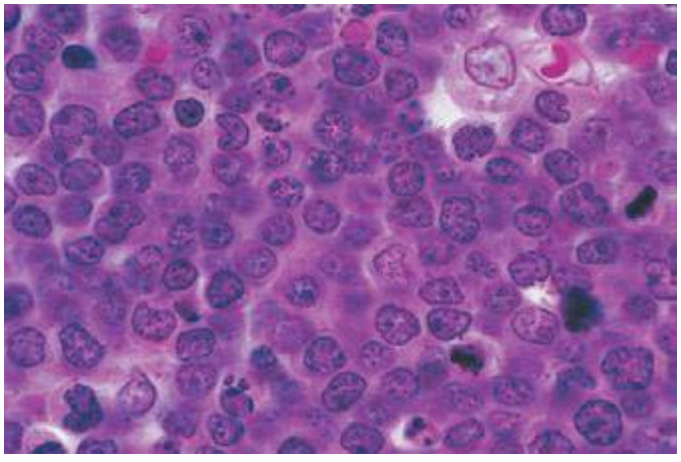

FIGURE 134-9 Burkitt's lymphoma. The neoplastic cells are homogeneous, medium-sized B cells with frequent mitotic figures, a morphologic correlate of high growth fraction. Reactive macrophages are scattered through the tumor, and their pale cytoplasm in a background of blue-staining tumor cells gives the tumor a so-called starry sky appearance.

Immunodeficiency-associated Burkitt's lymphoma is seen in patients with HIV infection.

Pathologists sometimes have difficulty distinguishing between Burkitt's lymphoma and diffuse large B-cell lymphoma. In the past, a separate subgroup of non-Hodgkin's lymphoma intermediate between the two was recognized. When tested, this subgroup could not be diagnosed accurately. Distinction between the two major types of B-cell aggressive non-Hodgkin's lymphoma can sometimes be made based on the extremely high proliferative fraction seen in patients with Burkitt's lymphoma (i.e., essentially 100% of tumor cells are in cycle) caused by *c-myc* deregulation.

Most patients in the United States with Burkitt's lymphoma present with peripheral lymphadenopathy or an intraabdominal mass. The disease is rapidly progressive and has a propensity to metastasize to the CNS. Initial evaluation should always include an examination of cerebrospinal fluid to rule out metastasis in addition to the other staging evaluations noted in Table 134-11. Once the diagnosis of Burkitt's lymphoma is suspected, a diagnosis must be made promptly, and staging evaluation must be accomplished expeditiously. This is the most rapidly progressive human tumor, and any delay in initiating therapy can adversely affect the patient's prognosis.

TREATMENT BURKITT'S LYMPHOMA

Treatment of Burkitt's lymphoma in both children and adults should begin within 48 h of diagnosis and involves the use of intensive combination chemotherapy regimens incorporating high doses of cyclophosphamide. Prophylactic therapy to the CNS is mandatory. Burkitt's lymphoma was one of the first cancers shown to be curable by chemotherapy. Today, cure can be expected in 70–80% of both children and young adults when effective therapy is administered precisely. Salvage therapy has been generally ineffective in patients in whom the initial treatment fails, emphasizing the importance of the initial treatment approach.

Other B-Cell Lymphoid Malignancies *B-cell prolymphocytic leukemia* involves blood and marrow infiltration by large lymphocytes with prominent nucleoli. Patients typically have a high white cell count, splenomegaly, and minimal lymphadenopathy. The chances for a complete response to therapy are poor.

Hairy cell leukemia is a rare disease that presents predominantly in older males. Typical presentation involves pancytopenia, although occasional patients will have a leukemic presentation. Splenomegaly is usual. The malignant cells appear to have "hairy" projections on light and electron microscopy and show a characteristic staining pattern with tartrate-resistant acid phosphatase. Bone marrow is typically not able to be aspirated, and biopsy shows a pattern of fibrosis with diffuse infiltration by the malignant cells. Patients with this disorder have monocytopenia and are prone to unusual infections, including infection by *Mycobacterium avium intracellulare*, and to vasculitic syndromes. Hairy cell leukemia is responsive to chemotherapy with interferon α, pentostatin, or cladribine, with the latter being the usually preferred treatment. Clinical complete remissions with cladribine occur in the majority of patients, and long-term disease-free survival is frequent. Many of these tumors have the V600E *BRAF* mutation and accordingly are responsive to BRAF inhibitors like vemurafenib.

Splenic marginal zone lymphoma involves infiltration of the splenic white pulp by small, monoclonal B cells. This is a rare disorder that can present as leukemia as well as lymphoma. Definitive diagnosis is often made at splenectomy, which is also an effective therapy. This is an extremely indolent disorder, but when chemotherapy is required, the most usual treatment has been chlorambucil.

Lymphoplasmacytic lymphoma is the tissue manifestation of Waldenström's macroglobulinemia (Chap. 136). Many of these tumors harbor a specific mutation, L265P, in *MYD88,* a change that leads to NF-κB activation. This type of lymphoma has been associated with chronic hepatitis C virus infection, and an etiologic association has been proposed. Patients typically present with lymphadenopathy,