splenomegaly, bone marrow involvement, and occasionally peripheral blood involvement. The tumor cells do not express CD5. Patients often have a monoclonal IgM protein, high levels of which can dominate the clinical picture with the symptoms of hyperviscosity. Treatment of lymphoplasmacytic lymphoma can be aimed primarily at reducing the abnormal protein, if present, but will usually also involve chemotherapy. Chlorambucil, fludarabine, and cladribine have been used. The median 5-year survival for patients with this disorder is ~60%.

Nodal marginal zone lymphoma, also known as *monocytoid cell lymphoma*, represents ~1% of non-Hodgkin's lymphomas. This lymphoma has a slight female predominance and presents with disseminated disease (i.e., stage III or IV) in 75% of patients. Approximately one-third of patients have bone marrow involvement, and a leukemic presentation occasionally occurs. The staging evaluation and therapy should use the same approach as used for patients with follicular lymphoma. Approximately 60% of the patients with nodal marginal zone lymphoma will survive 5 years after diagnosis.

Other more uncommon B-cell malignancies are discussed in Chap. 135e.

PRECURSOR T-CELL MALIGNANCIES

Precursor T-Cell Lymphoblastic Leukemia/Lymphoma Precursor T-cell malignancies can present either as ALL or as an aggressive lymphoma. These malignancies are more common in children and young adults, with males more frequently affected than females.

Precursor T-cell ALL can present with bone marrow failure, although the severity of anemia, neutropenia, and thrombocytopenia is often less than in precursor B-cell ALL. These patients sometimes have very high white cell counts, a mediastinal mass, lymphadenopathy, and hepatosplenomegaly. Precursor T-cell lymphoblastic lymphoma is most often found in young men presenting with a large mediastinal mass and pleural effusions. Both presentations have a propensity to metastasize to the CNS, and CNS involvement is often present at diagnosis.

TREATMENT PRECURSOR T-CELL LYMPHOBLASTIC LEUKEMIA/LYMPHOMA

Children with precursor T-cell ALL seem to benefit from very intensive remission induction and consolidation regimens. The majority of patients treated in this manner can be cured. Older children and young adults with precursor T-cell lymphoblastic lymphoma are also often treated with "leukemia-like" regimens. Patients who present with localized disease have an excellent prognosis. However, advanced age is an adverse prognostic factor. Adults with precursor T-cell lymphoblastic lymphoma who present with high LDH levels or bone marrow or CNS involvement are often offered bone marrow transplantation as part of their primary therapy.

MATURE (PERIPHERAL) T-CELL DISORDERS

Mycosis Fungoides Mycosis fungoides is also known as *cutaneous T-cell lymphoma*. This lymphoma is more often seen by dermatologists than internists. The median age of onset is in the mid-fifties, and the disease is more common in males and in blacks.

Mycosis fungoides is an indolent lymphoma with patients often having several years of eczematous or dermatitic skin lesions before the diagnosis is finally established. The skin lesions progress from patch stage to plaque stage to cutaneous tumors. Early in the disease, biopsies are often difficult to interpret, and the diagnosis may only become apparent by observing the patient over time. In advanced stages, the lymphoma can spread to lymph nodes and visceral organs. Patients with this lymphoma may develop generalized erythroderma and circulating tumor cells, called *Sézary's syndrome*.

Rare patients with localized early-stage mycosis fungoides can be cured with radiotherapy, often total-skin electron beam irradiation. More advanced disease has been treated with topical glucocorticoids, topical nitrogen mustard, phototherapy, psoralen with ultraviolet A (PUVA), extracorporeal photopheresis, retinoids (bexarotene), electron beam radiation, interferon, antibodies, fusion toxins, histone deacetylase inhibitors, and systemic cytotoxic therapy. Unfortunately, these treatments are palliative.

Adult T-Cell Lymphoma/Leukemia Adult T-cell lymphoma/leukemia is one manifestation of infection by the HTLV-1 retrovirus. Patients can be infected through transplacental transmission, mother's milk, blood transfusion, and by sexual transmission of the virus. Patients who acquire the virus from their mother through breast milk are most likely to develop lymphoma, but the risk is still only 2.5% and the latency averages 55 years. Nationwide testing for HTLV-1 antibodies and the aggressive implementation of public health measures could theoretically lead to the disappearance of adult T-cell lymphoma/leukemia. Tropical spastic paraparesis, another manifestation of HTLV-1 infection **(Chap. 225e)**, occurs after a shorter latency (1–3 years) and is most common in individuals who acquire the virus during adulthood from transfusion or sex.

The diagnosis of adult T-cell lymphoma/leukemia is made when an expert hematopathologist recognizes the typical morphologic picture, a T-cell immunophenotype (i.e., CD4 positive), and the presence in serum of antibodies to HTLV-1. Examination of the peripheral blood will usually reveal characteristic, pleomorphic abnormal CD4-positive cells with indented nuclei, which have been called "flower" cells **(Fig. 134-10)**.

A subset of patients have a smoldering clinical course and long survival, but most patients present with an aggressive disease manifested by lymphadenopathy, hepatosplenomegaly, skin infiltration, pulmonary infiltrates, hypercalcemia, lytic bone lesions, and elevated LDH levels. The skin lesions can be papules, plaques, tumors, and ulcerations. Lung lesions can be either tumor or opportunistic infection in light of the underlying immunodeficiency in the disease. Bone marrow involvement is not usually extensive, and anemia and thrombocytopenia are not usually prominent. Although treatment with combination chemotherapy regimens can result in objective responses, true complete remissions are unusual, and the median survival of patients is ~7 months. A small phase II study reported a high response rate with interferon plus zidovudine and arsenic trioxide.

Anaplastic Large T/Null-Cell Lymphoma Anaplastic large T/null-cell lymphoma was previously usually diagnosed as undifferentiated carcinoma or malignant histiocytosis. Discovery of the CD30 (Ki-1) antigen and the recognition that some patients with previously unclassified malignancies displayed this antigen led to the identification of a new type of lymphoma. Subsequently, discovery of the t(2;5) and the resultant frequent overexpression of the anaplastic lymphoma kinase (ALK) protein confirmed the existence of this entity. This lymphoma accounts for ~2% of all non-Hodgkin's lymphomas. Table 134-10 shows the clinical characteristics of patients with anaplastic large T/null cell lymphoma.

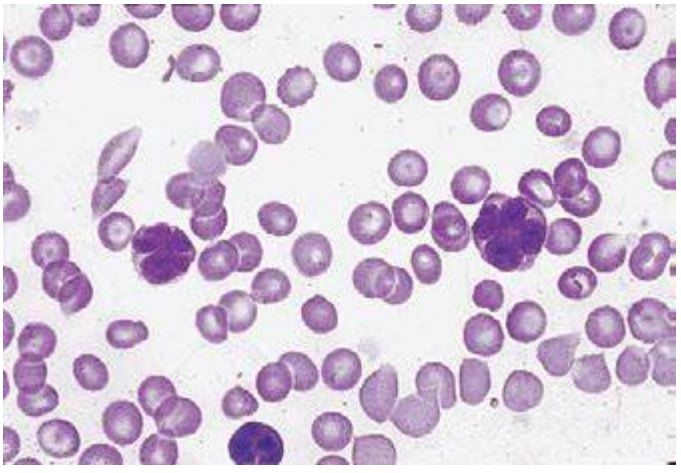

FIGURE 134-10 Adult T-cell leukemia/lymphoma. Peripheral blood smear showing leukemia cells with typical "flower-shaped" nucleus.