A 66-year-old woman presented with a palpable left breast mass. A mammogram was performed that showed a 3-cm radiodense area with calcifications at about 2 o'clock, slightly above the plane of the nipple. The calcified components of the lesion measured 1.2 cm in greatest dimension. Calcifications were surrounded by dense tissue (Figure 1, a). This lesion was not present on a mammogram 6 months earlier, which was completely unremarkable (Figure 1, b). Ultrasound examination showed a complex mass with irregular margins, with significant shadowing indicating the presence of calcium. There was no axillary lymphadenopathy. A lumpectomy was performed. The specimen cut surface showed a 3.9-cm greatest dimension gray-white fleshy mass with focal areas of calcification and hemorrhage. Histologic examination showed a biphasic epithelial-stromal tumor. The prominent stromal component was composed of spindle cells and formed protrusions into cleftlike spaces (Figure 2). These spaces were focally dilated and lined by a 2-layered epithelium. The degree of stromal cellularity and cytologic atypia varied from mild to severe. Multiple areas of focally calcified woven bone were present (Figure 3) as well as foci with immature neoplastic bone and highly atypical osteoblasts (Figure 4). The surrounding breast parenchyma showed focal areas of florid ductal hyperplasia and intraductal papillomatosis with some epithelial cytologic atypia. Immunohistochemical staining for cytokeratin AE1/AE3 was negative in the stromal areas of the tumor and positive in the benign ductal epithelium of the tumor and the surrounding breast parenchyma.

What is your diagnosis?
Pathologic Diagnosis: Osteosarcoma Arising in a High-Grade Phyllodes Tumor

A phyllodes tumor or cystosarcoma phyllodes is a biphasic neoplasm of the breast, and the synonymous names emphasize its leaflike architectural pattern (phyllos = leaf, Greek). Phyllodes tumors are composed of a connective tissue component that forms protrusions into cleftlike spaces, and these spaces are lined by the usual 2 layers of myoepithelial and ductal epithelium. Phyllodes tumors are classified as benign, low-grade malignant (borderline), and malignant lesions. Benign tumors have circumscribed borders and, compared to fibroadenomas, an expansion of the stromal component with increased stromal cellularity. Cytologic atypia is absent, and there are only few mitotic figures (<1 mitosis per 10 high-power fields). On the other end of the spectrum, fully malignant lesions show invasive tumor borders and stromal overgrowth resulting in substantial separation of epithelial elements. There is considerable cellular pleomorphism, and the stroma is mitotically active (>5 mitoses per 10 high-power fields). Low-grade malignant phyllodes tumors fill the gap between benign and frankly malignant lesions, featuring invasive borders, moderate stromal cellularity, and 2 to 5 mitoses per 10 high-power fields. Heterologous stromal elements can be found in benign, borderline, and malignant phyllodes tumors. Malignant tumors may show lipo-, fibro-, rhabdo-, chondro-, or osteosarcomatous differentiation. In cases with an osteosarcomatous component, the differential diagnosis includes metaplastic carcinoma with an osteosarcomatous component, metastatic osteosarcoma, and primary osteosarcoma of the breast.

Silver and Tavassoli recently published a study reporting that 1.3% of phyllodes tumors in the Armed Forces Institute of Pathology files had a component of osteogenic sarcoma. There were 22 patients in this series with a mean age of 59.8 years (range, 40–83 years), and 73% of the patients had a palpable mass from 3 weeks to 4 months. Tumors varied from 1.9 to 15 cm (mean, 6.4 cm) in diameter. Most lesions had infiltrative margins and showed the characteristic leaflike architecture of phyllodes tumors. The osteosarcomatous component merged with the phyllodes stroma and histologically resembled osteosarcomas of skeletal origin or the rare primary mammary osteosarcomas. Half of the cases were classified as fibroblastic osteosarcomas, which showed less cytologic atypia than the highly pleomorphic osteoclastic and osteoblastic variants. Mitotic activity ranged from 6 to 40 mitotic figures per 10 high-power fields and was most pronounced at the tumor periphery. By immunohistochemistry, all cases were negative for epithelial markers including broad-spectrum cytokeratins and epithelial membrane antigen. Treatment ranged from excisional biopsy to radical mastectomy. Axillary lymph nodes, evaluated in 11 patients, were all free of tumor. Local recurrences or metastatic disease occurred in 43% of the patients, and 7 patients died within 12 months of initial metastasis detection. Recurrent and metastatic lesions, reviewed in 5 patients, morphologically resembled the osteosarcomatous component of the primary tumor but with greater cellularity and pleomorphism. By univariate analysis, gross tumor size and osteosarcoma subtype significantly correlated with prognosis; however, in a multivariate analysis, neither of these factors was an independent prognosticator. Phyllodes tumors with an osteosarcomatous component are potentially aggressive neoplasms, particularly when they are large (>5 cm) or associated with an osteoclastic or osteoblastic sarcomatous component. A complete excision without axillary lymph node dissection is advised.

References