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Case Report

Fibrosarcoma with Deceptive Benign Presentations: a Report of Two Cases

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Abstract

Low-grade fibromyxoid sarcoma and myxofibrosarcoma are malignant soft tissue tumors, fibrosarcomas, of shared clinical and imaging appearances. We report sarcomatous lesions in soft tissue with deceptively benign clinical and imaging appearances, and correlate findings with those of histologic analysis. Two patients presented with a long history of painless swelling at the dorsum and upper extremity and denied any constitutional symptoms. Sonography and magnetic resonance imaging suggested the presence of benign soft tissue lesions of a predominant fluid-like consistency. Despite indolent clinical and imaging characteristics, in both cases, histopathology disclosed a diagnosis of spindle cell-type soft tissue sarcoma, designating an aggressive tumor. Knowledge of the seemingly benign clinical and imaging features of fibrosarcomas is required to raise the possibility of malignancy in soft tissue that may be underdiagnosed or misdiagnosed. The importance of a correct diagnosis and the implications of surgical resection, irradiation, and systemic oncological therapy are quite obvious.

Keywords

low-grade fibromyxoid sarcoma, myxofibrosarcoma, soft tissue, sarcoma, ultrasound, magnetic resonance imaging

INTRODUCTION

Soft tissue sarcomas constitute a diverse group of solid tumors with mesenchymal differentiation accounting for less than 1% of all adult malignancies.[1] Low-grade fibromyxoid sarcoma (LGFMS) is a rare malignant soft tissue sarcoma that is recognized in the World Health Organization (WHO) classification as a variant of fibrosarcoma arising in skeletal muscle, or the subcutaneous tissue. More than 150 LGFMS cases have been reported so far, although it is postulated that this tumor is often misdiagnosed as myxofibrosarcoma, low-grade myxoid sarcoma, or other sarcomatous or non-sarcomatous fibrous or myxoid neoplasms.[1,2] LGFMS typically occurs in young adults and originates in the deep soft tissue of the trunk or the lower extremities. In addition to mild atypical symptoms, our case presentation, to our knowledge, is the first to describe LGFMS assuming a benign, cyst-like appearance on imaging, which proved a diagnostic challenge to the oncology team.

Another mesenchymal tumor, myxofibrosarcoma, is acknowledged as a distinct myxoid variant of malignant fibrous histiocytoma with fibroblastic differentiation. This fibrosarcoma usually originates in the dermal and subcutaneous tissue of the extremities and is more common in the elderly. Despite its indolent presentation as a slowly growing mass, myxofibrosarcoma is often highly infiltrative, rendering local recurrence frequent. Additional characteristics of this sarcoma that make it particularly noteworthy include the extension of the tumor along the fascial planes, following a route that virtually facilitates distant recurrence.[1,3-5]

Although both of these malignant fibrous neoplasms of soft tissue can have a silent clinical course and a fallacious bland histological appearance, recurrence after surgery and late distant metastasis have been reported at variable but significant rates. Because malicious biological characteristics substantiate early recognition and specialized oncology treatment[1,3-7], consideration of this family of sarcomatous tumors arising in soft tissue is of fundamental clinical importance. We aimed to identify key features that might help characterize the nature of soft tissue sarcomas, assuming latent characteristics.

CASE REPORTS

Case 1

A 30-year-old woman presented with a slowly growing mass in her left back that gradually increased in size for three years. The patient reported no past medical problems, trauma, or constitutional symptoms including fever. Physical examination revealed a palpable and moderately tender mass in the left side of her trunk, extending laterally below the axilla. Mild erythema and a focal area of fluctuance approximately 4×4 cm were present. Laboratory evaluation yielded no findings.

Radiographs of the dorsum were obtained which showed obliteration of the fat planes with no evidence of osseous irregularity in the scapula. Upon imaging assessment of the lesion with sonography, an ovoid mass was identified in soft tissues of the dorsum with thin border, measuring 11.5×11×2.8 cm. The structure appeared as a unicompartmental, cyst-like fluid collection ***(Fig. 1).*** *An MR imaging examination was then performed to provide more detailed information about the anatomic relationships of the lesion. MR images revealed a large, well-defined cyst-like lesion in the dorsal trunk soft tissue. The intramuscular lesion was situated in the belly of left latissimus dorsi muscle and exhibited fluid-like characteristics* ***(Fig. 2).***

Myxoid material was aspirated from the dorsal trunk lesion in the urgent care unit. No growth was noted in bacterial cultures. Further investigation of the lesion with needle biopsy yielded histopathological features of soft tissue sarcoma with fibroblastic differentiation, and a myxoid stroma.

The mass was excised and histologic sections revealed an admixture of alternating loose fibrous and myxoid stroma that contained eosinophilic collagen fibers ***(Figs 3A, 3B)****. Bland fibroblastic spindle cells were deposited within this stroma, in a fascicular or storiform arrangement. Immunohistochemistry showed strong staining for vimentin, S-100 protein, CD34, and the epithelial membrane antigen (EMA). The neoplastic cells were positive in the reverse transcription polymerase chain reaction (RT-PCR) assay and did not express immunoreactivity to actin and desmin. The final pathologic diagnosis was low-grade fibromyxoid sarcoma. Postoperative course was uncomplicated and the patient remains well 18 months later, with no evidence of local recurrence or metastasis.*

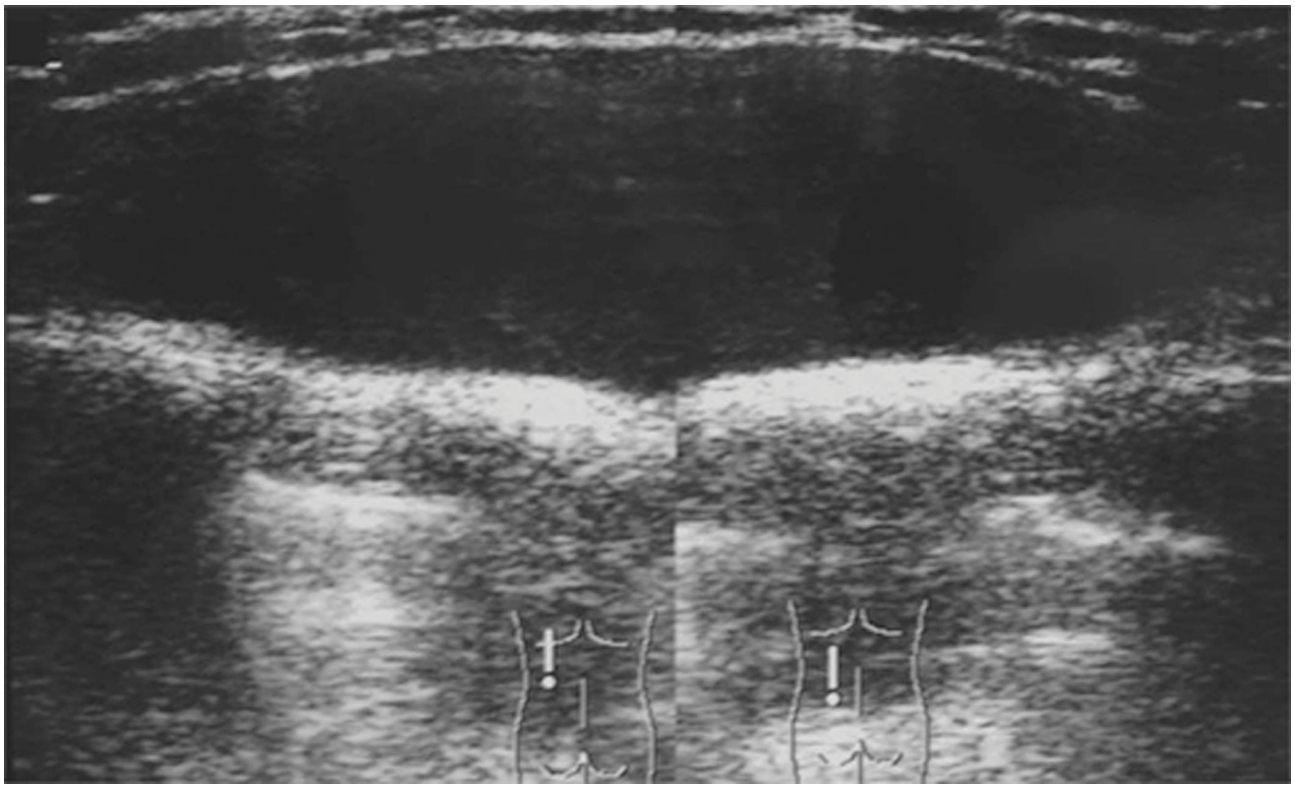

Figure 1. Longitudinal sonography of the left dorsum shows a nearly anechoic, cyst-like lesion in soft tissue. The margins of lesion are distinct.

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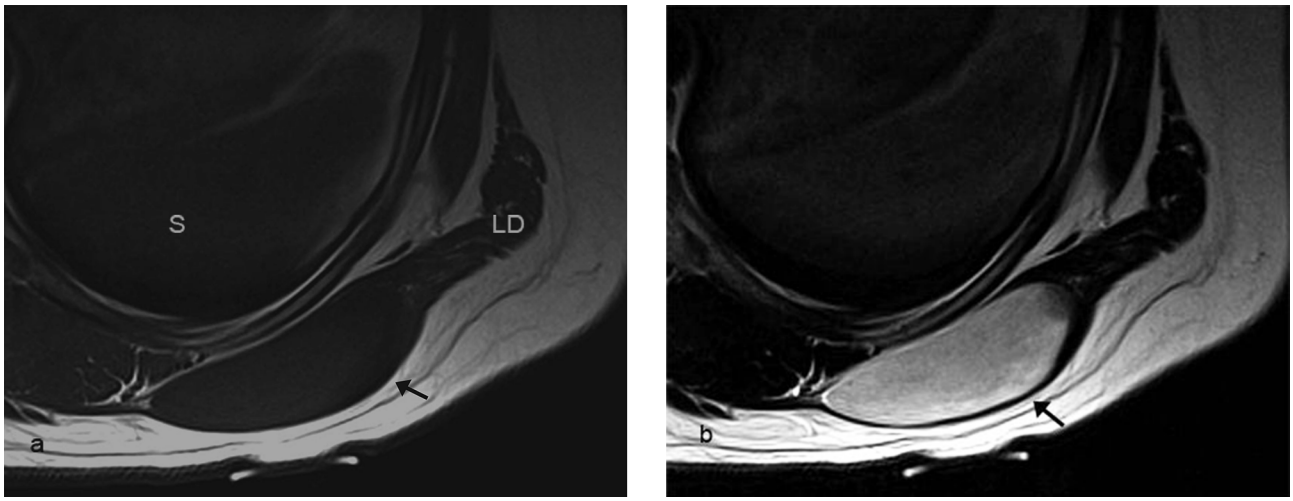

Figure 2. A. Axial T1-weighted image shows well-defined homogeneous soft tissue mass (arrow) of low signal intensity arising from the latissimus dorsi (LD) muscle. S: spleen; **B**. Corresponding T2-weighted image shows mass (arrow) of increased signal intensity arising in muscle.

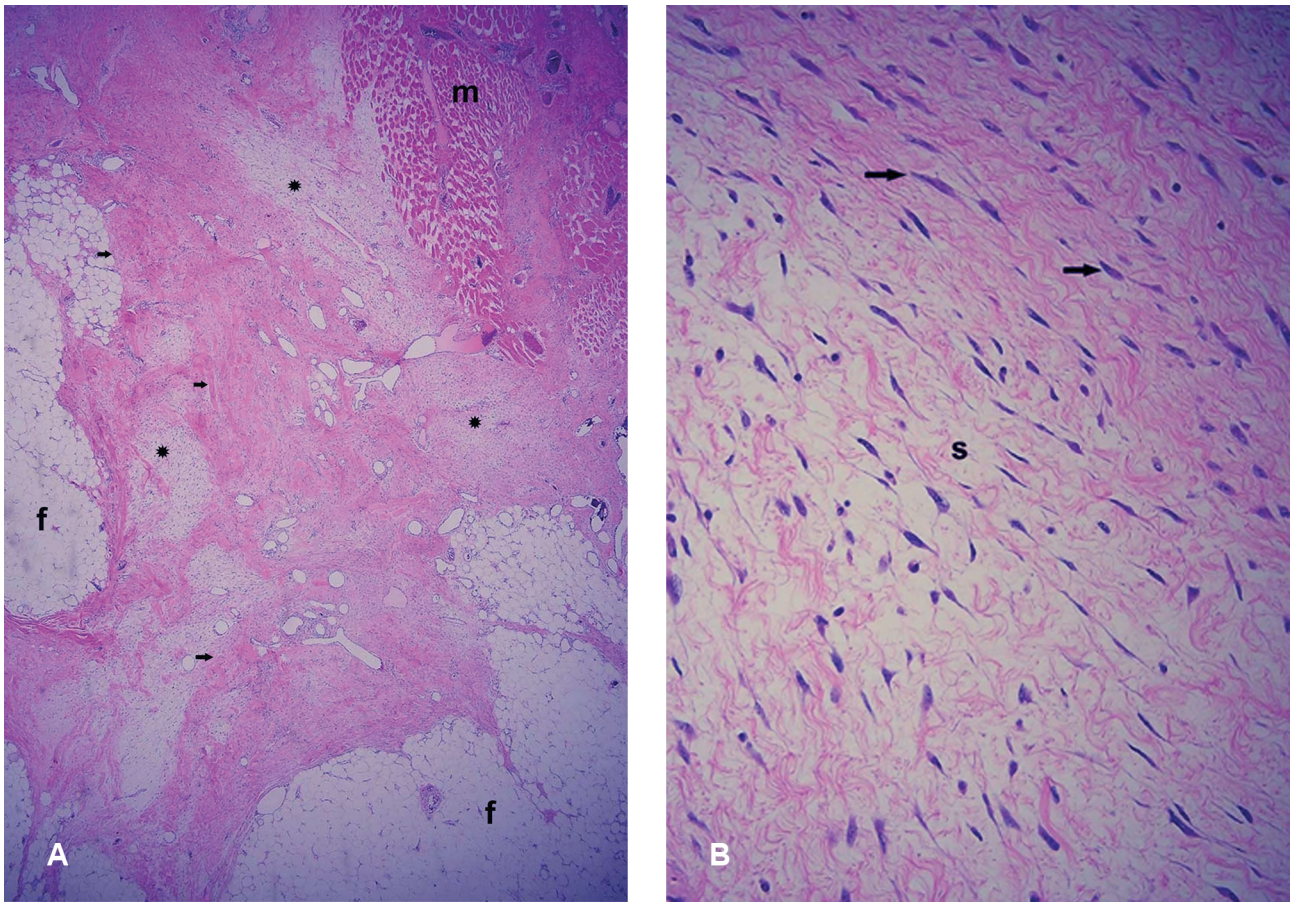

Figure 3. A. Photomicrograph shows tumor composed of abundant, pale myxoid material (asterisks) alternating with loose fibrous tissue (arrows). **f**: fat; **m**: muscle tissue; (original magnification, ×40; hematoxylin-eosin stain); **B**. Photomicrograph shows spindle cells (arrows) arranged in a fascicular growth pattern within loose fibrous and myxoid stroma (**s**). Mitoses are absent. (original magnification, ×200; hematoxylin-eosin stain).

Case 2

The second, much similar, and deceptively benign-appearing case involves a 67-year-old woman. The patient presented with a discrete mass in her left forearm that had been gradually enlarging for two years. There was no history of trauma. The medical problems of the patient included adult-onset diabetes mellitus and hypertension that were treated with appropriate medications. Laboratory findings excluded hyperuricemia that would possibly account for gouty tophus.

On physical examination, there was a large soft tissue mass at the midportion of the left forearm. The skin overlying the lesion was mildly swollen and erythematous. The patient had no pain over the obvious mass. Radiographs of the entire forearm were obtained. The soft tissue mass demonstrated no areas of asymmetric density, abnormal calcification, or change in the neighboring bones. Sonography depicted a below-elbow, unilocular lesion of mixed echogenicity in soft tissue measuring 9×4.2×4 cm. The patient was subsequently scheduled for an MR imaging study of the forearm. MR images showed a large, subcutaneous soft tissue mass of heterogeneous decreased signal intensity on T1- and increased signal intensity on T2-weighted images ***(Fig. 4)****. The mass had no effect on the adjacent bone.*

The lesion was aspirated, and white and chalky material was copiously retrieved. A needle core biopsy yielded spindle cells and abundant myxoid material.

Wide excision of the mass was then performed. Histopathology revealed both elongated and polygonal tumor cells embedded in a markedly myxoid stroma ***(Fig. 5)****. Diagnosis of myxoid malignant fibrous histiocytoma (myxofibrosarcoma) was instituted. No metastases or recurrences were documented in the 2-year follow-up period.*

DISCUSSION

Low-grade fibromyxoid sarcoma is a rare malignant mesenchymal tumor, a spindle cell sarcoma that usually arises in the deep soft tissues - i.e., the skeletal muscle of the trunk or thigh of young to middle-aged adults. Additional sites of involvement may include the chest wall/axilla, the shoulder, and the inguinal region.[1,2] Another subtype of fibrosarcoma, termed myxofibrosarcoma, is predominantly myxoid and usually arises in the subcutaneous tissue of the lower extremities in older patients.[1] Notably, patients with either type of sarcoma often have an initial presentation of a painless and slowly growing soft tissue mass that is already large at the time of diagnosis.[8] Both of our cases feature a typical presentation of this family of malignancies with regard to age, location, and depth of involvement in soft tissue. Our two patients presented with an asymptomatic soft tissue mass, and virtually no clinical suggestion of malignancy.

Because of a deceptively bland histologic appearance, the fibrosarcoma variants may initially be misdiagnosed as benign processes. Distinction between the two fibrosarcomas on histology is difficult, and is usually made in conjunction with the evaluation of specific tumor characteristics including cellular atypia and potential for metastasis.[1] In regard to the first criterion used for diagnosis, mitotic figures and nuclear pleomorphism are commonly absent or sparse

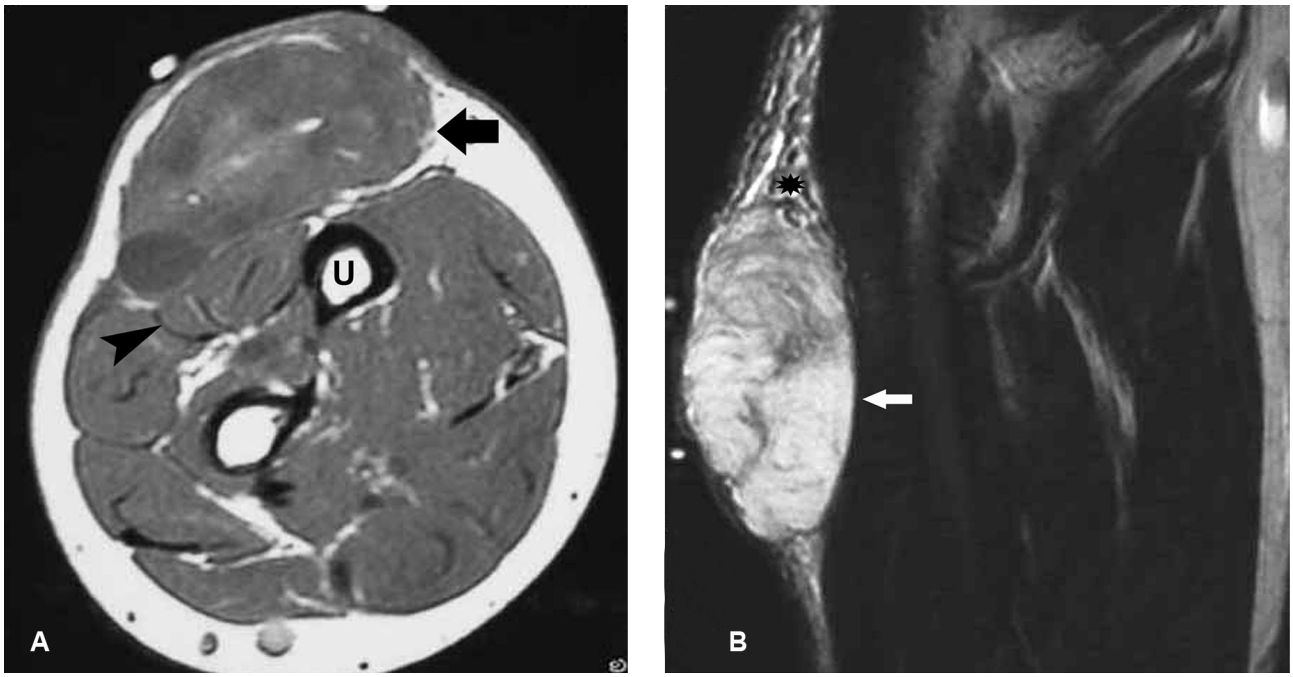

Figure 4. A. Axial T1-weighted image shows mass lesion (arrow) of abnormal, decreased signal intensity situated superficial to the extensor carpi ulnaris muscle (arrowhead). **U**: ulna; **B**. Corresponding sagittal T2-weighted image shows lesion (arrow) of increased signal intensity in the posterior forearm. Note the subcutaneous edema (asterisk).

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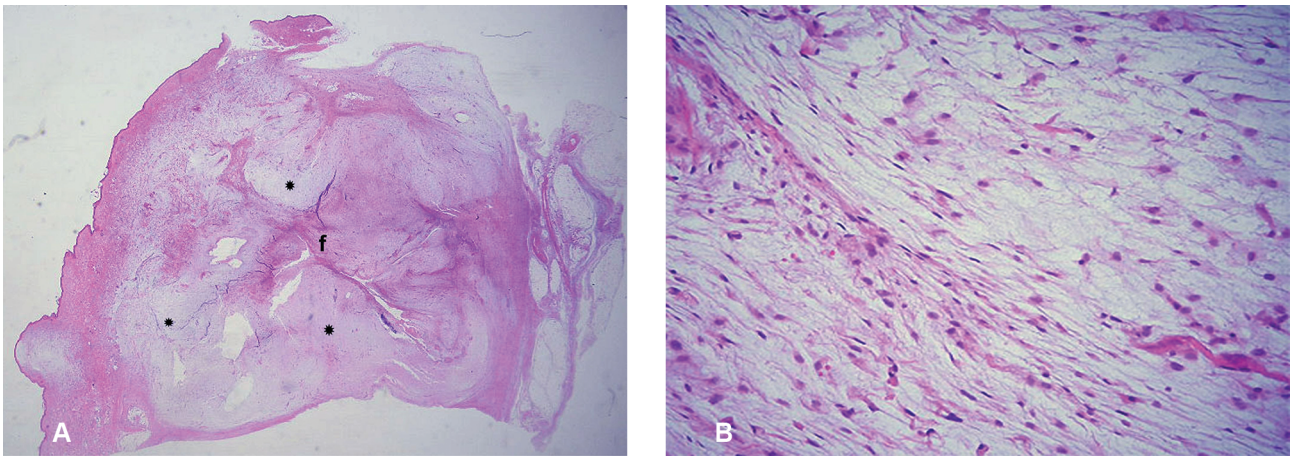

Figure 5. A. Photomicrograph shows tumor composed of predominant pale myxoid elements (asterisks) and a more central fibrous area (**f**), (original magnification, ×40; hematoxylin-eosin stain); **B**. Photomicrograph reveals spindle cells embedded in a markedly myxoid stroma (original magnification, ×200; hematoxylin-eosin stain).

in LGFMS, whereas cellular pleomorphism and nuclear atypia is prominent in myxofibrosarcoma.[9] Further, both (fibro)-myxoid sarcomas may demonstrate an infiltrating growth pattern, although this is more typical of myxofibrosarcoma.[1] Metastasis, the second confounding criterion used to differentiate these sarcomatous tumors, is usually to the lung. Indeed, metastasis tends to occur in up to 50% of the patients with LGFMS, which, in contrast, is relatively less in the myxofibrosarcoma variant, ranging from 20% to 25% of the cases.[1,7] The histologic grade, however, is directly correlated with the biological behavior in terms of tumor recurrences or metastases.[1] Unlike myxofibrosarcoma, LGFMS reportedly shows a definite propensity for late recurrence or metastasis.[1,2,6,10] Interestingly, in the presence of metastases survival may be prolonged.[6,11,12] The reason for this unique tumor biology is unknown at present. Finally, an additional diagnostic consideration of importance that proves useful in the differential diagnosis of the two fibrosarcoma variants appears to involve the *FUS* gene translocation that is merely confirmatory for LGFMS.[1,9,10,12] Both our patients showed histopathological findings corresponding to their respective individual fibrosarcoma subtypes.

Imaging plays a pivotal role in the identification and localization of a mass lesion residing in soft tissue. In the fibrosarcoma family of malignancies, the imaging characteristics reflect primarily the alternating fibrous and myxoid components of tumor.[8] Despite nonspecific imaging appearances of sarcomatous soft tissue tumors, the variability in histologic findings holds as a pervasive theme the presence of fibrous tissue and myxoid components. For example, the LGFMS is of a predominant myxoid nature. Histopathology of this fibroblastic neoplasm is that of a spindle cell sarcoma harboring an admixture of collagenous and myxoid zones that are arranged in a fascicular or storiform pattern.[1,2] Macroscopic signs of malignancy, such as necrosis, hemorrhage, nodularity, and infiltrative border are quite rare. In our patient with LGFMS, non-infiltrative cyst-like appearance of tumor on imaging was clearly misleading and could have been mistaken for other, benign fluid-containing lesions. To our knowledge, LGFMS manifesting with merely fluid-like echogenicity on US images has not been reported previously. Similar to the US findings, MR images showed signal intensity alterations consistent with the predominant myxoid component of tumor. On histology, the single intralesional nodule that enhanced avidly on MR images represented hypervascular myxoid material.[11,13]

In our patient with myxofibrosarcoma, the matrix was of a mixed fibrous, but predominantly myxoid consistency. Tumor cells were mildly pleomorphic and were seen arranged in a fascicular pattern, exhibiting some mitotic figures. US revealed an inhomogeneous lesion, which on histology was found to correspond to abundant myxoid material. On MR images, the myxoid component of the tumor exhibited decreased signal intensity on the T1- and increased signal on the T2-weighted images. Fibrous tissue within tumor exhibited low signal intensity on both the T1- and T2-weighted images.

Although the imaging findings of the lesions could not be used to determine the aggressive or nonaggressive behavior of each individual process, the exact histologic composition, or the potential for complications, there is no doubt that the imaging studies offered us a window through which to view the histologic nature of abnormal tissue.[13] The primary diagnostic considerations for soft tissue lesions with mixed fibrous and cyst-like elements are broad and besides LGFMS and low-grade myxofibrosarcoma include myxoliposarcoma, myxoid variant of dermatofibrosarcoma protuberans (DFSP), nodular fasciitis, desmoid fibromatosis, myxoid neurofibroma, and neurogenic tumors.[1,13] Myxoliposarcoma typically demonstrates a fatty component on imaging. Myxoid DFSP is a more cellular neoplasm infiltrating subcutaneous tissue in a lace-like fashion. Nodular fasciitis is situated in subcutaneous tissue and consists of bland myofibroblasts embedded in

a prominent myxoid matrix, and chronic inflammatory cells. Desmoid fibromatosis is a less cellular and more collagen-forming process. Mild enhancement of hyperintense areas on corresponding T2-weighted MR images, and the presence of entering and exiting nerve favor neurogenic tumors versus LGFMS.[13]

Because of a nonaggressive clinical course, soft tissue sarcomatous tumors can initially be misdiagnosed as lesions of a benign nature. Clinicians need to understand that a soft tissue mass exhibiting bland characteristics urges performance of diagnostic imaging and immediate biopsy to avoid misdiagnosis and to prevent delayed diagnosis and complications. The standard treatment for patients with localized disease is surgery with an intended wide margin. Patients with local recurrences are treated with repeat surgery and radiotherapy for local disease control. In those cases with metastatic fibrosarcomas, treatment includes multiagent palliative chemotherapy (doxorubicin, ifosfamide) for short-term stabilization of disease progression, and selective surgery of operable metastases.[14]

CONCLUSIONS

We report the constellation of imaging findings, histologic analyses, and clinical follow-up favoring the diagnosis of soft tissue sarcoma containing both fibrous and fluid-like elements in two patients with slow-growing mass lesions. Our LGFMS case presentation as a simple cyst on US has not been described before, and as such, we believe this observation should be considered in the differential diagnosis of soft tissue mass lesions. These cases illustrate the difficulty in evaluating soft tissue sarcomas that may assume non-aggressive clinical, imaging, and histologic characteristics.

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Competing Interests

The authors have declared that no competing interests exist.

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Фибросаркома с обманчивыми доброкачественными проявлениями: отчёт о двух случаях

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Резюме

Фибромиксоидная саркома низкой степени злокачественности и миксофибросаркома представляют собой злокачественные опухоли мягких тканей, фибросаркомы, имеющие общие клинические и визуализационные проявления. Мы сообщаем о саркоматозных поражениях мягких тканей с обманчиво доброкачественными клиническими и визуальными проявлениями и сопоставляем результаты с результатами гистологического анализа. У двух пациентов в анамнезе были длительные безболезненные припухлости на спине и верхних конечностях, и отрицались какие-либо конституциональные симптомы. Эхография и магнитно-резонансная томография позволили предположить наличие доброкачественных образований мягких тканей преимущественно жидкообразной консистенции. Несмотря на вялотекущие клинические и визуализационные характеристики, в обоих случаях гистопатология выявила диагноз саркомы мягких тканей типа веретенообразных клеток, обозначающий агрессивную опухоль. Знание кажущихся доброкачественными клинических и визуализационных особенностей фибросаркомы необходимо, чтобы повысить вероятность злокачественного новообразования в мягких тканях, которое может быть недодиагностировано или неправильно диагностировано. Совершенно очевидна важность правильного диагноза и последствия хирургической резекции, облучения и системной онкологической терапии.

Ключевые слова

фибромиксоидная саркома низкой степени злокачественности, миксофибросаркома, мягкие ткани, саркома, УЗИ, магнитно-резонансная томография