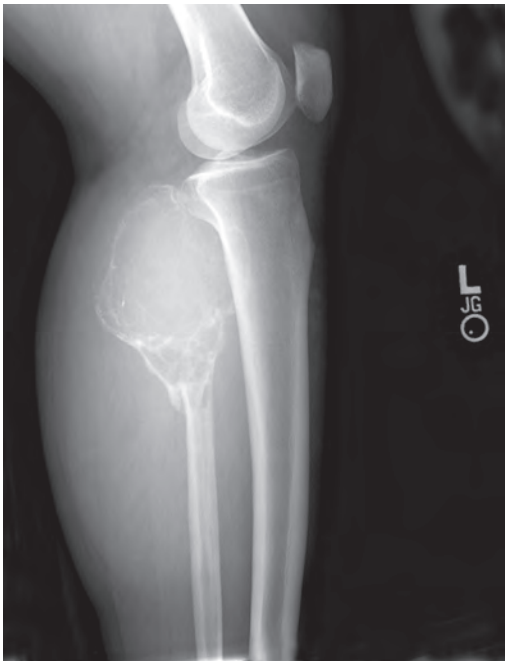

Figure 26-32 Giant cell tumor of the proximal fibula is predominantly lytic, expansile with destruction of the cortex. A pathologic fracture is also present.

bone (Fig. 26-32). These are large, red-brown masses that frequently undergo cystic degeneration. Histologically, the tumor consists of sheets of uniform oval mononuclear cells and numerous osteoclast-type giant cells with 100 or more nuclei (Fig. 26-33). The nuclei of the mononuclear cells and the osteoclasts are similar, ovoid with prominent nucleoli. Thus, the neoplastic population of osteoblast precursors is difficult to identify on routine histology. Necrosis and mitotic activity may be prominent. Although reactive bone, especially at the periphery of a lesion, may be present, the tumor cells do not synthesize bone or cartilage.

Clinical Course. Giant cell tumors are typically treated with curettage, but 40% to 60% recur locally. Up to 4% of tumors metastasize to the lungs, but these sometimes spontaneously regress and they are seldom fatal. Recently, the RANKL inhibitor, denosumab has shown promise as an adjuvant therapy in giant cell tumor.

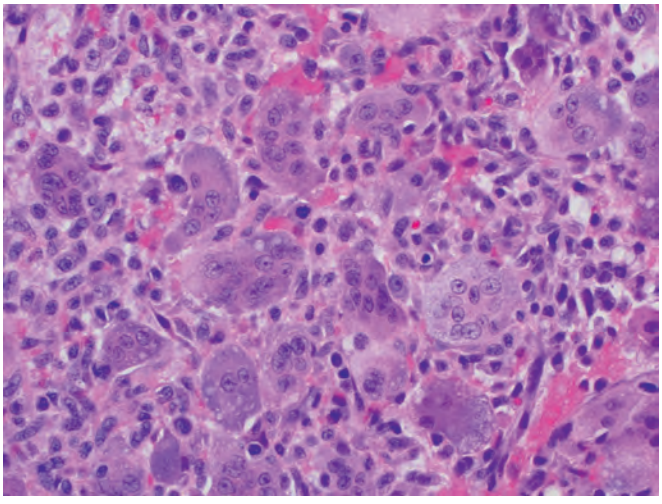

Figure 26-33 Benign giant cell tumor illustrating an abundance of multinucleated giant cells with background mononuclear stromal cells.

Aneurysmal Bone Cyst

Aneurysmal bone cyst (ABC) is a tumor characterized by multiloculated blood-filled cystic spaces. Interestingly, radiographic and histologic findings typical of ABC can also be seen as a secondary reaction to other primary bone tumors. Primary ABC affects all age groups but generally occurs during the first 2 decades of life and has no sex predilection. It most frequently develops in the metaphysis of long bones and the posterior elements of vertebral bodies. The most common signs and symptoms are pain and swelling. When an ABC involves the vertebrae, it can compress nerves and cause neurologic symptoms. Rarely, pathologic fractures occur. Secondary ABC can be present in the setting of a number of primary neoplasms, especially giant cell tumor and chondroblastoma.

Radiographically, ABC is usually an eccentric, expansile lesion with well-defined margins (Fig. 26-34*A*). Most lesions are completely lytic and often contain a thin shell of reactive bone at the periphery. Computed tomography and magnetic resonance imaging may demonstrate internal septa and characteristic fluid-fluid levels (Fig. 26-34*B*).

Pathogenesis. The spindle cells of ABC frequently demonstrate rearrangements of chromosome 17p13 resulting in fusion of the coding region of *USP6* to the promoters of genes that are highly expressed in osteoblasts, leading to USP6 overexpression. *USP6* encodes an ubiquitin specific protease that regulates the activity of the transcription factor NFκB. Increased NFκB activity appears to upregulate genes such as matrix metalloproteases that lead to cystic resorption of bone. Secondary ABCs do not have *USP6* rearrangements and appear to be triggered by epigenetic mechanisms.

MORPHOLOGY

Aneurysmal bone cyst consists of multiple blood-filled cystic spaces separated by thin, tan-white septa (Fig. 26-35). The septa are composed of plump uniform fibroblasts, multinucleated osteoclast-like giant cells, and reactive woven bone. The bone is lined by osteoblasts, and its deposition typically follows the contours of the fibrous septa. Approximately one third of cases contain an unusual densely calcified matrix called "blue bone." Necrosis is uncommon unless a pathologic fracture is present.

Clinical Course. The treatment of aneurysmal bone cyst is surgical, usually curettage or, in certain situations, en bloc resection. The recurrence rate is low, and spontaneous regression may occur following incomplete removal.

Lesions Simulating Primary Neoplasms

Fibrous Cortical Defect and Nonossifying Fibroma

Fibrous cortical defects (also known as **metaphyseal fibrous defects**) are extremely common, present in 30% to 50% of children older than 2 years. The vast majority arise eccentrically in the metaphysis of the distal femur and proximal tibia, and almost half are bilateral or multiple. Often they are small, about 0.5 cm in diameter. Those that