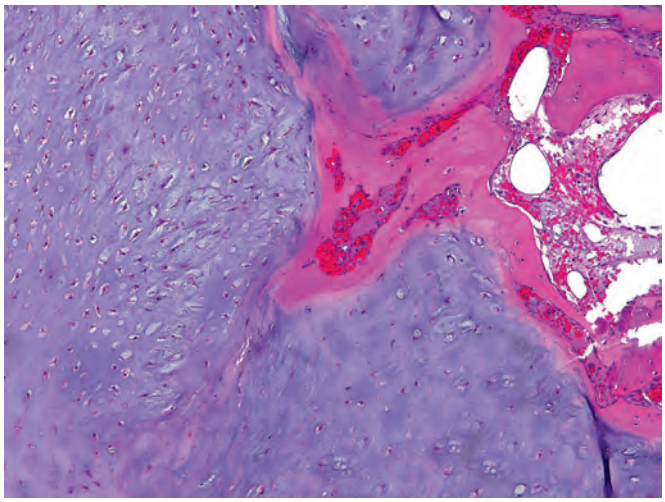

Figure 26-29 Enchondroma composed of a nodule of hyaline cartilage encased by a thin layer of reactive bone.

Chondrosarcoma

Chondrosarcomas are malignant tumors that produce cartilage. They are subclassified histologically as *conventional* (hyaline cartilage producing), *clear cell*, *dedifferentiated*, and *mesenchymal* variants. Conventional tumors are further subdivided by site as *central* (intramedullary) and *peripheral* (juxtacortical). Conventional central tumors constitute about 90% of chondrosarcomas. Chondrosarcoma is about half as common as osteosarcoma and is the second most common malignant matrix-producing tumor of bone. Individuals with chondrosarcoma are usually in their 40s or older. The clear cell and especially the mesenchymal variants occur in younger patients, in their teens or 20s. These tumors affect men twice as frequently as women. Chondrosarcomas commonly arise in the axial skeleton, especially the pelvis, shoulder, and ribs. Unlike benign enchondroma, the distal extremities are rarely involved. On imaging, the calcified matrix appears as foci of flocculent densities. A slow-growing, low-grade tumor causes reactive thickening of the cortex, whereas a more aggressive high-grade neoplasm destroys the cortex and forms a soft tissue mass. The clear cell variant is unique in that it originates in the epiphyses of long tubular bones. About 15% of conventional chondrosarcomas are secondary, arising from a preexisting enchondroma or osteochondroma.

Although chondrosarcomas are genetically heterogeneous, a few reproducible abnormalities have been identified. Chondrosarcomas arising in multiple osteochondroma syndrome exhibit mutations in the *EXT* genes, and both chondromatosis-related and sporadic chondrosarcomas may have *IDH1* and *IDH2* mutations. Silencing of the *CDKN2A* tumor suppressor gene by DNA methylation is also relatively common in sporadic tumors.

MORPHOLOGY

Conventional chondrosarcomas are large bulky tumors made up of nodules of glistening gray-white, translucent cartilage but matrix is often gelatinous or myxoid (Fig. 26-30*A*). The myxoid matrix can ooze from the cut surface. Spotty calcifications are typically present, and central necrosis may create cystic spaces. The tumor spreads through the cortex into surrounding muscle or fat. Histologically, the cartilage infiltrates the marrow space and surrounds pre-existing bony trabeculae. The tumors vary in cellularity, cytologic atypia, and mitotic activity and are assigned a grade from 1 to 3. Grade 1 tumors have relatively low cellularity, and the chondrocytes have plump vesicular nuclei with small nucleoli. By contrast, grade 3 chondrosarcomas are characterized by high cellularity, extreme pleomorphism with bizarre tumor giant cells, and mitoses (Fig. 26-30*B*).

Dedifferentiated chondrosarcoma is defined as a low-grade chondrosarcoma with a second, high-grade component that does not produce cartilage. **Clear cell chondrosarcoma** contains sheets of large, malignant chondrocytes that have abundant clear cytoplasm, numerous osteoclast-type giant cells, and intralesional reactive bone formation, which often causes confusion with osteosarcoma. **Mesenchymal chondrosarcoma** is composed of islands of well-differentiated hyaline cartilage surrounded by sheets of small round cells, which can mimic Ewing sarcoma.

Clinical Course. Chondrosarcomas usually present as painful, progressively enlarging masses. There is a direct correlation between the grade and the biologic behavior of the tumor. Fortunately, most conventional chondrosarcomas are grade 1 tumors with 5-year survival rates of 80% to 90% (versus 43% for grade 3 tumors). Grade 1

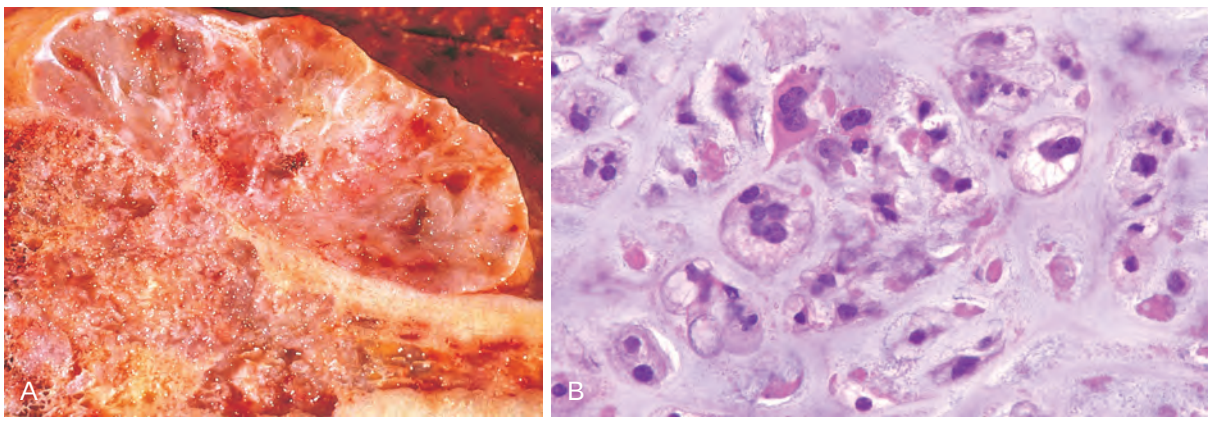

Figure 26-30 Chondrosarcoma. **A,** Nodules of hyaline and myxoid cartilage permeating throughout the medullary cavity, growing through the cortex, and forming a relatively well-circumscribed soft tissue mass. **B,** Anaplastic chondrocytes amid hyaline cartilage matrix in a grade 3 chondrosarcoma.