A Report of a Rare Case of Myxoinflammatory Fibroblastic Sarcoma

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Myxoinflammatory fibroblastic sarcoma of the soft tissues is a rare low-grade tumor of uncertain origin that most often occurs on the extremities of adults. The tumor predominantly involves the subcutaneous tissues of the hands and feet. Despite being a rare neoplasm, owing to its varied histologic appearance, myxoinflammatory fibroblastic sarcoma should be differentiated from various benign and malignant soft-tissue lesions. Myxoinflammatory fibroblastic sarcoma has been well described in pathology journals but not in the surgical literature. We report a case of myxoinflammatory fibroblastic sarcoma in a 19-year-old man with a plantar ulcer lesion in his left foot. To our knowledge, this is the first reported case in the literature involving the epidermis. (J Am Podiatr Med Assoc 100(6): 497-501, 2010)

Myxoinflammatory fibroblastic sarcoma of the soft tissues is a rare low-grade tumor of uncertain origin that most often occurs on the extremities of adults. In an analysis of 51 cases occurring between 1989 and 1996, Montgomery et al[1] originally described the lesion in 1998 with the term *inflammatory myxohyaline tumor of distal extremities with virocyte or Reed-Sternberg–like cells*. Simultaneously, Meis-Kindblom and Kindblom[2] proposed the term *acral myxoinflammatory fibroblastic sarcoma* for the same lesion. Moreover, in the same year, Michal[3] reported an *inflammatory myxoid tumor of the soft parts with bizarre giant cells*, which basically corresponds to the same entity. Because a percentage of the cases were not acral in location, some authors[4] recommended avoiding use of the adjective *acral* in the name of this entity. The term *acral* was dropped in the 2002 World Health Organization classification.[5]

Approximately half of all of the cases in the literature were reported separately in the first two articles describing this entity.[1, 2] Most lesions were located in the extremities, and only five cases (3.2%) have been described in more proximal regions.[6-9] Sixty-four percent of lesions were found in the upper extremities, most commonly in the fingers and hands (52%). Thirty-three percent of lesions were found in the lower extremities, most commonly in the toes and feet. Approximately 25% of the cases described in the literature were localized in the feet and ankles, especially in the dorsum and toes.[1, 2, 4, 6]

Histologically, the lesions are composed of a mixed acute and chronic inflammatory infiltrate associated with alternating hyaline and myxoid zones in variable proportions. The neoplastic cells are large polygonal and spindle, with a bizarrely shaped nucleus and prominent nucleoli.

To date, 193 cases of myxoinflammatory fibroblastic sarcoma have been identified but clinical follow-up information was available only in 183 cases. Clinically, this tumor is usually present with slow-growing, painless masses.[1, 2, 4, 6] Recurrences after surgical excision were not uncommon; 28 of 138 patients (20%) with follow-up had at least one recurrence. The usual treatment (local excision, wide re-excision, and amputation) was performed in 53 patients (29%).

The clinical presentation of myxoinflammatory fibroblastic sarcoma can be similar to several benign processes. An inflammatory infiltrate may obscure the neoplastic nature of the lesions and is commonly associated with fibrosis and focal hemosiderin deposition. The dominating inflammatory infiltrate may conceal the sarcomatous component, which frequently leads to the erroneous diagnosis of

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a benign reactive process and raises the possibility of an infectious etiology. However, to date, there has been no evidence of an infectious etiology.[1, 2, 10] Some authors[2] believe that the intimate relationship with the synovium, the frequent association with tenosynovitis, and the prominent inflammatory infiltrate suggest that inflammation may play a role in the pathogenesis of myxoinflammatory fibroblastic sarcoma.

The histologic differential diagnosis is broad and varied, depending on whether the inflammatory, myxoid, or bizarre atypical component predominates in the lesion. Conditions such as tenosynovitis, ganglion cyst, pigmented villonodular synovitis, giant cell tumor of the tendon sheath, and myxoid malignant fibrous histiocytoma (myxofibrosarcoma) are the main elements of the histopathologic differential diagnosis.[10-12]

Radiologic features of myxoinflammatory fibroblastic sarcoma may be present, with various magnetic resonance imaging patterns that probably reflect their variable histologic composition. Differential diagnosis with other benign conditions, especially with ganglion cyst and giant cell tumor of the tendon sheath, may be difficult.[7, 13]

Several authors[14-17] have performed cytogenetic analysis on patients with myxoinflammatory fibroblastic sarcoma that had clonal chromosomal changes. These findings support classifying myxoinflammatory fibroblastic sarcoma as a separate neoplastic entity, and they potentially could be used to help diagnostically distinguish it from other conditions. Given the variations in the cytogenetic results hitherto reported in cases of myxoinflammatory fibroblastic sarcoma, further research is required to confirm the findings that best characterize this tumor.[14-17]

The myxoinflammatory fibroblastic sarcoma cases reported in the literature have been described as poorly circumscribed and multinodular, with the tumor often invading the adjacent synovial lining, tendon sheaths, subcutaneous fat, dermis, surrounding sweat glands, and skeletal muscle.[1-3] To our knowledge, only one case of myxoinflammatory fibroblastic sarcoma involving the bone has been reported in the literature,[11] but no lesions with invasion of the epidermis have been reported. Most reported cases involved the dermis, and some closely approached the epidermis.[6, 18]

Case Report

A 19-year-old man was referred by his podiatric physician (private surgery) to the Podiatry Clinic of Seville University with a 6-month-old 0.8-cm growth on the plantar side of his left forefoot. The lesion was not increasing in size but was constantly painful when wearing shoes, and an abnormal sensation was noted when walking. The lesion was treated topically as a plantar wart with local recurrence. No medical problems were reported. On physical examination, a firm ulcerated lesion was located in the plantar aspects of the internal longitudinal arch of the left foot. The lesion was fixed to the skin and showed ulceration. A clear, viscous, jelly-like substance was obtained on pressure (Fig. 1). Surgical excisional biopsy was performed under local anesthesia 1 month after the initial visit.

Grossly, an ill-defined white lesion measuring 0.9 $\times$ 0.5 cm was seen in cutaneous tissue with epidermal ulceration that invaded subjacent subcutaneous tissue. The lesion was characterized by multinodular growth infiltrating fascia, dermis, and subcutaneous fat.

Microscopic examination revealed a tumor in the subcutaneous tissues, infiltrating the dermis and ulcerating epidermis and showing a variable admixture of myxoid matrix and fibrous areas (Fig. 2). Histologic analysis of the specimen showed that the excision was marginal in some zones and intralesional in others. The specimen showed diffusely infiltrated inflammatory cells, most of which were neutrophils and lymphocytes. Large ovoid and spindle epithelioid cells with prominent nucleus and eosinophilic nucleoli were scattered (Fig. 3).

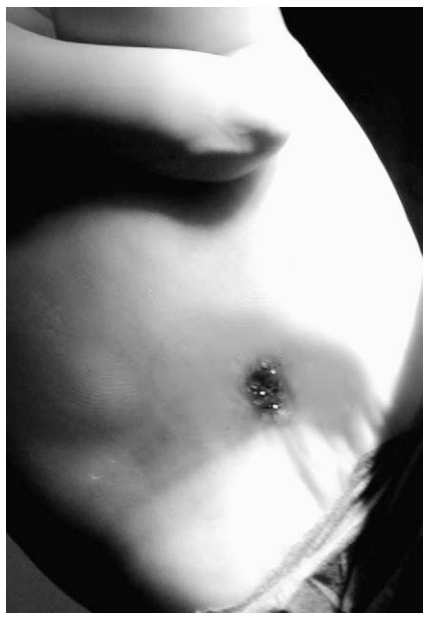

Figure 1. The ulceration of the skin.

Figure 2. Histologic panoramic view showing the neoplasm infiltrating the dermis and ulcerating epidermis (H&E, ×10).

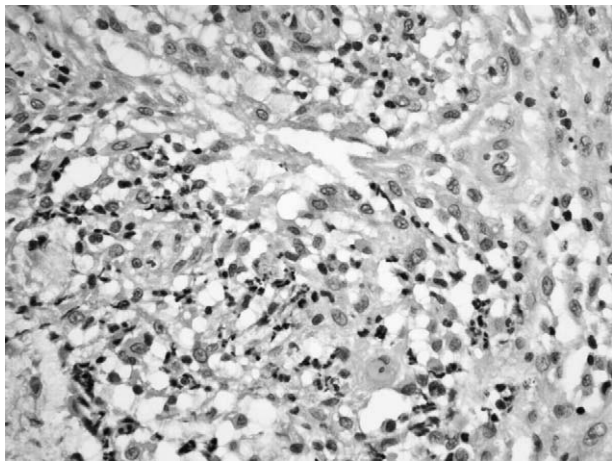

Figure 3. Histopathologic specimen showing large epithelioid cells with eosinophilic nucleoli. High inflammatory cellularity is seen (H&E, ×100).

Immunohistochemical study revealed tumoral cells focally positive to immunohistochemical stains for vimentin, CD68, and CD34. Immunoreaction for S-100, Melan-A, HMB-45 CK, and cytokeratin was negative.

The diagnosis of myxoinflammatory fibroblastic sarcoma was confirmed. After surgery, the patient was referred to the oncology service of the reference hospital for monitoring. Physical examination for the presence of local or regional metastatic disease and a chest radiograph to evaluate for distant metastatic disease were performed.

Based on the high recurrence rate reported in the literature,[2, 19] the patient was advised to undergo wide excision. A wide excision was performed with adequate tumor-free margins 2 months after the primary excision. No adjuvant therapy was given, and the patient had no evidence of disease (no local recurrence or metastasis) 15 months after the primary excision.

Discussion

Myxoinflammatory fibroblastic sarcoma is a malignant tumor with a high rate of local recurrence and a low rate of metastasis that predominantly involves the subcutaneous tissues of the hands and feet. It is claimed that the potential for local recurrence of myxoinflammatory fibroblastic sarcoma far surpasses the risk of metastasis. In the literature review, only nine cases of metastases have been registered (6.5%).[2, 10-12] The relatively high rate of recurrence reports (20%–67%) is probably a consequence of inadequate clearance at primary surgery as a result of a wrong assumption of a benign soft-tissue tumor and concomitant ignorance of the character of this newly discovered abnormality. In the present case, microscopic examination revealed inadequate clearance of the primary surgery, and the patient was advised to undergo a wide excision with adequate tumor-free margins.

Based on the protracted clinical course, Meis-Kindblom and Kindblom[2] established a high rate of local recurrence (sometimes needing amputation) and a low rate of metastasis; they believed that these tumors were low-grade sarcomas. Despite some authors having suggested that these neoplasms have a high capacity for local recurrence and locally aggressive behavior, their findings support the contention that these are not all low-grade neoplasms.[10]

In limited immunohistochemical studies performed on the previously reported cases, vimentin was strongly and diffusely positive in all of the lesions in which it was performed. CD68 was commonly performed and was positively reported in 69% of the cases. Tumors showed fairly variable positivity for CD34 in previous reports, and lesions were inconsistently positive for epithelial membrane antigen. Sporadic positivity for S-100 protein and smooth muscle actin was present in some cases. Melan-A was negative in all cases.[2, 6, 10, 11, 17, 19] In the present case, of the same

form, the lesion was focally positive to immunohistochemical stains for vimentin, CD68, and CD34 and negative to immunoreaction for S-100, Melan-A, HMB-45 CK, smooth muscle actin, and cytokeratin (Table 1).

Although most lesions reported in the literature were frequently present as a painless mass usually in the subcutaneous tissues, they can be painful in feet when wearing shoes, and an abnormal sensation can be noted during gait. Most lesions reported in the literature were subcutaneous, and they frequently infiltrated the synovium and the dermis, and some closely approached the epidermis. To our knowledge, this rare case is the first reported of myxoinflammatory fibroblastic sarcoma involving the epidermis. On the other hand, in the reviewed literature, most cases described in feet were localized in the dorsum and toes; in the present case, the lesion was localized in the plantar side of the forefoot. This circumstance originated because at first the lesion was confused with a recurrent plantar wart by his podiatric physician.

The presence in many of the reported cases of abundant myxoid material extracted by fine needle aspiration biopsy or obtained during surgical procedure and the frequent presence in some cases of ganglion-like cells has sometimes originated misdiagnoses. Some patients with myxoinflammatory fibroblastic sarcoma were diagnosed as having a ganglion cyst.[9, 14, 18, 20] In the present case, a clear, viscous, jelly-like substance was obtained on pressure, and the patient was believed to have a benign condition, such as an ulcerated ganglion cyst, at the time of initial evaluation.

Table 1. MIFS Immunohistochemical Staining Results

	Literature (No. of Cases/ Total No. [%])	The Present Case
Vimentin	67/67 (100)	Positive
EGFR	14/16 (87.5)	NA
CD68	44/64 (68.8)	Positive
CD34 (endothelial)	35/66 (53.0)	Positive
EMA	13/64 (20.3)	NA
S-100 protein (melanoma)	3/63 (4.8)	Negative
SMA (sarcoma markers)	3/45 (6.7)	Negative
Melan-A (melanoma)	0/11	Negative
HMB-45 CK	0/38	Negative
Cytokeratin (epithelial)	0/30	Negative

Abbreviations: EGFR, epidermic growth factor receptor; EMA, epithelial membrane antigen; MIFS, myxoinflammatory fibroblastic sarcoma; NA, not available; SMA, smooth muscle actin.

In the same way, we think that although myxoinflammatory fibroblastic sarcoma commonly involves the dermis and subcutis, its clinical presentation in the foot can be similar also to several epidermal benign tumors (epidermoid inclusion cysts), infectious benign processes (plantar warts), and mechanical injuries (foreign bodies and puncture wounds).

To date, no standard treatment protocol has been worked out. Local excision, wider local excision, and amputation have all been used primarily. The use of chemotherapy in two cases and radiotherapy in five cases after local recurrence has also been reported, but without providing details of the chemotherapeutic agents or radiation dosages.[2, 21] Postoperative radiotherapy may be best reserved for patients who are likely to undergo wide local excision with adequate tumor-free margins.

Conclusions

Myxoinflammatory fibroblastic sarcoma is a rare neoplasm that predominantly affects the distal extremities. Its clinical presentation can be similar to several benign processes. The lesion is generally asymptomatic and often invades the subcutaneous fat, dermis, and skeletal muscle but rarely involves the bone or epidermis. A rare clinical case of myxoinflammatory fibroblastic sarcoma that involved the epidermis has been presented. The lesion, localized in the plantar side of the forefoot, was constantly painful and was diagnosed as a plantar wart with local recurrence by his podiatric physician. This case should alert clinicians to the presence of plantar lesions that can be misdiagnosed as benign epidermal or infectious processes. Foot surgeons should be familiar with the clinical, radiographic, and histologic appearances of this tumor because it has a high rate of local recurrence (sometimes leading to amputations) and can metastasize.

It is important for podiatric physicians to include myxoinflammatory fibroblastic sarcoma in their differential diagnosis to appropriately treat the lesion and reduce the chance of metastasis. Complete excision with clear margins is recommended for these neoplasms. Postoperative tumor surveillance should include physical examination for the presence of local or regional metastatic disease and a chest radiograph to evaluate for distant metastatic disease.

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References

1. Montgomery E, Devaney KO, Giordano TJ, et al: Inflammatory myxohyaline tumor of distal extremities with virocyte or Reed-Sternberg–like cells: a distinctive lesion with features simulating inflammatory conditions, Hodgkin's disease, and various sarcomas. Mod Pathol **11:** 384, 1998.
2. Meis-Kindblom JM, Kindblom LG: Acral myxoinflammatory fibroblastic sarcoma: a low-grade tumor of the hands and feet. Am J Surg Pathol **22:** 911, 1998.
3. Michal M: Inflammatory myxoid tumor of the soft parts with bizarre giant cells. Pathol Res Pract **194:** 529, 1998.
4. Jurcić V, Zidar A, Montiel MD, et al: Myxoinflammatory fibroblastic sarcoma: a tumor not restricted to acral sites. Ann Diagn Pathol **6:** 272, 2002.
5. Meis-Kindblom JM, Kindblom LG: "Myxoinflammatory Fibroblastic Sarcoma," in *Tumors of the Soft Tissue and Bone: WHO Classification of Tumors*, *Pathology and Genetics Classification of Tumors*, *Pathology and Genetics*, 1st Ed, ed by CMD Fletcher, KK Unni, F Mertens, p 96, IARC Press, Lyon, France, 2002.
6. Kovarik CL, Barrett T, Auerbach A, et al: Acral myxoinflammatory fibroblastic sarcoma: case series and immunohistochemical analysis. J Cutan Pathol **35:** 192, 2008.
7. Narváez JA, Martinez S, Dodd LG, et al: Acral myxoinflammatory fibroblastic sarcomas: MRI findings in four cases. Am J Roentgenol **188:** 1302, 2007.
8. McFarlane R, Meyers AD, Golitz L: Myxoinflammatory fibroblastic sarcoma of the neck. J Cutan Pathol **32:** 375, 2005.
9. Premalata CS, Rao CR, Padma M, et al: Myxoinflammatory fibroblastic sarcoma: report of a rare case at an unusual site with review of the literature. Int J Dermatol **47:** 68, 2008.
10. Hassanein AM, Atkinson SP, Al-Quran SZ, et al: Acral myxoinflammatory fibroblastic sarcomas: are they all low-grade neoplasms? J Cutan Pathol **35:** 186, 2008.
11. Sakaki M, Hirokawa M, Wakatsuki S, et al: Acral myxoinflammatory fibroblastic sarcoma: a report of five cases and review of the literature. Virchows Arch **442:** 25, 2003.
12. Pohar-Marinsek Z, Flezar M, Lamovec J: Acral myxoinflammatory fibroblastic sarcoma in FNAB samples: can we distinguish it from other myxoid lesions? Cytopathology **14:** 73, 2003.
13. Tateishi U, Hasegawa T, Onaya H, et al: MR appearance and pathologic correlation. AJR Am J Roentgenol **184:** 1749, 2005.
14. Gonzalez-Cámpora R, Ríos-Martín JJ, Solórzano-Amoretti A, et al: Fine needle aspiration cytology of an acral myxoinflammatory fibroblastic sarcoma: case report with cytological and cytogenetic findings. Cytopathology **19:** 118, 2008.
15. Ida CM, Rolig KA, Hulshizer RL, et al: Myxoinflammatory fibroblastic sarcoma showing t(2;6)(q31;p21.3) as a sole cytogenetic abnormality. Cancer Genet Cytogenet **177:** 139, 2007.
16. Lambert I, Debiec-Rychter M, Guelinckx P, et al: Acral myxoinflammatory fibroblastic sarcoma with unique clonal chromosomal changes. Virchows Arch **438:** 509, 2001.
17. Mansoor A, Fidda N, Himoe E, et al: Myxoinflammatory fibroblastic sarcoma with complex supernumerary ring chromosomes composed of chromosome 3 segments. Cancer Genet Cytogenet **152:** 161, 2004.
18. Lang JE, Dodd L, Martinez S, et al: Acral myxoinflammatory fibroblastic sarcoma. Clin Orthop Relat Res **445:** 254, 2006.
19. Baumhoer D, Glatz K, Schulten HJ, et al: Myxoinflammatory fibroblastic sarcoma: investigations by comparative genomic hybridization of two cases and review of the literature. Virchows Arch **451:** 923, 2007.
20. Alkuwari E, Gravel DH: A 30-year-old man with a soft tissue mass on the right elbow: inflammatory myxohyaline tumor of the distal extremities with prominent eosinophilic infiltrate. Arch Pathol Lab Med **130:** 35, 2006.
21. Ebhardt H, Kosmehl H, Katenkamp D: Acral myxoinflammatory fibroblastic sarcoma: six cases of a tumor entity [in German]. Pathologe **22:** 157, 2001.