focuses on *mycosis fungoides*, a lymphoma of skin-homing CD4+ T helper cells that presents in the skin. In most affected individuals, the disease remains localized to the skin for many years, but it may eventually evolve into a systemic lymphoma. This tumor may occur at any age, but most commonly afflicts persons older than age 40.

Lesions of mycosis fungoides usually involve truncal areas and include scaly, red-brown *patches*; raised, scaling *plaques* that may even be confused with psoriasis; and fungating *nodules*. Prognosis is related to the percentage of body surface involved and progression from patch to plaque to nodular forms. Eczema-like lesions typify early stages of disease when obvious visceral or nodal spread has not occurred. Raised, indurated, irregularly outlined, erythematous plaques may then supervene. Development of multiple, large red-brown nodules correlates with systemic spread. Sometimes plaques and nodules ulcerate (Fig. 25-18*A*). Ultimately, lesions may affect numerous body surfaces, including the trunk, extremities, face, and scalp. In some individuals, seeding of the blood by malignant T cells is accompanied by diffuse erythema and scaling of the entire body surface (erythroderma), a condition known as *Sézary syndrome* (Chapter 13).

The proliferating cells in CTCL are clonal populations of CD4-positive T helper cells that home to the skin due expression of cutaneous lymphocyte antigen. The neoplastic cells have clonal T-cell receptor gene rearrangements and sometimes express aberrant combinations of T-cell surface antigens. Topical therapy with steroids or UV light is often used for early skin lesions, whereas more aggressive systemic chemotherapy is indicated for advanced disease.

MORPHOLOGY

The histologic hallmark of CTCL of the mycosis fungoides type is the presence of the **Sézary-Lutzner cells**, which characteristically form bandlike aggregates within the superficial dermis (Fig. 25-18*B*) and invade the epidermis as single cells and small clusters **(Pautrier microabscesses).** These cells have markedly infolded nuclear membranes, imparting a hyperconvoluted or cerebriform contour. Although patches and plaques show pronounced epidermal infiltration by Sézary-Lutzner cells (epidermotropism), in more advanced nodular lesions the malignant T cells often lose this epidermotropic tendency, grow deeply into the dermis, and eventually spread systemically.

Mastocytosis

The term *mastocytosis* encompasses a spectrum of rare disorders characterized by increased numbers of mast cells in the skin and, in some instances, in other organs as well. A cutaneous form of the disease that affects predominantly children and accounts for more than 50% of all cases is termed *urticaria pigmentosa.* The cutaneous lesions are usually multiple, although solitary mastocytomas may also occur in very young children. About 10% of individuals with mast cell disease have systemic disease, with mast cell infiltration of many organs. These individuals are often adults, and unlike localized cutaneous disease, the prognosis may be poor.

Many of the signs and symptoms of mastocytosis are due to the effects of histamine, heparin, and other substances released when mast cells degranulate. *Darier sign* refers to a localized area of dermal edema and erythema (wheal) that occurs when lesional skin is rubbed. *Dermatographism* refers to an area of dermal edema resembling a hive that occurs as a result of localized stroking of apparently normal skin with a pointed instrument. In systemic disease, all of the following may be seen: pruritus and flushing, variously triggered by certain foods, temperature changes, alcohol, and certain drugs (morphine, codeine, aspirin); watery nasal discharge (rhinorrhea); rarely, gastrointestinal or nasal bleeding, possibly due to the anticoagulant effects of heparin; and bone pain, which may be caused by mast cell infiltration or by pathologic fractures stemming from osteoporosis. Osteoporosis is caused by excessive histamine release in the marrow microenvironment and can be a clue to the diagnosis, particularly in premenopausal women and in men.

Pathogenesis. Many cases of mastocytosis have acquired activating point mutations in the KIT receptor tyrosine kinase. The resulting increase in KIT signaling drives mast cell growth and survival. This insight has led to trials of KIT kinase inhibitors in patients with disseminated disease.

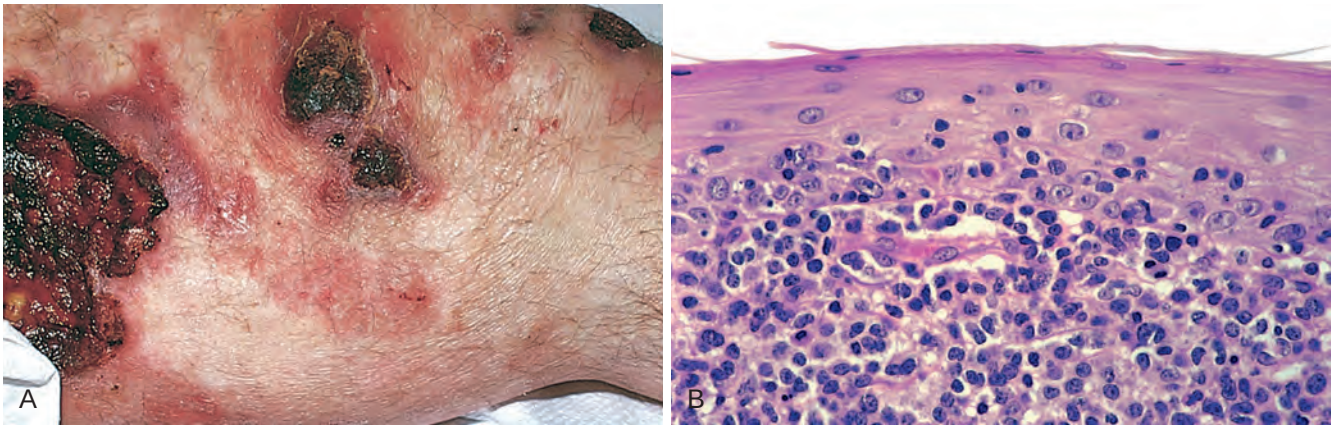

Figure 25-18 Cutaneous T-cell lymphoma. **A,** Several erythematous plaques with scaling and ulceration are evident. **B,** Microscopically, there is an infiltrate of atypical lymphocytes that accumulates beneath and invades the epidermis.