Chapter 73
Myofibroblastic Sarcoma

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Definition: Sarcomas composed of myofibroblasts.

Myofibroblastic sarcomas display a range of differentiation. Low-grade myofibroblastic sarcoma is identified as a specific entity in the WHO 2013 classification, while the definition of high-grade myofibroblastic sarcoma is not well established. There is evidence that myofibroblastic differentiation in pleomorphic sarcomas is associated with a more aggressive behavior.

Epidemiology: Low-grade myofibroblastic sarcomas occur predominantly in adult patients (age range: 4–75 years, mean 38), while high-grade myofibroblastic sarcomas can also occur in children. There is a slight male predominance.

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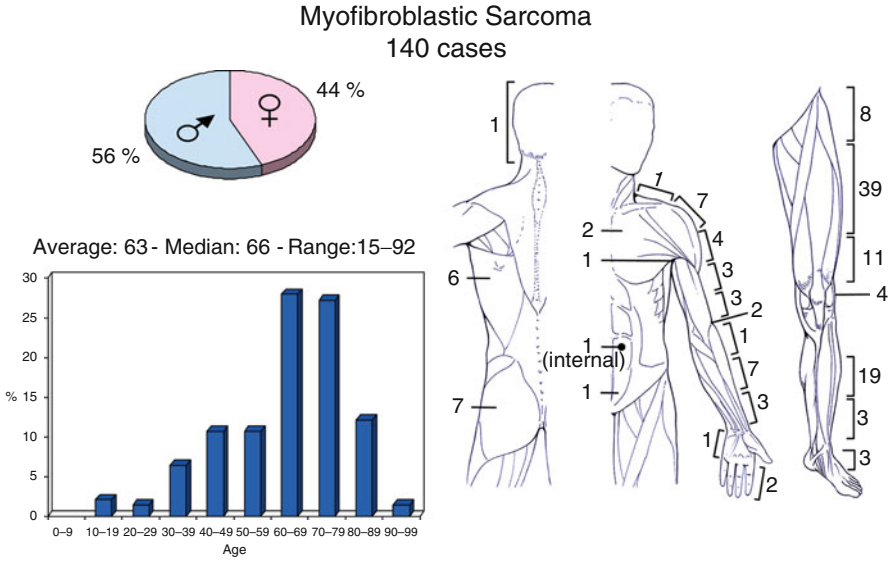


Location: Low-grade myofibroblastic sarcomas most commonly occur in the head and neck region, including the oral cavity, pharynx and parapharyngeal regions, and proximal extremities and trunk; occasional cases can occur in the abdomen or pelvis. They usually arise in the deep soft tissues, but cases have been seen in the subcutis and submucosa. Visceral lesions are rare. Cases have also been described in bone, including maxilla, mandible, femur, and ilium. High-grade myofibroblastic sarcomas arise in deep soft tissues, predominantly in lower limbs and trunk, with occasional cases in head and neck.

Clinical and Imaging: Enlarging painless mass, very often with infiltrative margins. High-grade sarcomas with hemorrhage and necrosis are heterogeneous at MRI.

Histopathology: Grossly, low-grade myofibroblastic sarcomas are firm with a pale fibrous-appearing cut surface, ill-defined infiltrative margins, or sometimes with pushing margins. High-grade myofibroblastic sarcomas are large solid tumors with hemorrhage and necrosis. Histologically, low-grade myofibroblastic sarcomas are characterized by a proliferation of spindle cells arranged in a fascicular or in a storiform pattern. The neoplastic cells show tapered fusiform elongated to wavy nuclei with discernible eosinophilic cytoplasm. Sometimes the nuclei are rounded

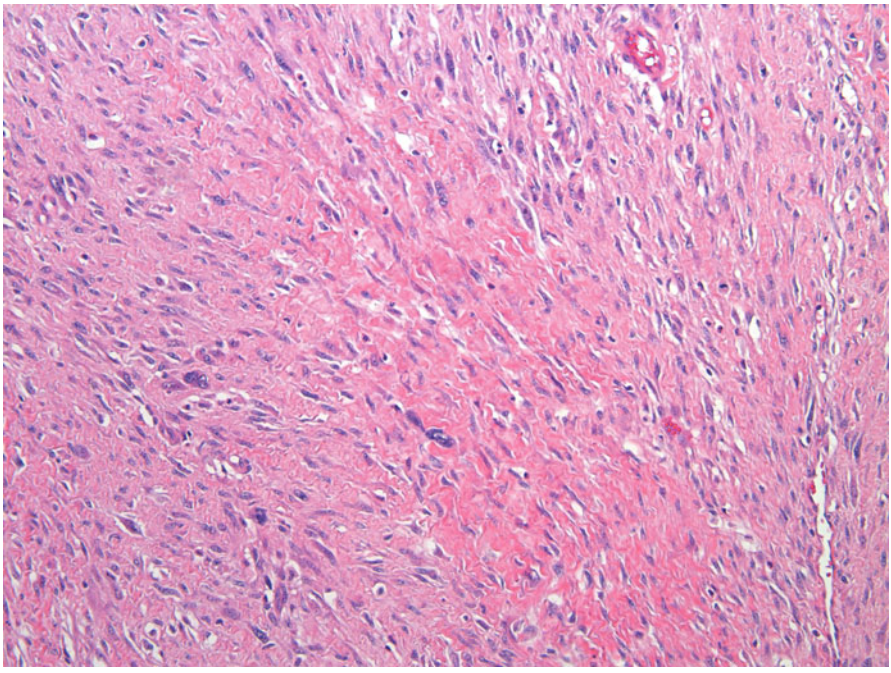
and vesicular with small punctuated nucleoli. There is at least focally moderate nuclear atypia. The margins are predominantly infiltrative, with separation rather than destruction of skeletal muscle bundles. Mitotic activity is variable but atypical mitoses are rare. Stroma is often minimal and can be variably collagenous. High-grade myofibroblastic sarcomas are composed of pleomorphic, spindle, or epithelioid cells arranged in a fascicular or in a storiform growth pattern, with scattered atypical mitotic figures. Both low- and high-grade myofibroblastic sarcomas show variable positivity for actins and/or desmin. Calponin and CD34 can be positive. EMA, S100, beta-catenin, and caldesmon are negative. Ultrastructure is the gold standard in defining normal myofibroblasts which are distinguished from smooth muscle cells by fibronectin fibril and fibronexus junctions, which are considered the most characteristic ultrastructural markers of myofibroblasts. Fibronexus, a cell-to-matrix junction, first described and designated by Singer in 1979, is a unit composed of fibronectin and 5 nm microfilaments that converge at the cell surface. It is not perfectly clear whether these features are always present in myofibroblastic sarcomas.

Course and Staging: About 33 % of low-grade myofibroblastic sarcomas locally recur, especially after incomplete excision. Metastases have been reported in approximately 10 % of cases. Progression to high-grade sarcoma has been documented. High-grade myofibroblastic sarcomas recur in 33 % of cases with metastases in over 70 %. These tumors, like the other pleomorphic sarcomas with myogenic differentiation, have a worse outcome than undifferentiated sarcomas.

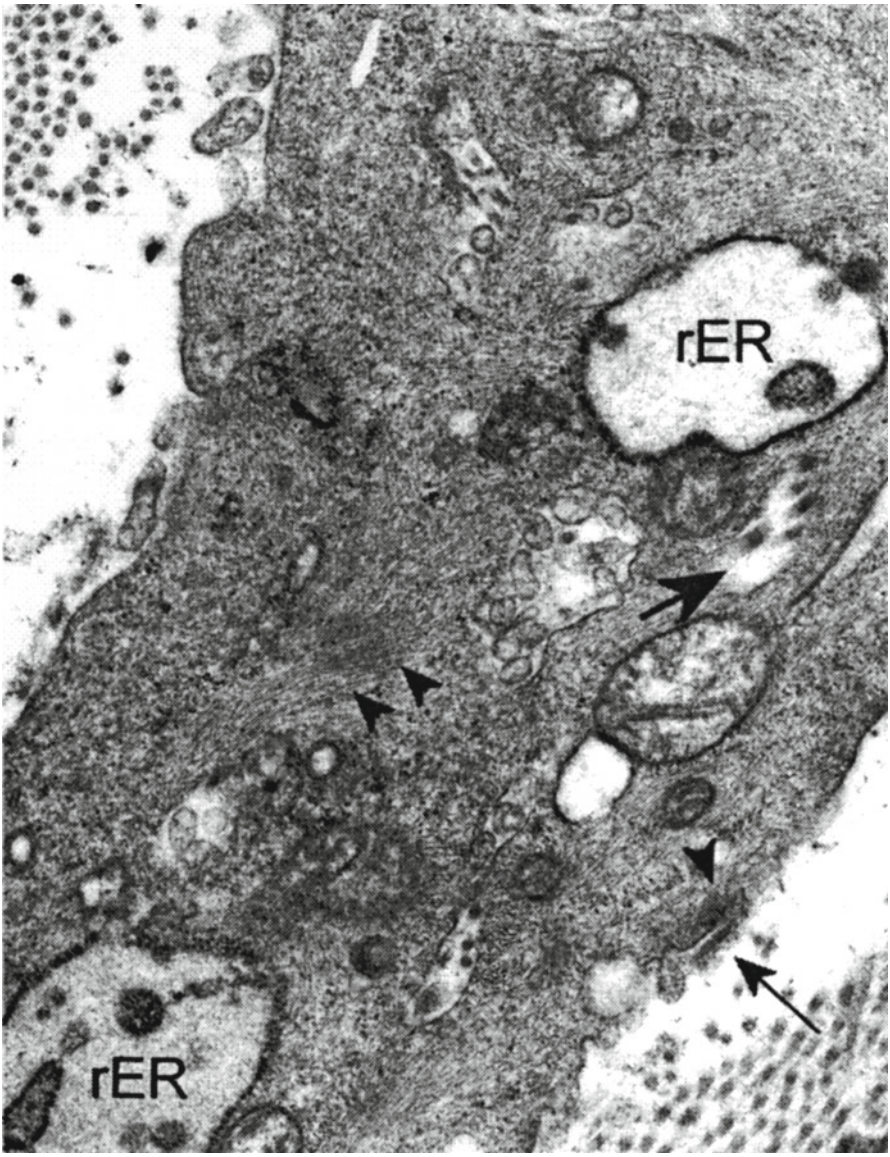
Treatment: Low-grade myofibroblastic sarcomas are best managed by wide surgical excision and long-term follow-up to detect possible late metastases. High-grade myofibroblastic sarcomas should be managed by excision with wide margins and adjuvant radiation therapy and/or systemic chemotherapy.

Immunohistochemical Panel

VIM	+
MS act	±
Smooth M act	±
Desmin	±
Caldesmon	−
Calponin	+



Fascicular to storiform arrangement of spindle cells with short tapered wavy nuclei. Stroma is variably collagenous. Some tumors show a tissue culture-like growth pattern that closely resembles nodular fasciitis



Portion of a myofibroblast showing intermediate filaments, actin filaments (*arrowheads*), dilated rough endoplasmic reticulum cisternae (rER), collagen inclusions (*large* and *short arrows*), and fibronexus (*thin* and *long arrow*), ×9,000

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