

Myxoinflammatory Fibroblastic Sarcoma: New Case Report of a Rare Entity

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Abstract

Myxoinflammatory fibroblastic sarcoma (MIFS) is a malignant mesenchymal tumor most commonly occurring in the distal extremities of adults, it generally behaves like a low-grade tumor but is still able to progress locally and metastasize to distant sites, rarely resulting in death. It is a tumor whose unusual morphology can lead to misdiagnosis, either in the non-neoplastic sense (infectious or inflammatory) or as another sometimes malignant tumor entity. The genetic abnormalities detected in MIFS are the t(1;10)(p22;q24) translocation, with rearrangements of TGFBR3 and MGEA5 genes associated with increased levels of FGF8, with chromosome 3 marker/ring formation, and amplification of the VGLL3 locus.

Keywords: Sarcoma; fibroblastic; low; Histology; Génétics.

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INTRODUCTION

Myxoinflammatory fibroblastic sarcoma (MIFS) is a rare malignant soft tissue tumor first described in 1997 by Montgomery [1] with more descriptions the following year by Montgomery et al., [2] (51 cases), Meis -Kindblom and Kindblom [3] (44 cases) and Michal [4] (5 cases). The first designation given by Montgomery et al., was “inflammatory myxohyalin tumor of the distal extremities with Reed Sternberg-like cells” [2], by Michal as “inflammatory myxoid tumor of the soft parts with bizarre giant cells” [4], and by Meis-Kindblom and Kindblom as “Acral myxoinflammatory fibroblastic sarcoma” [3].

MIFS remains a low-grade soft tissue tumour of the distal extremities with a strong tendency to local recurrence. As other studies have shown, this tumour cannot be limited to the acraal sites, and apart from local recurrence, 6 cases with metastatic disease have been reported in the literature to date [3].

It is an entity that can occur in patients of any age, 4 to 91 years of age, and which generally presents itself as a painless mass of the distal part of a limb and often taken for a synovial cyst, tenosynovitis or a giant cell tumour of the sheaths and tendons [3].

CASE PRESENTATION

Our case concerns a 55-year-old diabetic patient on OAD, who was admitted for painless swelling of the big toe of the right foot, evolving for 6 months. The clinical examination finds a subcutaneous mass, measuring 6 cm of main axis, fixed in relation to the deep plane with radiology in favour of a benign process. A surgical biopsy was done by the treating physician and sent to our structure. Three fragments of hard consistency were received, measuring between 1.5 and 3 cm of wide axis, of a greyish-white appearance; included in full. Histological examination showed a multinodular lesion composed of myxoid and fibrous/hyalinized heterogeneous zones with a very rich inflammatory infiltrate background (Figure 1). The growth pattern was confined to subcutaneous tissue with polymorphic inflammatory cells with neutrophils, lymphocytes, plasma cells, histiocytes and eosinophilic polynuclear cells (Figure 2). The tumour cell population was composed of epithelioid or fusiform cells with large dispersed cells, with large bizarre nuclei and strongly nucleolated, resembling viral inclusions (virocyte-like cells) or Reed-Sternberg cells (Figure 3). Multivacuoletic cells resembling pleomorphic lipoblasts (pseudolipoblasts) were noted (Figure 4). Giant tumour cells, mainly in myxoid areas, showed imperogenesis. Low mitosis levels were noted despite the presence of

also labelled cytonuclear atypia. In the end, the diagnosis of fibroblastic myxoinflammatory sarcoma was retained.

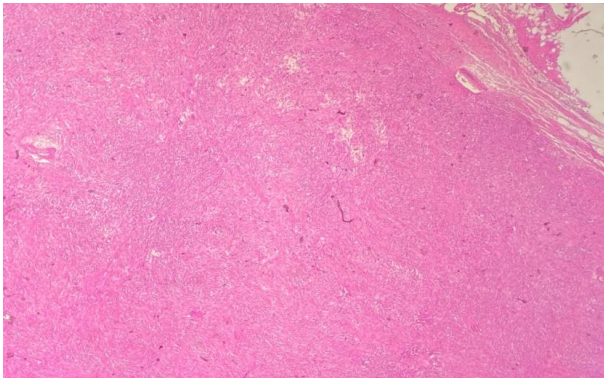


Figure 1: Histological image showing a multinodular lesion composed of variable myxoid and fibrous/hyalinized areas with an associated dense inflammatory infiltrate Gx10

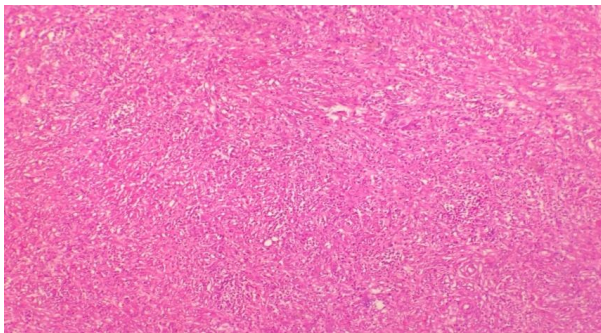


Figure 2: Histological image showing the growth pattern is confined to the subcutaneous tissue with polymorphic inflammatory cells including neutrophils, lymphocytes, plasma cells, histiocytes and eosinophils, which mix through the myxoid and fibrous areas Gx20

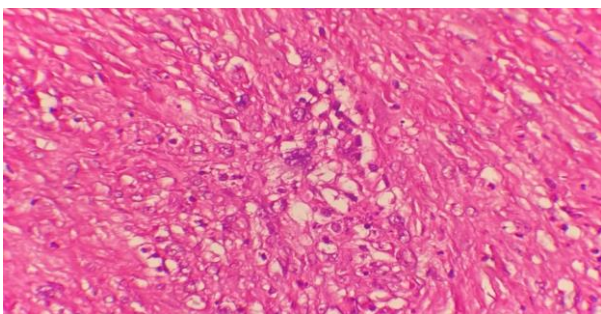


Figure 3: Histological image showing tumor cell population is composed of spindle-shaped epithelioid cells with scattered large cells with odd nuclei and prominent nucleoli resembling viral inclusions (virocyte-like cells) or Reed-Sternberg cells Gx40

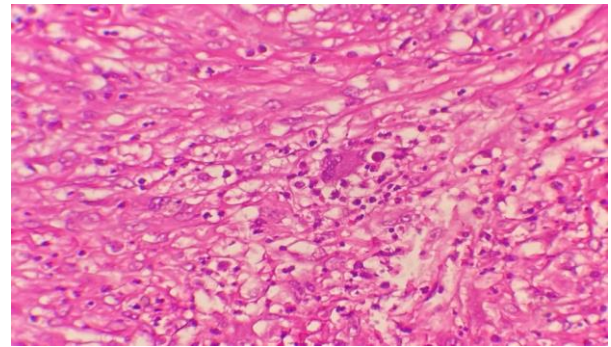


Figure 4: Histological image showing the presence of multivacuolated cells resembling pleomorphic lipoblasts (pseudolipoblasts - tumor cells with cytoplasmic vacuoles containing myxoid material) Gx40

DISCUSSION

Sarcomas of the soft tissues of the lower limb are generally of high grade and aggressive. Locally aggressive tumours or low-grade sarcomas, such as MIFS, are relatively rare in the foot and leg [3]. Clinically, this tumour is described mainly in the soft tissues of the distal limbs, in the fingers, hands or feet, representing 61% of the reported locations. As indicated in previous studies [5], the lesion usually occurs in a benign setting, in the form of an asymptomatic mass or swelling and this was indeed the case for our patient. Histologically, most MIFS have characteristics as described by Weiss *et al.*, [5]. Indeed, it is a growth along the interlobular septa of subcutaneous fat or along the tendon sheaths, with only few cases involving the dermis and even less invading skeletal muscle [6, 7]. The tumour stroma is predominantly fibrosclerotic, punctuated by myxo-oedematous foci of varying size (75% of cases), with the presence of large epithelioid cells with abundant cytoplasm filled with sometimes eosinophilic mucin and nuclei with irregular contours with prominent nucleoli giving an "Owl eye" appearance resembling Reed-Sternberg cell nuclei; and / or mottled heterochromochromat (93%), pseudolipoblasts (63%) and a permanently present intralesional inflammatory infiltrate [7]. Most recently published studies show the presence of a low mitotic index (usually 5 mitosis or less per 50 HPF) [8], while some mention the presence of atypical mitotic figures, accentuated vascularisation especially in myxoid zones [9] and hypercellularity [10]. The majority of these histopathological characteristics have been described in our case.

Immunohistochemical results show that neoplastic cells diffusely express vimentin positively, with variable immunopositivity for cytokeratin, SMA, CD68 and CD34. Meis-Kindblom *et al.*, report that the positivity of the MIB-1 proliferation index was less than 1% in the majority of cases [3].

Cytogenetically, Lambert *et al.*, [9] find a complex karyotype with reciprocal translocation t(1;10) (p22;q24) as well as the loss of chromosomes 3 and 13 in a case of acral myxoinflammatory fibroblastic sarcoma. The presence of these clonal chromosomal changes supports the neoplastic nature of the tumour and emphasises its distinction as an entity [9]. In our case, immunohistochemical and cytogenetic studies were not done for a reason related to the patient's social status. The differential diagnosis is broad and varied and depends on the predominance of the inflammatory or myxoid character at the level of the lesion, or the existence of an atypical component as already mentioned above [3]. Cytogenetically, Lambert *et al.*, [9] find a complex karyotype with reciprocal translocation t(1;10) (p22;q24) as well as the loss of chromosomes 3 and 13 in a case of acral myxoinflammatory fibroblastic sarcoma. The presence of these clonal chromosomal changes supports the neoplastic nature of the tumour and emphasises its distinction as an entity [9]. In our case, immunohistochemical and cytogenetic studies were not done for a reason related to the patient's social status. The differential diagnosis is broad and varied and depends on the predominance of the inflammatory or myxoid character at the level of the lesion, or the existence of an atypical component as already mentioned above [3]. Most of the differential diagnoses mentioned so far were: a tumor-like process related to an infectious disease, an inflammatory lesion such as tenosynovitis and proliferative or nodular fasciitis, a neoplastic process such as giant cell tumor, the inflammatory myofibroblastic tumour, in particular when the inflammatory cells are represented by lymphocytes and plasma cells predominated, liposarcoma, epithelioid sarcoma and myxoid malignant fibrous histiocytoma (MFH). An inflammatory lesion, giant cell tumour, myofibroblastic inflammatory tumour and inflammatory fibrosarcoma can be distinguished by recognising the atypical nature of MIFS epithelioid cells [12]. Inflammatory myofibroblastic tumour and inflammatory fibrosarcoma are most often located in the abdomen or chest [12] and leiomyosarcoma in the retroperitoneum or abdomen unlike the distal localisation of MIFS. The presence of mucin in the form of intracytoplasmic vacuole instead of extracellular mucin at the fat level eliminates liposarcoma [3]. MFH is thus described as a difficult and important differential diagnosis [2, 3, 9]. As with inflammatory myofibroblastic tumour and inflammatory fibrosarcoma, proximal localisation promotes the diagnosis of myxoid MFH compared to MIFS. When the lesion has focal immunopositivity for keratin or obvious tumour necrosis, the possibility of epithelioid sarcoma must be mentioned [12].

Treatment essentially consists of a complete surgical removal of the tumour with verification of surgical margins [13].

CONCLUSION

In summary, myxoinflammatory fibroblastic sarcoma, being so far considered a low-grade sarcoma occurring primarily at acral sites, is an entity that encompasses the full spectrum of lesions ranging from low-grade, relatively indolent neoplasms to high-grade tumors. Grade or fully undifferentiated spindle cell/pleomorphic sarcomas with aggressive biological behavior, examples of which were once diagnosed in the past as high-grade myxofibrosarcomas or myxoid/pleomorphic MFH. While the immunoprofile of MIFS remains variable, it has been shown to have emergent genetic features, in particular the t(1;10) rearrangement which is shared with malignant fibrous histiocytoma. Fluorescent FISH in situ hybridization for TGFBR3 and MGEA5 rearrangements is likely to be a valuable adjunct to determining the correct diagnosis in the future.

ABBREVIATIONS

MIFS: Mixoinflammatory fibroblastic sarcoma
 OAD: Oral Anti Diabetics
 MFH: Malignant Fibrous Histiocytoma
 FISH: Fluorescence in situ hybridization
 SMA: Smooth Muscle Actin

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