Pathologic Quiz Case

Myxoid Tibial Lesion in a 31-Year-Old Man

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The patient was a 31-year-old man with a left lower extremity mass that had gradually enlarged during the preceding year, resulting in mild discomfort and poor cosmesis. He had no history of local trauma or surgery. Radiologic studies revealed a pedunculated mass arising from the junction of the middle and distal thirds of the anterior cortex of left tibia. The mass was variably calcified and radiolucent, suggesting a paraosteal or periosteal osteosarcoma. The mass was surgically enucleated and sent for histologic examination. A follow-up computed tomographic scan, performed 6 months after surgical resection, demonstrated no evidence of recurrence.

The mass was oval and well circumscribed, and had a yellow-gray and uniformly gelatinous cut surface. It measured 5 cm in maximum dimension (Figure 1). There were no areas of hemorrhage or necrosis. Microscopic examination revealed a neoplasm with well-defined nodular contours and prominent myxoid areas (Figure 2). Embedded in the myxoid stroma were spindle to stellate cells exhibiting mild cytologic atypia and rare mitoses (Figure 3). The tumor infiltrated the surrounding adipose tissue and cortical bone. Immunohistochemical stains revealed strong reactivity for vimentin (Figure 4) and focal staining for smooth muscle actin in the tumor cells.

What is your diagnosis?

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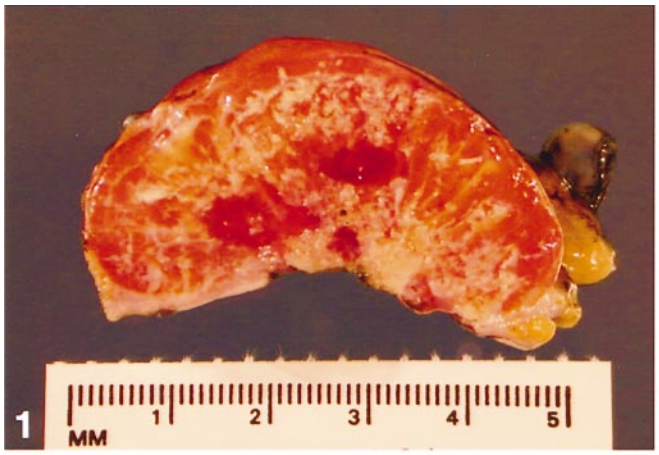

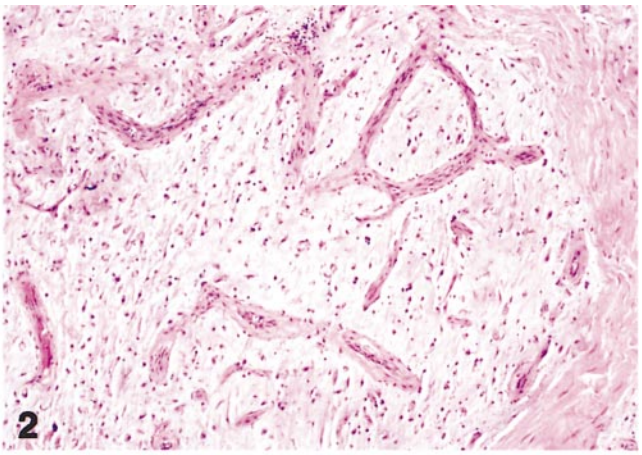

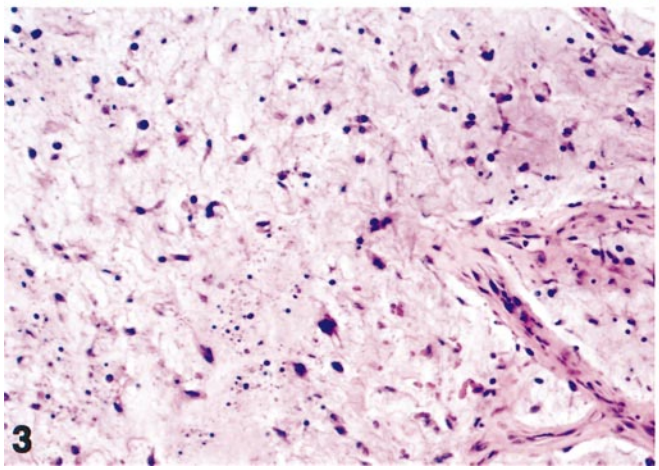

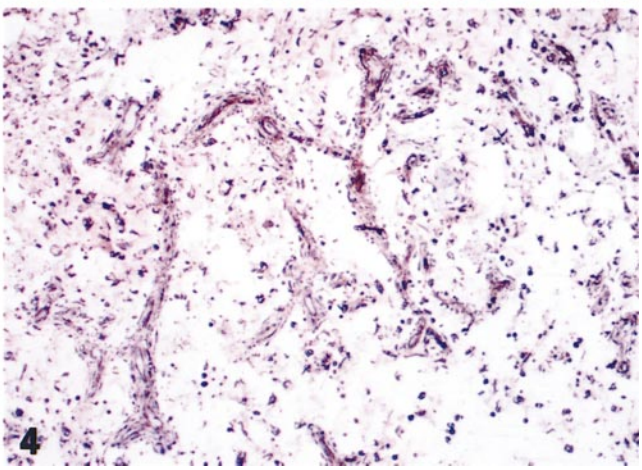

Pathologic Diagnosis: Low-Grade Myxofibrosarcoma

Angervall et al[1] originally described myxofibrosarcomas in 1977 as tumors of fibroblastic differentiation, characterized by a nodular appearance, prominent myxoid matrix, plexiform capillaries, and location in dermis and superficial soft tissues. The authors categorized these tumors into grades I through IV, depending on cellularity, mitotic activity, and nuclear atypia. Weiss and Enzinger[2] in the same year defined a myxoid variant of malignant fibrous histiocytoma (MFH) as a tumor with at least 50% myxoid component. Myxoid MFH had a better prognosis than MFH with less than 50% myxoid component, and the degree of myxoid change was inversely related to the metastatic rate of the tumor.

In 1996, Mentzel et al[3] reported 75 cases of myxofibrosarcomas and divided these tumors into low-, intermediate-, and high-grade categories, depending on the degree of atypia and the presence or absence of pleomorphic MFH component within the tumor. Tumors of the low-grade category were purely myxoid with mild cytologic atypia. None of the low-grade tumors had metastasized. Recently, Weiss and Goldblum[4] proposed that highly myxoid fibroblastic/fibrohistiocytic sarcomas (>50% myxoid component) should be divided into 2 groups. Tumors with minimal cellular atypia (myxofibrosarcoma/myxoid fibrosarcomas) should be classified as grade I. Those with significant nuclear atypia (myxoid MFH) should be categorized as grade II tumors. The nonmyxoid lesions should be graded as fibrosarcomas or MFH, depending on the degree of atypia.[4]

The most common clinical presentation of low-grade myxofibrosarcoma is that of a slowly enlarging and painless mass in the lower extremities of elderly patients. There is a slight male predominance.[5] Although it is seen most commonly in the fifth to seventh decades of life, it has also been reported as early as 7 years of age.[6] The most common sites for this tumor are the extremities, with a slightly greater incidence in the lower extremity. Other sites include head, trunk, retroperitoneum, and mediastinum.[3] It arises most frequently in the superficial subcutaneous tissue and has a tendency to spread into the underlying skeletal muscle. Deep-seated tumors are larger, less nodular, and more infiltrative than their superficial counterparts.[3] The duration of symptoms ranges from 2 weeks to 15 years.[3,5]

On gross examination, these tumors are oval to spherical, multinodular, and range from a few millimeters to several centimeters in greatest dimension. The cut surface is translucent, gray-white, glistening, and gelatinous. Areas of hemorrhage and necrosis are uncommon. Histologically, the tumor has a multinodular contour with a predominant myxoid background (>50%) and low cellularity. Elongated and curvilinear thin-walled capillaries are a prominent feature. The tumor cells are often aligned along the vessel periphery. The tumor cells are noncohesive, fusiform, round to stellate, and embedded in a myxoid matrix. The matrix is composed chiefly of hyaluronic acid.[4] The tumor cells have slightly eosinophilic cytoplasm, indistinct cell borders, hyperchromatic and irregular nuclei, mild pleomorphism, and rare to occasional mitoses, ranging from 0 to 6 per 10 high-power fields.[3] Occasional cells contain small mucin-containing cytoplasmic vacuoles, but no lipoblasts are present. Cellular areas are absent.

Immunohistochemically, the tumor demonstrates diffuse cytoplasmic positivity for vimentin and focal staining for muscle-specific and smooth muscle actins, suggesting myofibroblastic differentiation. The tumor cells are consistently negative for CD68, Mac-387, factor XIIIa, and desmin. In most cases, the tumor cells stain positively for both epithelial growth factor and its receptor. Ultrastructurally, these cells are elongated with occasionally clefted nuclei containing peripherally condensed chromatin. The cytoplasm contains dilated rough endoplasmic reticulum with well-developed Golgi apparatus and a fair number of mitochondria.[3] Cytogenetic aberrations have included (2:15)(p23;q21.2), ring chromosomes, del(1)(q12), and highly complex karyotypes with intratumoral heterogeneity; however, no specific abnormality has emerged. DNA flow cytometric analysis revealed these tumors to be predominantly aneuploid.[5,7] Adequate surgical resection appears to be the treatment of choice. However, 38% to 50% of these tumors recur.[3,5] The recurrent tumor often has a higher histologic grade. To date, no case has been shown to metastasize. Deep-seated (or higher grade) tumors have similar rates of local recurrence; however, they have higher rates of metastasis and mortality.[5]

The main differential diagnoses include myxoma, myxoid liposarcoma, and low-grade fibromyxoid sarcoma. Myxomas are hypovascular and lack the curvilinear vessels. The cells are less atypical but are mitotically active. Myxoid liposarcomas contain lipoblasts and do not have the perivascular tumor cell condensation. Low-grade fibromyxoid sarcomas have greater cellular atypia and more fibrous stroma, and they can metastasize.[8]

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