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= **Abstract** =

Cytological Features of Low Grade Fibromyxoid Sarcoma
-Report of a Case with a Review of the Literature-

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Low-grade fibromyxoid sarcoma (LGFMS) is a rare soft tissue tumor. There have been only a few prior fine-needle aspiration (FNA) cytological reports. Recognition of this tumor is important because of its potential for metastasis despite its indolent nature and its deceptively bland cytologic appearance. A 60-year-old male presented with a slowly growing mass in the left calf detected 10 years ago. The patient underwent surgical excision. FNA cytology was performed directly on the mass. The smears showed low cellularity composed of hypercellular tissue fragments, hypocellular loose aggregates, and stripped nuclei. The cytoplasm was seen as either collagenous material or very thin fibrillary collagen strands. Tumor cells had spindle, ovoid, or irregular nuclei, fine chromatin, and small nucleoli. Focally slight degree of nuclear pleomorphism is noted. There were no mitotic figures. Blood vessels were frequently seen. Immunocytochemically, tumor cells were negative for S-100 protein, desmin, smooth muscle actin, and CD34. The diagnosis of LGFMS is rarely possible by cytology alone; however, LGFMS should be included in the differential diagnosis of spindle-cell tumors consisting of hypercellular and hypocellular components with some capillary-sized vessels arising in the deep soft tissue of the lower extremities, particularly the thigh. The immunocytochemical findings are of help in the differential diagnosis.

Key words: Soft tissue neoplasm, Low-grade fibromyxoid sarcoma, Aspiration biopsy

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INTRODUCTION

Soft tissue sarcomas are relatively rare and constitute fewer than 1% of all cancers.[1] Low-grade fibromyxoid sarcoma (LGFMS), a distinctive variant of fibrosarcoma, is a rare soft tissue sarcoma[2] and was first recognized by Evans[3,4] and subsequently by Fletcher and colleagues.[5] Identification of this tumor is of clinical and pathological importance because its aggressive clinical course includes recurrences, metastases, and death despite its deceptively bland histologic appearance.[3,4,6] There have been only a few prior fine-needle aspiration (FNA) cytological reports of LGFMS.[7-10] We illustrate the FNA cytology findings of LGFMS arising in the thigh of a 60-year-old male with review previous reports.

CASE

A 60-year-old male presented with a slowly growing mass in the left calf that was detected 10 years ago. Magnetic resonance imaging demonstrated a solid mass in the left flexor hallucis longus. The patient underwent surgical excision. FNA cytology was performed directly on the mass using a 20-gauge needle. A histological diagnosis of LGFMS was made. No postoperative chemotherapy or radiation therapy was administered. The patient was alive with no clinical or imaging evidence of recurrent or metastatic disease 19 months after excision.

Cytological Findings

FNA smears were fixed in 95% ethanol and stained with Papanicolaou and hematoxylin-eosin (H-E) stain. The smears had low cellularity and were composed of hypercellular tissue fragments, hypocellular loose aggregates, and stripped nuclei (Fig 1A). The cytoplasm was seen as either collagenous material or thick or thin fibrillary collagen strands (Fig 1B and C). The cells had spindle, ovoid, or irregular nuclei, fine chromatin, and small nucleoli (Fig. 1D). A focally slight degree of nuclear pleomorphism was noted in a hypercellular tissue fragment. There were no mitotic figures. Curvilinear capillary-sized blood vessels were frequently seen (Fig 1A inset). In some areas cellularity was increased around these vessels. Occasional background mononuclear cells were present. Immunocytochemically S-100 protein (4C4.9, 1:100; NeoMarkers, Fremont, CA, USA), desmin (D33, 1:100; DAKO, Copenhagen, Denmark), smooth muscle actin (αsm-1, 1:50; Novocastra, Newcastle upon Tyne, UK), and CD34 (QBEnd/10, 1:50, DAKO) immunostains were negative.

Histological Findings

The mass measuring 7.0×6.0 cm was well circumscribed and showed a gray-white to ivory trabeculated glistening cut surface with some myxoid areas (Fig. 2A). Neither necrosis nor hemorrhage was present. Microscopically this tumor showed nodular growth pattern at low power (Fig. 2B). Relatively hypercellular areas alternated with less cellular areas. The tumor showed whorled, fascicular, or haphazard, arrangements. The cells had a benign appearance; spindle, oval, or irregular nuclei, finely granular chromatin, one to several small nucleoli, and eosinophilic fibrillary cytoplasm, either thick in hypercellular areas or thin in hypocellular areas. Nuclear pleomorphism was slight. There were no mitotic figures. Curvilinear or branching capillary-sized blood vessels were frequently found. In some areas cellularity was increased around these vessels in a vaguely organoid pattern. Perivascular sclerosis was noted. Several lymphocytes were present. Immunohistochemically, tumor cells were strongly and diffusely positive for vimentin (V9, 1:50, Biogenex, San Ramon, CA, USA) and negative for cytokeratin (5D3 and LP34, 1:50; Novocastra), epithelial membrane antigen (EMA, GP1.4, 1:200; Novocastra), S-100 protein, desmin, smooth muscle actin, and CD34. The Ki-67 (polyclonal, 1:200; DAKO) index was less than 5%.

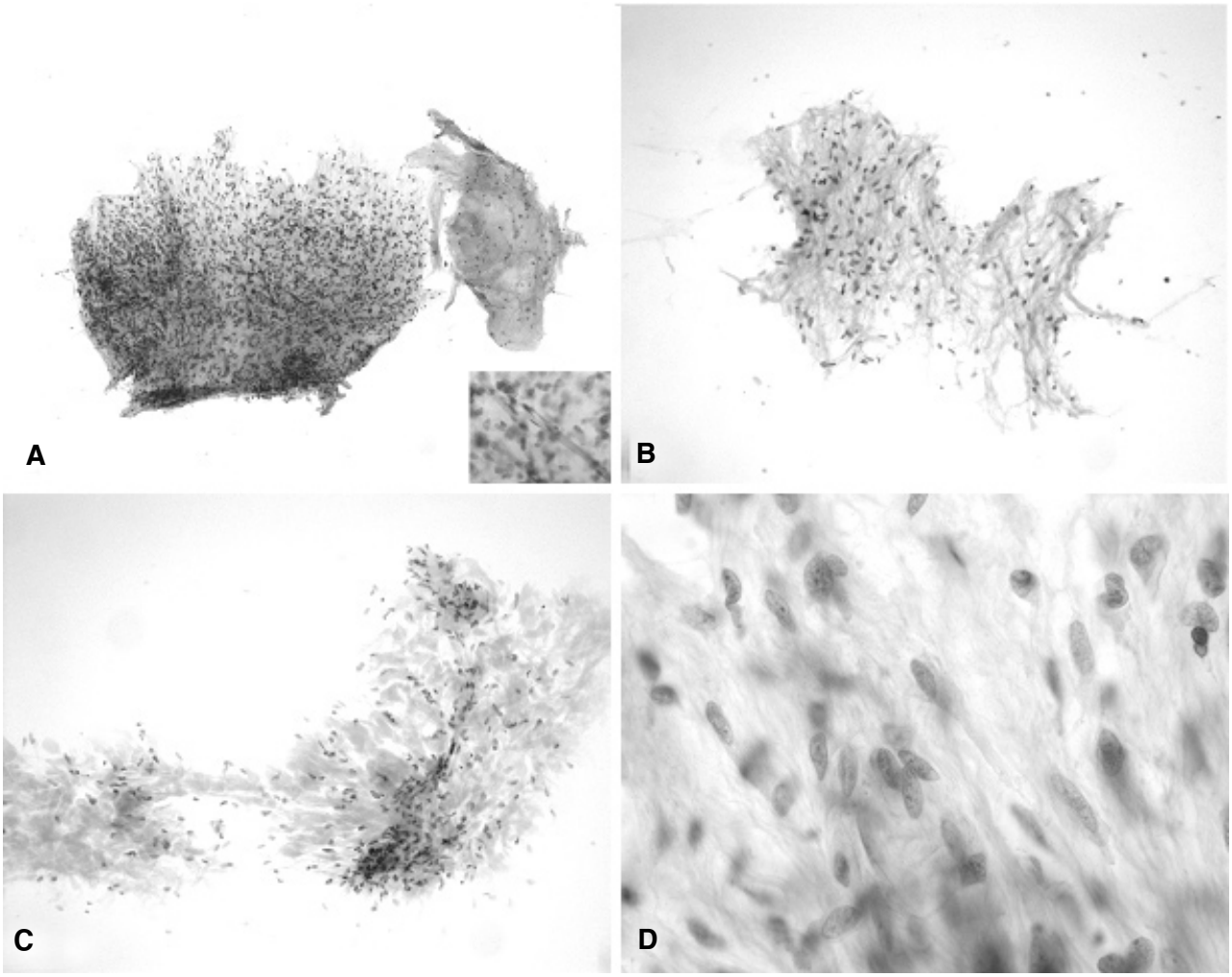

Fig. 1. The smears were composed of hypercellular tissue fragments with capillary-sized vessels (inset) and hypocellular myxoid material **(A)**. The cytoplasm is seen as either thin fibrillary collagen strands **(B)** or collagenous material **(C)** The tumor cells have spindle, ovoid, or irregular nuclei, fine chromatin, and small nucleoli **(D)**. (Papauicolaou)

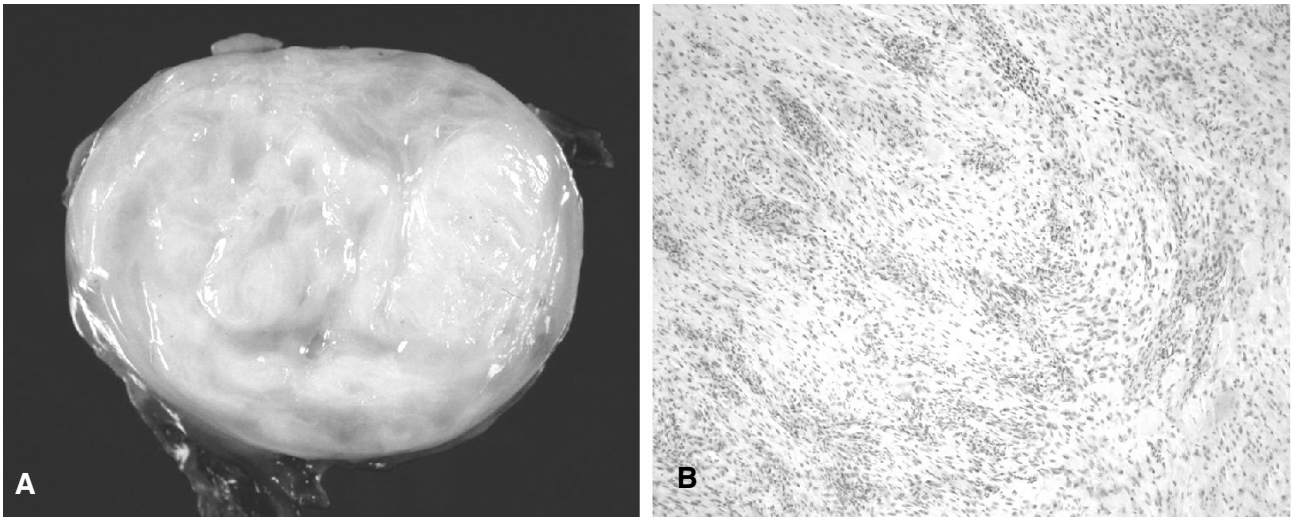

Fig. 2. The mass shows a gray-white to ivory trabeculated glistening cut surface with some myxoid areas **(A)**. Histologic section shows relatively hypercellular areas alternated with less cellular areas **(B)**.

DISCUSSION

LGFMS is characterized by an admixture of heavily collagenized and myxoid zones, deceptively bland spindled cells with a whirling growth pattern and arcades of curvilinear blood vessels.[2] LGFMS typically affects young adults and presents with a slowly growing, painless, deep soft tissue mass in the lower extremities, particularly the thigh, followed, in decreasing order of frequency, by the chest wall/axilla, shoulder region, inguinal region, buttock, and neck.[2,3,6,11]

Densely cellular aggregates suggestive of fibrous composition were rare or absent in the previous reports.[8,9] Therefore, in these cases the cytological findings were not specific enough to make a definitive diagnosis based on FNA alone.[9] Our case had particular cytological features considered to be specific to LGFMS: hypercellular and hypocellular components with relatively bland spindle cells with thick or thin fibrillary collagen strands and curvilinear capillary-sized blood vessels. Unlike previous reports, small indistinct nucleoli were also found in our case. The previously reported cytological features of LGFMS are summarized in Table 1.

The differential diagnosis of LGFMS includes a variety of benign or malignant fibrous or myxoid neoplasm such as neurogenic tumors, desmoid-type fibromatosis, nodular fasciitis, solitary fibrous tumor, myxoid spindle cell lipoma, myxoid synovial sarcoma, myxoid liposarcoma, hyalinizing spindle cell tumor with giant rosettes, myxofibrosarcoma, and myxoid variant of dermatofibrosarcoma protuberans.[2,11] Neurogenic tumors have long, slender, wavy nuclei with tapered ends and S-100 protein positivity that are not present in LGFMS.[9] In desmoid-type fibromatosis, stromal myxoid change is unusual, except in the mesentery and the pelvis.[2] Some nodular fasciitis may resemble LGFMS, but the former lesion is characterized by plump immature-appearing fibroblasts with oval, pale staining nuclei and prominent nucleoli. Mitotic figures are fairly common. Other features of fasciitis, such as the presence of erythrocytes, hemosiderin containing macrophages, or multinucleated giant cells, are also found. Clinically nodular fasciitis occurs especially on the chest, back, and upper extremities, typically grows rapidly, and usually measures 2 cm or less.[2,11,12] Recognizing cytological features and clinical scenarios helps establish the diagnosis of nodular fasciitis. Although the spindle-shaped cells are similar to those seen in the LGFMS, CD34 positivity is present in solitary fibrous tumors. Although some spindle cell lipomas show myxoid stromal change, it is a circumscribed subcutaneous lesion that occurs typically on the neck and back and the spindle cells in spindle cell lipoma are strongly positive for CD34.[2] Monophasic synovial sarcoma may be extremely difficult to distinguish from LGFMS.[13] Epithelial marker[14] help in the diagnosis of synovial sarcoma. Myxoid liposarcoma usually demonstrates multivacuolated lipoblasts and anastomosing vessels embedded in the myxoid background material.[13] The immunohistochemical profile of myxoid liposarcoma reveals positive staining of neoplastic cells for S-100 protein.[8] The hyalinizing spindle cell tumor with giant rosettes is the subset of LGFMSs where the collagen rosettes, a central core of collagen arranged centrifugally from the center surrounded by rounded to ovoid cells,[11] are particularly prominent and well formed.[2] This feature was not seen in our case. The myxoid variant of dermatofibrosarcoma protuberans may resemble the LGFMS, but this lesion tends to be more superficial, predominantly involving the dermis and subcutaneous tissue. Moreover, positive immunostaining with CD34 can be useful in the differential diagnosis.[11,12,15] Myxofibrosarcoma commonly arises in the subcutaneous tissues of the extremities, unlike LGFMS, which typically arises in the skeletal muscle. Also, myxofibrosarcoma has a greater degree of nuclear pleomorphism and hyperchromasia and is uniformly myxoid lacking fibrous zones. In contrast, myxoid areas in LGFMS seem to also have stromal collagen and are not as transparent as the myxoid areas of myxofibrosarcoma.[11]

The diagnosis of LGFMS is rarely possible by cytology alone; however, LGFMS should be included in the differential diagnosis of spindle-cell tumors consisting of hypercellular and hypocellular components with capillary-sized vessels arising in the deep soft tissue of the lower extremities, particularly thigh. The immuno-

Table 1. Cytological Features of three previous FNA cytological reports of LGFMS

	Cellularity	Presentation	Cellular Shape	Cytoplasm	Nucleus	Chromatin	Nucleoli	Mitosis	Pleomorphism	Cytologic Diagnosis
Dawamneh et al.[10]	Low	▪ Singly and in small clusters embedded in myxoid material and associated with a collagenous matrix ▪ No coarse blood vessel fragments ▪ No inflammatory cells	Spindle	Wispy, fagile	Elongated, ovoid, and occasionally plump	Evenly distributed, slightly coarse	(−)		(−)	
Estrada Villasenor et al.[7]	Low	▪ Tumor cells in an abundant myxoid background with occasional thick bands of collagen ▪ Capillary-sized vessels in some of the myxoid areas	Spindle, bipolar	Pale blue long wispy cytoplasmic processes	▪ Spindle shaped ▪ Two nuclei in some cells ▪ Focally slight degree of nuclear enlargement and hyperchromasia	Bland	(−)	(−)	Focally slight	Low grade myxoid sarcoma
Silverman et al.[8]		▪ Microtissue fragments (hypocellular in many of the fragments)consisting of tumor cells in myxoid matrix ▪ Thin-walled capillary-type channels	Spindle		Slightly elongated, oval to tapered				(−)	Myxoid proliferation, reactive vs. low grade myxoid sarcoma
Lind-berg et al.[9]										
Case 1	Low	▪ Scattered tumor cells (single dispersed cells in the majority of smears and rare densely cellular aggregates) in an abundant myxoid background ▪ No capillaries or fibrous stromal fragments ▪ Occasional foamy histiocytes		Loose and tapered along the long axis of the nuclei	▪ Ovoid to spindle ▪ 15 μm	Fine powdery	(−)	(−)	(−)	Myxoid spindle cell neoplasm
Case 2	Low	▪ Scattered tumor cells in a prominent myxoid background (rare foci of thicker myxoid material with increased tumor cells) ▪ No capillaries or fibrous stromal fragments ▪ Occasional histiocytes	Spindle		▪ Ovoid to spindle ▪ 15 μm				(−)	Myxoid spindle cell lesion, myxoma vs. mucocele
Case 3	Low	▪ Myxoid background with numerous tumor cells (no larger, hypercellular fragments) ▪ No capillaries or fibrous stromal fragments	Small ovoid and spindle		▪ Ovoid to spindle ▪ 15 μm	Fine powdery	(−)	(−)	Minimal	Spindle cell neoplasm, favor low grade sarcoma

cytochemical findings are of help in the differential diagnosis.

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