SECTION EDITOR: ENID GILBERT-BARNESS, MD

Pathologic Case of the Month

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AN 11-YEAR-OLD African American boy presented to his local physician with a complaint of painless swelling in the right calf. The lesion subsequently increased in size, and 2 months later he was limping and complaining of pain in the leg. Magnetic resonance imaging of the knee revealed a lobulated heterogeneous soft tissue mass in the lateral head of the gastrocnemius muscle with associated edema in the surrounding musculature (**Figure 1**). A deep-seated, tennis ball–sized mass was subsequently resected 2 weeks later. The resection included the lateral head of the gastrocnemius muscle, underlying soleus muscle, and surrounding soft tissues. The closest margin was along the neurovascular bundle in the popliteal space. There was no attachment of tumor to the periosteum or synovium.

Grossly, the fairly well-circumscribed, vaguely lobulated, fusiform tumor measured 6.0 cm in greatest diameter and consisted of soft to firm, tan-white tissue with a focally gelatinous cut surface. Focal areas of cystic hemorrhage were present (**Figure 2**). Microscopically, the tumor was composed of strands of epithelioid to spindle-shaped cells with uniform, round to oval, hyperchromatic nuclei and variably clear to eosinophilic cytoplasm embedded in a fibromyxoid matrix. Densely cellular areas were separated by thick bands of fibrous stroma, and loosely cellular clusters of cells were embedded in a more abundant myxoid matrix (**Figure 3**) that was reactive with Alcian blue (pH 2.5) in the presence or absence of hyaluronidase. Well-differentiated hyaline cartilage was not identified. The mitotic activity was generally low. No necrosis was observed. The tumor cells were reactive immunohistochemically with vimentin and epithelial membrane antigen in a focal pattern. Results of staining for S100 protein and cytokeratins were negative.

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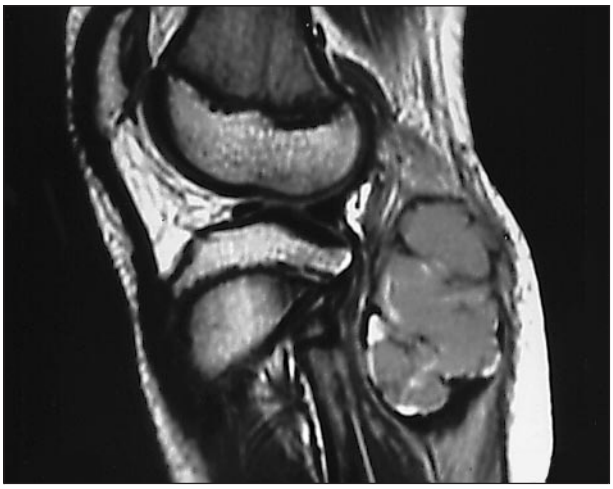

Figure 1.

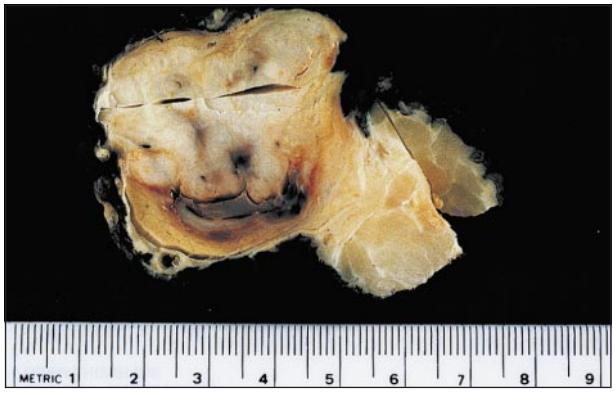

Figure 2.

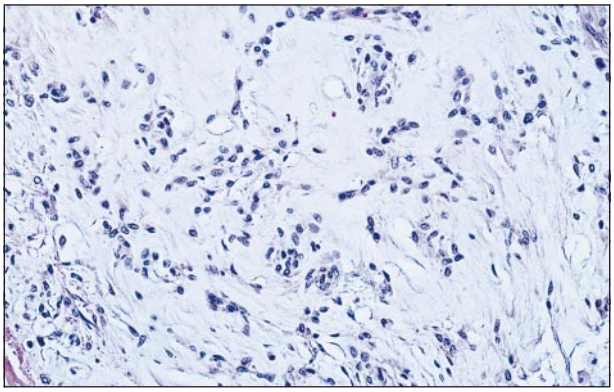

Figure 3.

Diagnosis and Discussion

Extraskeletal Myxoid Chondrosarcoma

Figure 1. *Sagittal proton density magnetic resonance image of the knee reveals a lobulated heterogeneous mass in the lateral head of the gastrocnemius muscle. High signal consistent with edema is seen in the surrounding muscle.*

Figure 2. *Tan-white, vaguely lobulated gross appearance of the soft tissue tumor with a gelatinous cut surface and focal areas of cystic hemorrhage. Scale is in centimeters.*

Figure 3. *Section reveals small rounded tumor cells in cords and sheets embedded within an abundant extracellular myxoid matrix (hematoxylin-eosin, original magnification ×10).*

A diagnosis of extraskeletal myxoid chondrosarcoma was rendered based on histologic findings. Extraskeletal myxoid chondrosarcomas are rare malignant soft tissue neoplasms that are usually seen in patients older than 35 years but can be seen in children.[1] As in this case, most are deep seated and are located primarily in the musculature of the extremities. The thigh and popliteal fossa are the most common sites, and the male-female patient ratio is 2:1. Our patient had a typical presentation of nonspecific signs and symptoms.

Typically well-circumscribed, extraskeletal myxoid chondrosarcomas are commonly encapsulated by a rim of fibrous tissue. The abundant myxoid matrix gives the cut surface a gelatinous appearance. The degree of cellularity is variable; less well-differentiated, highly cellular tumors generally have less extracellular matrix and behave more aggressively. As illustrated in this case, the neoplastic cells characteristically are epithelioid to spindly and contain centrally placed, uniformly round to oval, hyperchromatic nuclei and clear to vacuolated eosinophilic cytoplasm. A peripheral rim of eosinophilic cytoplasm can be distinctive, suggesting chondroblastic differentiation. The extracellular matrix stains deeply with Alcian blue; in contrast to myxomas and parachordomas, this staining reaction is resistant to hyaluronidase.

Immunohistochemical studies classically result in positive reactions for S100 protein and vimentin and negative staining for epithelial markers such as epithelial membrane antigen and cytokeratins. However, a recent report indicates that S100 immunopositivity is less common in extraskeletal myxoid chondrosarcomas than generally accepted.[2] Ultrastructural features characteristically include distinctive aggregates of microtubules within the rough endoplasmic reticulum. Distinctive, nonmicrombular, lamellar inclusions have also been described.[3] Although not found in this case, cytogenetic studies characteristically reveal alterations of chromosomes 9 and 22, t(9;22)(q22-q31;q11-q22). Molecular analysis has shown this translocation to represent fusion of the *EWS* gene at 22q12 to a novel orphan nuclear receptor gene at 9q22.[4]

Differential diagnoses include other myxoid neoplasms such as bony myxoid chondrosarcoma, myxoid liposarcoma, chordoma, and parachordoma. Myxoid chondrosarcomas of bone have an identical histologic appearance, necessitating a complete radiologic evaluation to exclude primary bone disease. The presence of lipoblasts and a distinctive plexiform vascularity distinguish myxoid liposarcomas from this neoplasm. Absence of stainable extracellular mucin using Alcian blue after treatment with hyaluronidase is a differentiating feature of myxochondromas, chordomas, parachordomas, and myxoid liposarcomas.

Clinically, extraskeletal myxoid chondrosarcomas are considered to be relatively slow-growing tumors with a long-term propensity for recurrence and metastasis. In a 10-year follow-up study of 10 patients, Saleh et al[5] reported metastasis or recurrence in all patients and death from disease in 7. In a larger series, Meiss and Martz[6] found a 53% recurrence rate and a 44% metastatic rate, with 73% of the patients alive after 10 years. In a pediatric series, 5 of 7 patients were dead within months after diagnosis.[1] The lungs, soft tissues, and lymph nodes are the most common sites of metastasis. The treatment of choice is wide local excision, and a good response to radiation therapy has been observed.[7] Resistance to standard soft tissue sarcoma chemotherapy has been demonstrated.[8]

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