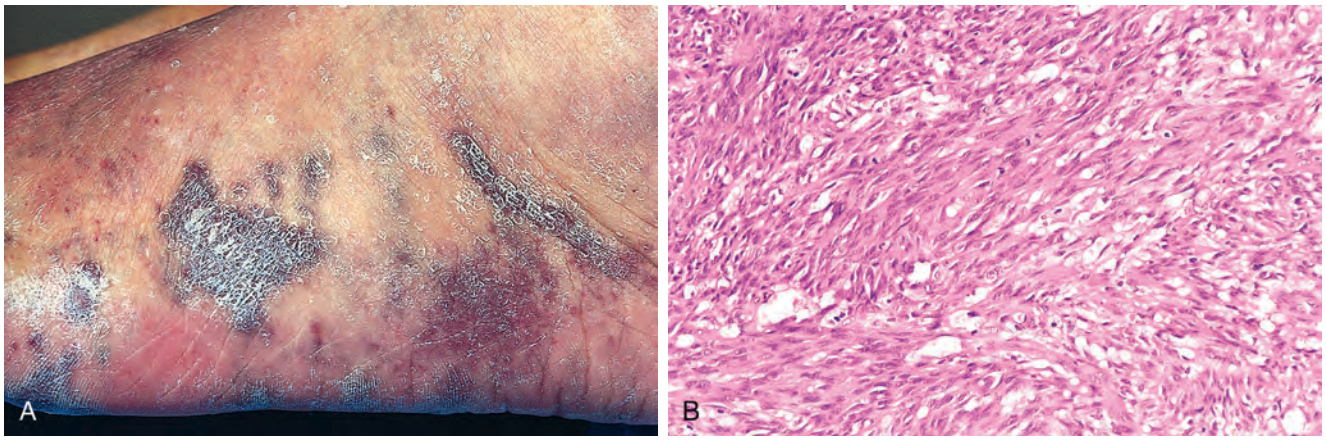

Figure 11-32 Kaposi sarcoma. **A,** Gross photograph, illustrating coalescent red-purple macules and plaques of the skin. **B,** Histologic appearance of the nodular stage of KS, demonstrating sheets of plump, proliferating spindle cells. (**B,** Courtesy Christopher DM Fletcher, MD, Brigham and Women's Hospital, Boston, Mass.)

- Eventually, lesions become **nodular** and more distinctly neoplastic. These lesions are composed of sheets of plump, proliferating spindle cells, mostly in the dermis or subcutaneous tissues (Fig. 11-32*B*), encompassing small vessels and slitlike spaces containing red cells. Marked hemorrhage, hemosiderin pigment, and mononuclear inflammation are present; mitotic figures are common, as are round, pink, cytoplasmic globules representing degenerating red cells within phagolysosomes. The nodular stage often heralds nodal and visceral involvement, particularly in the African and AIDS-associated variants.

Clinical Features. The course of KS varies widely and is significantly influenced by the clinical setting. Most primary KSHV infections are asymptomatic. Classic KS is—at least initially— largely restricted to the surface of the body, and surgical resection is usually adequate for an excellent prognosis. Radiation can be used for multiple lesions in a restricted area and chemotherapy yields satisfactory results for more disseminated disease, including nodal involvement. In immunosuppression-associated KS, withdrawal of immunosuppression (perhaps with adjunct chemotherapy or radiotherapy) is often effective. Antiretroviral therapy treatment has greatly decreased that frequency of KS in HIV infected patients, emphasizing the central role that T cell immunodeficiency has in the disease. Interferon-α and angiogenesis inhibitors are variably effective, while newer strategies aimed at specific kinases that lie downtream of VEGF receptors show promise.

Hemangioendothelioma. *Hemangioendotheliomas* encompass a spectrum of vascular neoplasms with clinical behaviors *intermediate between benign, well-differentiated hemangiomas and frankly anaplastic angiosarcomas,* described later.

Epithelioid hemangioendothelioma is an example; it is a vascular tumor of adults occurring around medium- and large-sized veins. Well-defined vascular channels are inconspicuous, and neoplastic cells are plump and often cuboidal (resembling epithelial cells). The clinical behavior is extremely variable; most are cured by excision, but up to 40% recur, 20% to 30% eventually metastasize, and perhaps 15% of patients die of their tumor.

Malignant Tumors

Angiosarcoma. *Angiosarcoma* is a malignant endothelial neoplasm that primarily affects older adults. There is equal gender predilection, and the tumor may occur at any site, but most often involves skin, soft tissue, breast, and liver.

Hepatic angiosarcoma is associated with carcinogenic exposures, including arsenic (e.g., in pesticides), Thorotrast (a radioactive contrast agent formerly used for radiologic imaging), and polyvinyl chloride (a widely used plastic). All of these agents have long latencies between initial exposure and eventual tumor development. The increased frequency of angiosarcoma among polyvinyl chloride workers is one of the well-documented instances of human chemical carcinogenesis.

Angiosarcoma can also arise in the setting of lymphedema, classically in the ipsilateral upper extremity several years after radical mastectomy (i.e., with lymph node resection) for breast cancer; the tumor presumably arises from lymphatic vessels *(lymphangiosarcoma)*. Angiosarcoma has also been induced by radiation and are rarely associated with foreign material introduced into the body either iatrogenically or accidentally.

Angiosarcomas are locally invasive and can readily metastasize; 5-year survival rates approach 30%.

MORPHOLOGY

Cutaneous angiosarcoma can begin as multiple deceptively small and asymptomatic red papules or nodules; these eventually become large, fleshy masses of red-tan to gray-white tissue with margins blurring imperceptibly into surrounding structures (Fig. 11-33*A*). Central areas of necrosis and hemorrhage are frequent.

Microscopically, **all degrees of differentiation can be seen,** from plump, atypical endothelial cells forming vascular channels (Fig. 11-33*B*) to wildly undifferentiated tumors with a solid spindled appearance and no discernible blood vessels that may be difficult to distinguish from carcinomas and melanomas. The endothelial origin of these tumors can be demonstrated by immunohistochemical staining for CD31 or von Willebrand factor (Fig. 11-33*C*).