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Case Research

Giant myxoinflammatory fibroblastic sarcoma with bone invasion: a very rare clinical entity and literature review

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Abstract

Myxoinflammatory fibroblastic sarcoma (MIFS) is a rare low-grade, malignant soft tissue tumor that is usually observed in the extremities of adult patients. Magnetic resonance imaging findings for this tumor type have rarely been reported. We report a case involving the distal left femur of a middle-aged man and tumoral invasion of the bone, which, to our knowledge, has been previously described only once. He was treated with distal femoral tumor resection and reconstruction with a modular prosthesis. Histopathologic diagnosis confirmed MIFS. We reviewed literature of the diagnostic imaging and bone invasion findings associated with this tumor type.

Key words Myxoinflammatory fibroblastic sarcoma, bone invasion, magnetic resonance imaging

Myxoinflammatory fibroblastic sarcoma (MIFS), first described in 1998[1,2], is a unique low-grade tumor that characteristically occurs in the distal extremities, but it has also been reported in the legs and arms[2]. The World Health Organization (WHO) describes MIFS as a "unique, low-grade, sarcoma with myxoid stroma, inflammatory infiltrate, and virocyte-like cells that predominately involves the hands and feet"[3]. The WHO classification system for cancer represents the common nomenclature for cancer worldwide. The synonym "atypical myxoinflammatory fibroblastic tumor" for lesions known as MIFS was introduced in the last WHO classification of tumors of the soft tissue and bone, published in 2013[4]. MIFS is grouped as an intermediate (rarely metastasizing) fibroblastic/myofibroblastic soft tissue tumor.

The mass often grows slowly but can infiltrate into the surrounding soft tissues [5]. The tumoral bone invasion represented in the current case report is very rare. Clinically, the invading tumor manifests as a slow-growing, painless mass that is characterized by a high rate of local recurrence and a low rate of metastasis. Cases have been reported over a wide age range; however, this rare tumor typically presents during the fourth to sixth decades of life, without a gender predilection[5,6]. Histologically, the lesions are composed of a myxoid matrix containing numerous inflammatory cell types, fibrosis, and scattered large tumor cells. The clinical and radiologic differential diagnosis includes the more commonly encountered ganglion cyst, tenosynovitis, and giant-cell tumor of the tendon sheath[7]. The magnetic resonance imaging (MRI) criteria include lesion location, size, borders, and signal intensity on T1-weighted, T2-weighted, fat-suppressed T2-weighted, and contrast-enhanced T1-weighted images. Diagnostic delays, misdiagnosis, and inadequate surgical excision remain problematic. We present the MRI findings associated with an unusually located and late-diagnosed case of MIFS.

Case Report

A 34-year-old man presented with a 6-month history of pain and swelling in his left knee. His medical history included prior presentation with a similar complaint for 5 years, involving left knee pain and difficulty walking. A mass had been detected in the center of his left distal femur, with a soft tissue component. The mass had increased in size and had become painful. There was no history of trauma.

Physical examination revealed a fixed, hard, painless, and palpable mass measuring 7–8 cm in diameter and locating on the patient's left distal femur. The patient had no neurovascular problems and no palpable lymphadenopathy. Standard laboratory test results were within normal limits. A roentgenographic study showed destruction of the distal femur and a corresponding dense soft tissue mass (**Figure 1**). An MRI examination revealed a mass with focal cortical bone destruction in the distal metadiaphyseal region of the femur. On MRI, this lesion was mainly located in the subcutaneous tissue but extended through the fascia and into the muscle and bone. Osseous involvement was detected on radiographs as subtle bone erosion of the distal femur anterior cortex. The associated soft tissue was isointense to muscle on the T1-weighted image and was intermediately hyperintense to muscle on the T2-weighted image and

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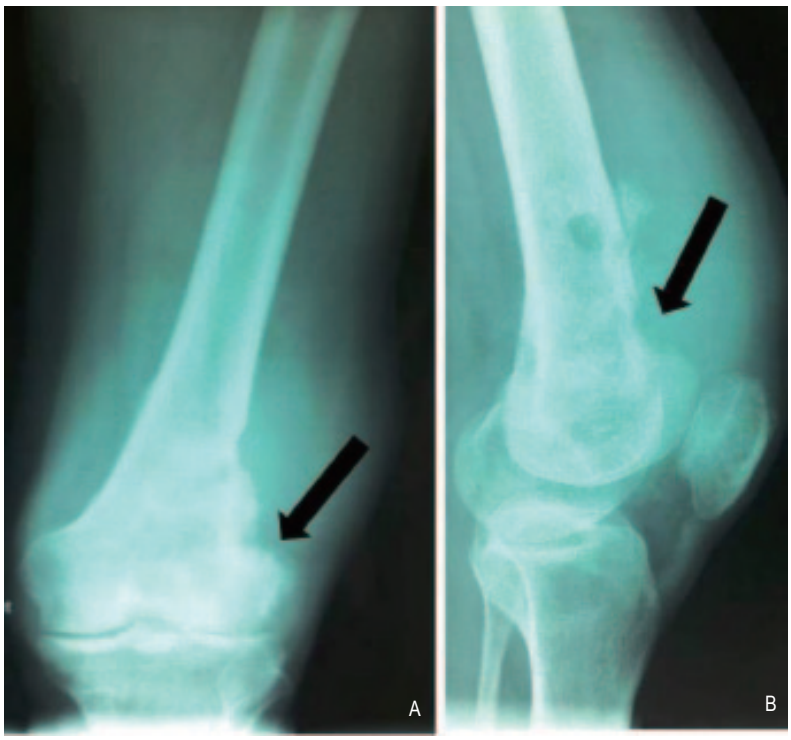

Figure 1. **Anteroposterior (A) and lateral (B) radiographs of the femur show a soft tissue mass, with bone destruction, on the surface of the distal femur.**

showed intense enhancement after contrast medium administration (**Figure 2**). No evidence of regional or distant metastasis was found in the patient. Biopsies of the neoplastic lesion contained elevated numbers of inflammatory cells.

In February 2011, the patient underwent distal femoral tumor resection and reconstruction with a modular prosthesis. During surgery, the tumor appeared encapsulated and consisted of multiple poorly circumscribed nodules, and the cortex appeared excavated from the outside. The excised lesion was 16 cm × 12 cm × 8.5 cm in size, with a capsule-like structure, and demonstrated a beige cut surface. The tumor had infiltrated the bone tissue as well as the soft tissue.

Histopathologically, the lesion demonstrated numerous polymorphonuclear leukocytes, each with a large vesicular nucleus. The tumor tissue was composed of atypical cells with boundaries that could not be clearly defined (**Figure 3**). Immunohistochemical examination of tumor cells revealed that they were negative for myoglobin, desmin, CD30, smooth muscle actin (SMA), epithelial membrane antigen, and HHF-35 (anti-muscle actin antibody) but positive for CD68-phosphoglucomutase 1 (PGM1). The patient was readmitted in his third year of clinical follow-up, with no evidence of disease.

Discussion

MIFS is a recently described low-grade sarcoma. The tumor usually appears as a slowly-growing, multinodular, poorly circumscribed, and painless mass located in the upper extremities. In all reported cases, the tumors were located in the distal extremities, and lesions were found in the upper extremities, most commonly in the fingers or hands. The foot, ankle, wrist, and knee were less common anatomic locations[1]. Many tumors were diagnosed as inflammatory or benign lesions on biopsies due to their histological appearances. Most lesions were subcutaneous, and they frequently infiltrated the synovium and the dermis, whereas bone invasion was very rare. In 2007, Narvaez *et al*.[8] reported a unique case of acral MIFS eroding the bone. We report a case involving the distal left femur of a middle-aged man and tumoral invasion of the bone, which, to our knowledge, has been previously described only once. We provide an updated review of the literature about MIFS in **Table 1**. The anatomic location of distal extremity soft tissue masses is important in the differential diagnosis of a patient's disease. The hands and fingers are the most frequent sites for the development of MIFS, ganglion cysts, epidermoid cysts, and giant-cell tumors of the tendon sheath. The malignant soft tissue tumors of the leg that are most commonly observed in middle-aged patients include synovial sarcoma, liposarcoma, malignant schwannoma, malignant fibrous histiocytoma, and fibrosarcoma. The sensitivity of MRI in identifying soft tissue tumors is high, but its specificity is low; MRI is also able to differentiate between fatty and fibrous tissues in tumors[8,9]. Ertener *et al*. [10] stated that the MRI features were different from the previously described findings of a presented case report, and a hyperintense lesion with a homogenous internal structure and regular and inflammatory cell contents was observed in this case.

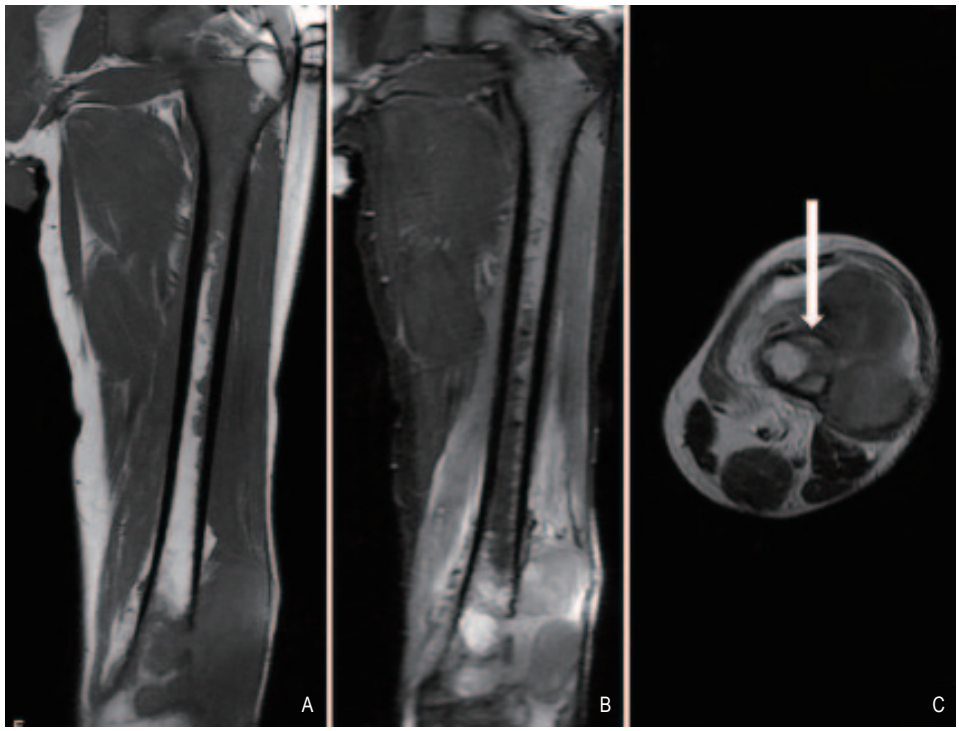

Figure 2. **Preoperative magnetic resonance images of the patient. A, coronal T1-weighted image shows a mass isointense to the muscle. B, coronal short T1 inversion recovery sequence shows an intermediate signal-intensity tumor with surrounding edema. C, axial T1-weighted image after contrast administration shows intense enhancement.**

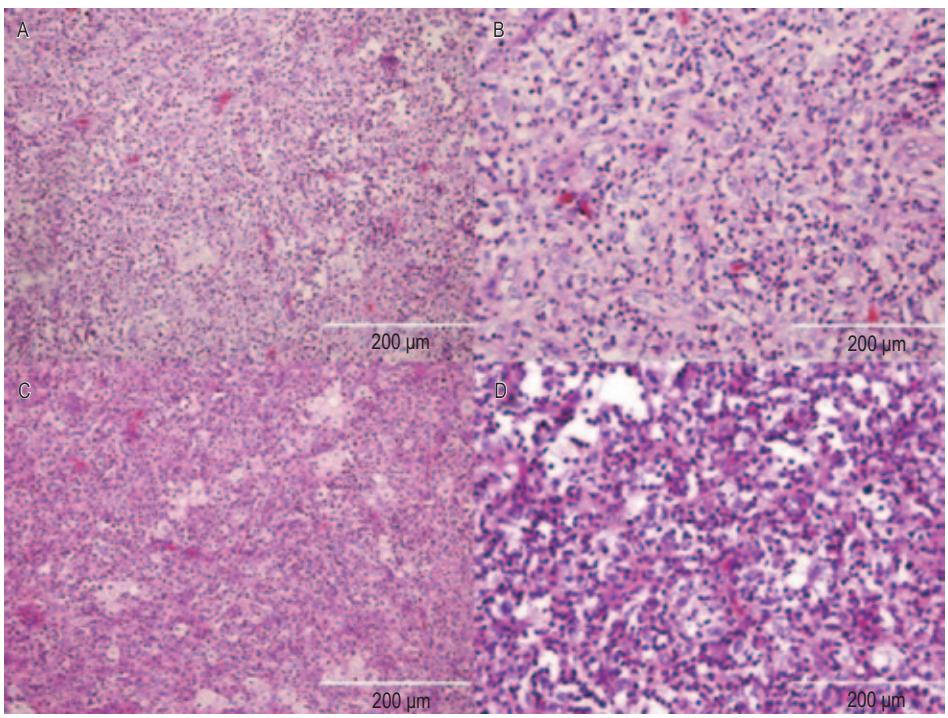

Figure 3. **Histological examination of an acral myxoinflammatory fibroblastic sarcoma with hematoxylin and eosin staining. A, high-power photomicrograph of the tumor specimen shows a large number of inflammatory cells with large, atypical nuclei. B, the tumor specimen shows a large number of inflammatory neoplastic cells with an irregular shape and large, atypical nuclei. C, the tumor shows an admixture of neoplastic and inflammatory cells, with certain large and histiocytic cells. D, the tumor specimen shows a large number of inflammatory cells with large, atypical nuclei.**

Therefore, the MRI signal features of MIFS are nonspecific. On MRI images, MIFS is typically observed as a poorly circumscribed mass with a multinodular appearance; extensive involvement adjacent to the tendon sheath is also a common feature. The MRI findings

Table 1. Literature review about myxoinflammatory fibroblastic sarcoma

Reference	No. of patients	Age range	Distal lesion	Treatment	Size (cm)	Recurrence	Metastases	Follow-up (months)
Meis-Kinblom *et al.*, 1998[1]	44	20–91	44/44	37 excision, 10 amputation, 5 RT, 2 CT	1–6	24/36	2/36	6–540
Montgomery *et al.*, 1998[2]	51	4–81	51/51	NA	NA	6/27	0/27	NA
Ebhardt *et al.*, 2001[13]	6	22–60	6/6	Excision	1–4	2/6	0/6	NA
Fetsch *et al.*, 2001[7]	37	14–72	37/37	33 excision, 4 amputation	0.6–5.0	3/18	0/18	11–319
Lambert *et al.*, 2001[14]	1	53	1/1	Excision	7.4	NA	NA	NA
Jurcic *et al.*, 2002[15]	9	22–87	6/9	Excision, 6 amputation	1.5–1.8	1/9	0/9	1–60
Sakaki *et al.*, 2003[16]	5	15–75	5/5	Excision	2.7	2/4	1/4	8–58
Kusumi *et al.*, 2005[17]	1	58	1/1	Excision	4.9	0/1	0/1	12
Lang *et al.*, 2006[18]	5	22–66	4/5	Excision	NA	0/5	0/5	14–22
Narvaez *et al.*, 2007[8]	4	22–66	3/4	Excision	NA	0/4	0/4	NA
Yasuda *et al.*, 2007[19]	1	68	1/1	Excision	NA	0/1	0/1	48
Hassanein *et al.*, 2008[20]	5	39–65	5/5	3 excision, 1 amputation, 1 loss to follow-up	1.4.0	2/4	1/4	0.5–95
Kovarik *et al.*, 2008[12]	18	21–66	10/18	Excision	1.0–10.0	0/13	0/13	1–23
Chahdi *et al.*, 2010[21]	1	51	1/1	Excision	3	0/1	0/1	10
Fukasawa *et al.*, 2012[22]	1	48	1/1	Excision	2	0/1	0/1	24
Wickham *et al.*, 2012[23]	1	40	1/1	Excision	3.5	0/1	0/1	NA
Ertener *et al.*, 2013[10]	1	53	1/1	Excision	2	0/1	0/1	7
Silver *et al.*, 2013[24]	1	33	1/1	Excision	2	1/1	0/1	60
Toll *et al.*, 2013[25]	3	40–70	3/3	2 excision, 1 amputation	NA	1/3	0/3	24–84
Raghavan *et al.*, 2012[26]	1	50	1/1	Excision	6	0/1	0/1	24

NA, not available; RT, radiotherapy; CT, chemotherapy. No patients had bone invasion except for one in Narvaez *et al.* study[8]. The data of recurrence and metastases are presented as the number of patients with recurrence or metastases / the number of patients with follow-up information.

of MIFS are also similar to those observed for giant-cell tumors of the tendon sheath, proliferative fasciitis, acral fibromyxoma, myxoid liposarcoma, and myxofibrosarcoma[9,11]. In our case, however, there was no involvement of the tumor around the tendon sheath, but bone invasion was present.

In MIFS, initial misdiagnosis and incomplete, marginal, or intralesional excision contribute to high rates of local, multiple, and aggressive recurrence. Local recurrence or metastasis may also occur years after the initial surgical excision. However, wide-margin excision during the surgical treatment of MIFS is usually sufficient to prevent recurrence. Radiation is commonly administered preoperatively, intraoperatively, or postoperatively [6]. Fortunately, the incidence of metastasis is low for this sarcoma, despite the local invasiveness of the tumor. A metastatic rate of 6% (2 of 36 patients) was reported in one study, with one case metastasizing to the inguinal lymph nodes and the other to the lungs. The metastases were detected 1.5 and 5 years, respectively, after the primary surgery[1]. Postoperative follow-up at 4–6 month intervals, with evaluation of the primary site and systemic imaging, has been recommended to ensure the absence of metastasis and recurrence[12].

In conclusion, MIFS behaves similarly to a low-grade sarcoma and is very rarely observed. We report tumoral invasion of the bone in a second case. We recommend complete excision and prolonged follow-up for local recurrence and metastasis. Definitive diagnosis of MIFS needs to be made by histopathologic examination because the associated MRI findings are nonspecific.

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