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CLINICAL CASE

High grade mixofibrosarcoma: a case report

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Abstract

Myxofibrosarcoma (MFS) is a soft-tissue sarcoma commonly found in older adults, characterized by its aggressive course and high recurrence rate. It primarily affects the lower extremities with local invasion. We present the case of a 73-year-old woman with a rapidly growing mass in the right thigh, showing evidence of bacterial superinfection. Biopsy confirmed a high-grade MFS. Computed tomography imaging revealed an exophytic mass with malignant features and soft-tissue invasion, without bone or vascular involvement. The patient subsequently underwent surgical excision with limb preservation. This case highlights the importance of thorough vascular assessment, as despite the tumor size, the absence of vascular invasion allowed for safe resection following discussion by a multidisciplinary medical team. This report provides clinical evidence on the feasibility of conservative resection in extensive MFSs and highlights the value of a multidisciplinary approach in complex cases.

Keywords: *Soft-tissue sarcoma. Neoplasm malignant. Case report.*

Mixofibrosarcoma de alto grado: reporte de caso

Resumen

El mixofibrosarcoma es un sarcoma de tejidos blandos frecuente en adultos mayores. Se caracteriza por su curso agresivo y una alta tasa de recurrencia, que afecta principalmente las extremidades inferiores con invasión local. Se presenta el caso de una mujer de 73 años con una masa de rápido crecimiento en el muslo derecho, que mostraba evidencia de sobreinfección bacteriana. La biopsia confirmó un mixofibrosarcoma de alto grado. La tomografía evidenció una masa exofítica con características malignas e invasión de tejidos blandos, sin compromiso óseo ni vascular, por lo que la paciente fue sometida a exéresis quirúrgica con preservación de la extremidad. Este caso resalta la importancia de una evaluación vascular detallada, ya que pese al tamaño tumoral, la ausencia de invasión vascular permitió una resección segura, previa discusión en junta médica multidisciplinaria. Este reporte aporta evidencia clínica sobre la posibilidad de resección conservadora en mixofibrosarcomas extensos y subraya el valor de un abordaje multidisciplinario en casos complejos.

Palabras clave: *Sarcoma de tejidos blandos. Neoplasia maligna. Presentación de caso.*

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Introduction

Myxoid soft-tissue sarcomas represent a heterogeneous group of neoplasms of mesenchymal origin that are characterized by the presence of a myxoid stroma. These include entities such as myxoid liposarcoma, fibromyxoid sarcoma, extraskeletal myxoid chondrosarcoma, myxofibrosarcoma (MFS), myxoinflammatory fibroblastic sarcoma, and myxoid dermatofibrosarcoma protuberans.[1,2]

MFS, formerly called myxoid malignant fibrous histiocytoma, is considered one of the most common soft-tissue sarcomas involving the extremities and usually affecting elderly patients. Its estimated incidence is < 0.1/100,000 inhabitants each year. The course of this neoplasm is usually aggressive because it presents a high rate of local recurrence and a significant risk of metastasis.[1-4] The present manuscript was written according to the CARE guidelines.

Case presentation

A 73-year-old female patient with a medical history notable only for age-related hearing loss, with no other significant non-pathological personal or family antecedents, presented to the physician's office reporting the presence of a progressively enlarging exophytic mass on her right thigh for approximately 1 year. The patient reported pain in the area of the lesion and the presence of purulent discharge.

At the time of examination, the patient had an Eastern Cooperative Oncology Group (ECOG) performance status of 2. The physical examination revealed the presence of an exophytic mass of approximately 15 × 10 cm located on the lateral side of the right thigh, with evidence of necrotic tissue, and a purulent discharge that emitted a foul odor and was tender to palpation (Fig. 1). No inguinal lymphadenopathy was found. Given the low frequency of the neoplasm, its size, the atypical clinical presentation, the patient's sex, and her medical history, several differential diagnoses, including MFS, liposarcoma, leiomyosarcoma, and angiosarcoma, were actively considered before reaching the definitive diagnosis. This process was complex and made the initial diagnostic impression a significant clinical challenge. Furthermore, due to the aggressive nature of the presentation, including impaired ECOG performance status, large tumor size, ulceration, and visible signs of necrosis, the initial prognosis was considered poor and guarded.

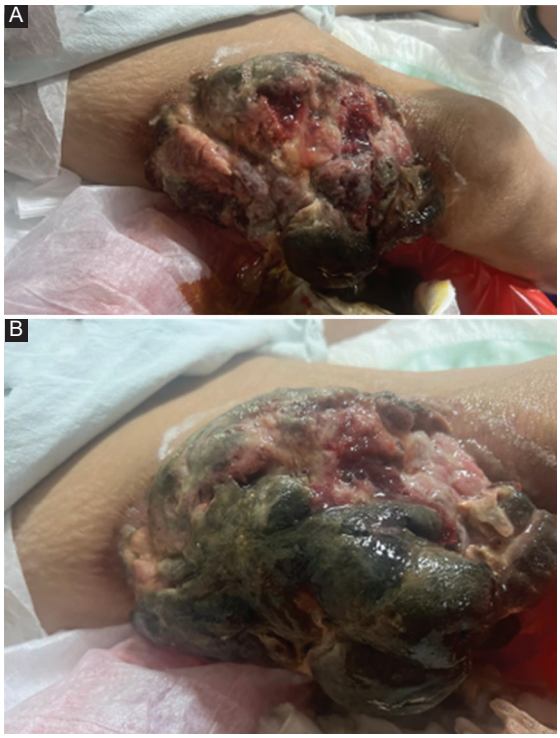


Figure 1. Clinical appearance of the exophytic thigh lesion. **A** and **B**: exophytic lesion located on the lateral aspect of the right thigh, showing necrotic tissue, ulceration, and effacement of the surrounding tissue.

Laboratory tests on admission revealed severe anemia (Hb: 4.3 g/dL, Hct: 13.4%), leukocytosis with neutrophilia and left shift (Leu: 19,930; PMN [polymorphonuclear neutrophils]: 87%, Ab: 7%); and elevated inflammatory markers erythrocyte sedimentation rate (ESR: 31 mm/h) and C-reactive protein (CRP: 3.031 mg/dL). Serology for human immunodeficiency virus-1/2, human T-lymphotropic virus 1, and Epstein-Barr virus was negative. Furthermore, no alterations were found in the electrophoretic proteinogram.

X-ray of the lower extremity showed no bone involvement or isolated osteolytic lesions. Contrast-enhanced computed tomography (CT) showed the presence of an exophytic lesion dependent on the vastus lateralis muscle of approximately 117 × 63 mm, which involved subcutaneous tissue and skin and showed enhancement with the administration of contrast (Fig. 2). In addition, a 3D reconstruction CT angiography was performed, which did not show involvement of the femoral artery on the right side (Fig. 3).

The biopsy of the lesion from surgical excision of the tumor revealed the presence of malignant cells with

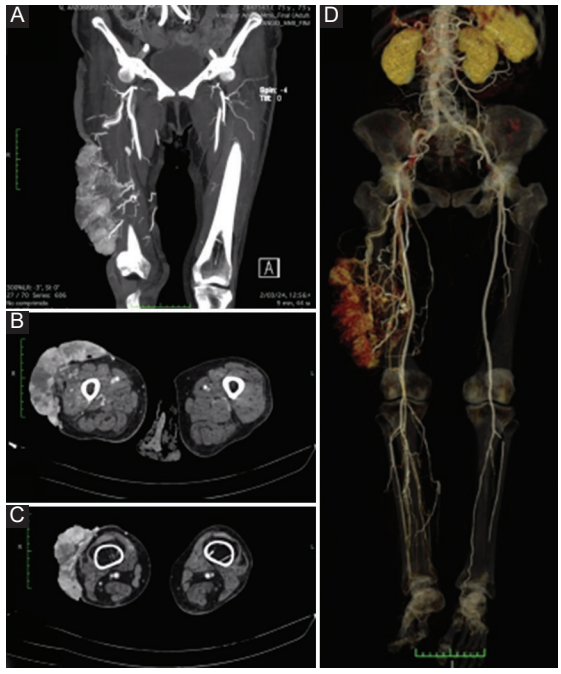


Figure 2. Computed tomography and angiography of the lesion. **A:** coronal view of the computed tomography scan showing an exophytic lesion in the right lower limb, presenting as a large heterogeneous mass with areas of intermediate and low density, suggestive of myxoid components and necrosis. Significant deformation of the surrounding muscle contour and neovascularization dependent on branches of the right femoral artery are observed, without evidence of direct femoral artery invasion. **B** and **C:** axial computed tomography sections at different levels showing a large heterogeneous lesion involving the deep muscle planes, with partially defined margins. **D:** three-dimensional reconstruction obtained by computed tomography angiography, showing the anatomical relationship between the exophytic lesion and the vascular tree of the lower extremity. The mass displaces the main arteries and veins, highlighting its extension and compressive effect without evidence of intravascular invasion.

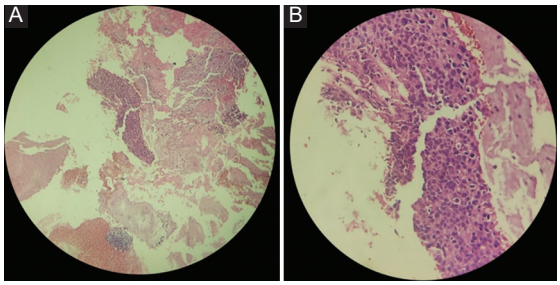


Figure 3. Histopathological findings of the lesion. **A:** histological section stained with hematoxylin and eosin at ×10 magnification, showing a characteristic myxoid matrix with hypocellular areas interspersed with regions of greater cellular density. Scattered spindle cells with nuclear pleomorphism and disordered arrangement are also observed. **B:** histological section stained with hematoxylin and eosin at ×40 magnification, showing pleomorphic, hyperchromatic, and occasionally multinucleated tumor cells. The myxoid matrix is infiltrated by spindle cells in a disordered pattern, associated with marked pleomorphism. These findings are consistent with high-grade myxofibrosarcoma.

marked pleomorphism, hypercellularity, high mitotic activity, with areas of necrosis, and high histological grade without evidence of lymphovascular invasion consistent with high-grade MFS. Immunohistochemistry of the lesion revealed positivity for vimentin and alpha smooth muscle actin and negativity for cytokeratin 20, desmin, S100a, and HMB-45. The Ki-67 proliferation index was 70%.

Because the patient showed severe anemia and infection of the lesion, transfusion therapy with 3 red blood cell package was indicated. Furthermore, intravenous antibiotic therapy with meropenem and vancomycin was administered. The patient had an adequate response to antibiotic treatment, and her hematological variables normalized over the next 48 h.

After an interdisciplinary evaluation by oncology, cardiovascular surgery, and traumatology, it was decided that the patient should undergo surgical resection as the first line of management. The patient underwent a wide local excision with limb preservation, under general anesthesia. A fusiform incision was made over the lesion, and the tumor was resected *en bloc* with adequate macroscopic margins, including involved subcutaneous tissue and part of the vastus lateralis muscle. Intraoperative findings confirmed no invasion of the femoral neurovascular bundle or bone structures. The procedure lasted approximately 2 h. The defect was reconstructed using a fasciocutaneous rotational flap, and surgical drains were placed. Histopathology later confirmed negative surgical margins, validating the completeness of the resection. The surgical specimen showed uncompromised surgical margins.

After surgery, the patient was scheduled to begin adjuvant chemotherapy with the ifosfamide/doxorubicin regimen. The treatment protocol consisted of four cycles, administered every 21 days. Each cycle included doxorubicin at 75 mg/m^2 intravenously on day 1, and ifosfamide at 2.5 g/m^2/day intravenously on days 1 to 3,

accompanied by mesna for uroprotection. All drugs were delivered via intravenous infusion under inpatient monitoring. The patient tolerated the regimen well, without requiring dose reductions or treatment delays. During follow-up, thoracoabdominal CT scans performed after the second cycle showed no evidence of local recurrence or distant metastasis. Hematologic monitoring revealed mild, transient neutropenia (grade I) after the first cycle, which resolved spontaneously. Liver and renal function remained within normal limits throughout treatment. Serial complete blood counts and inflammatory markers (CRP, ESR) normalized following the initial resection and remained stable. Clinical progress notes documented good general condition, adequate performance status (ECOG 1), and absence of new symptoms. She did not present major complications, and no dose-limiting toxicities were reported. She is currently alive and receiving her third cycle of chemotherapy.

Discussion

MFS is one of the most common myxoid soft-tissue sarcomas in older adult patients.[2,5] According to the World Health Organization 2020 Classification of Soft-tissue Tumors, MFS is classified within myofibroblastic/fibroblastic tumors.[6] The average age of presentation of this entity is 65 years old, with a slight male sex predominance. These usually originate from the dermal and subcutaneous tissues of the lower extremities, and appendicular girdle, and less frequently from the trunk, head, neck, hands, and feet.[5-7]

Clinically, high-grade MFS typically presents as a painless, rapidly growing mass in an extremity, often manifesting as a malignant lesion with ulceration, necrosis, and hemorrhage. These lesions are frequently infected due to their favorable environment for bacterial growth.[8] This case is consistent with theoretical descriptions in terms of the patient's age, tumor location, histological characteristics, immunohistochemical profile, and surgical management. However, it stands out due to the presence of exophytic growth, ulceration, and secondary infection – clinical features that are uncommon and typically associated with advanced stages or rapidly progressing tumors.[4,9,10]

The diagnostic process considered several differential diagnoses, including undifferentiated pleomorphic sarcoma, fibrosarcoma, leiomyosarcoma, and malignant peripheral nerve sheath tumor. The rarity of high-grade MFS, combined with its atypical presentation in this case, posed a significant diagnostic challenge and necessitated a multidisciplinary approach involving pathology, radiology, oncology, and surgical teams to establish an accurate diagnosis and determine the most appropriate treatment strategy.

Regarding genetic alterations, a study by Ogura et al. demonstrated that the presence of mutations in p53 and Kirsten rat sarcoma virus (KRAS) was associated with poor overall survival.[11] On the other hand, the expression of CD109, a transforming growth factor-beta coreceptor, is associated with a poor prognosis, particularly in high-grade MFSs. Another notable alteration is the expression of CD34, which has been shown to increase the risk of developing distant metastasis. It has been postulated that this could be due to the expression of this marker in CD34+ fibroblastic/fibrocystic stromal cells that have the capacity to remodel the extracellular matrix and contribute to fibrosis and the formation of tumor stroma.[4]

Histopathologically, spindle-shaped cells with multinodular growth can be observed in a myxoid stroma with fibrous areas with curvilinear blood vessels.[2,4] According to its cellularity, nuclear pleomorphism, mitotic activity, and percentage of necrosis, MFS can be classified into three grades: low grade, intermediate grade, and high grade.[2,6] Low-grade MFS is usually described as a hypocellular sarcoma with modified stellate spindle cells and a condensation of blood vessels that may be accompanied by pseudolipoblasts.[12] Low-grade MFS usually has a low risk of recurrence (42%) compared to high-grade MFS, which has a recurrence risk of 62%, and also has a high metastatic potential.[1] High-grade MFS are usually hypercellular tumors with atypical mitotic figures, evidence of hemorrhage, necrosis, and multinucleated giant cells. On the other hand, intermediate-grade MFS have characteristics of both types but lack areas of necrosis and significant cellular pleomorphism.[12,13] The patient in this case presented a high-grade MFS with local invasion; however, no distant metastases were found. The absence of a family history of cancer in this patient suggests that the tumor likely resulted from a *de novo* somatic mutation, favored by age-related cellular changes and accumulated DNA damage. At the cellular level, these alterations may drive uncontrolled mesenchymal proliferation, abnormal neovascularization, and tumor hypoxia, leading to necrosis, ulceration, and secondary infection. Molecularly, mutations in TP53 and KRAS, along with the expression of CD109 and CD34, can promote apoptosis evasion, stromal remodeling, and local invasiveness. These mechanisms may explain the clinical phenotype observed in this case: an exophytic, necrotic,

infected, and rapidly growing tumor with no evidence of distant dissemination.[2,4,9]

This neoplasm can be located in superficial or deep planes, with deep involvement being more common (20-70%). It exhibits a peripheral infiltrative growth pattern that extends into intra- and extra-muscular vascular and fascial planes.[4] In the present case, invasion of muscle tissue, adipose tissue, and small-caliber vessels originating from the femoral artery was observed, without direct involvement of the artery.

The standard treatment for localized disease consists of radical resection with clear surgical margins, combined with neoadjuvant or adjuvant radiotherapy, with the goal of preserving the affected limb. However, the role of radiotherapy in reducing the risk of local recurrence remains uncertain, as several studies have reported inconsistent results.[4] In this case, the patient underwent wide surgical resection of the tumor with limb preservation and negative margins. Chemotherapy cycles were completed in full, without the need for dose adjustments. These findings confirm not only the feasibility but also the early effectiveness and tolerability of the adjuvant chemotherapy regimen.

Regarding prognosis, MFS presents the highest recurrence rate compared to all soft-tissue sarcomas, ranging from 20 to 60% after 5 years, according to the case series.[14-16] Local recurrence of cases regardless of histological grade ranges from 10 to 61%.[17] MFS presents a median overall survival of 155 months (0.1-215) with a 5-year survival of 67.7%. In the present case, the patient underwent weekly, monthly, and quarterly oncological follow-up, showing a favorable clinical course with no evidence of recurrence to date; therefore, her current prognosis is considered encouraging. The most important prognostic factors are age, sex, tumor size, histological grade, and surgical margins.[18,19]

This case report presents several strengths, notably the detailed description of the clinical, radiological, histopathological, and therapeutic aspects of high-grade MFS in an elderly patient – a population in which this neoplasm is most prevalent. The multidisciplinary approach adopted, along with accurate imaging interpretation, surgical findings, and the favorable outcomes of chemotherapy, provides a comprehensive understanding of the clinical course and supports therapeutic decision-making. Moreover, the effectiveness of the adjuvant treatment and the patient's favorable evolution further underscore the clinical value of the chosen management strategy. Adherence to CARE guidelines also ensures methodological quality and reproducibility of the information presented.

Nevertheless, as with any single case report, its generalizability is limited. The absence of long-term follow-up restricts the assessment of recurrence or metastatic dissemination risk – factors that are particularly relevant in high-grade sarcomas. In addition, the genetic analysis was limited to immunohistochemical techniques, without the inclusion of molecular studies that could have provided more accurate prognostic information. Future reports could benefit from extended observation periods and the incorporation of molecular biomarkers, which would enhance both prognostic stratification and therapeutic guidance in this type of neoplasm.

From the patient's perspective, the post-operative course was well-tolerated and complication-free. She expressed satisfaction with the multidisciplinary care and felt reassured by the surgical outcomes, which favored adherence to follow-up and emotional stability.

Conclusion

This case of high-grade MFS in an elderly patient underscores the critical role of multidisciplinary management in addressing atypical and aggressive presentations. The integration of vascular assessment enabled a safe and function-preserving surgical approach, while the adjuvant chemotherapy regimen was both effective and well tolerated. This case highlights the importance of early intervention, coordinated care, and adherence to oncologic protocols, even in complex clinical scenarios. Furthermore, it contributes to the existing literature by illustrating a successful example of limb-sparing treatment in advanced soft-tissue sarcoma and reinforces the need for long-term follow-up and incorporation of molecular markers to enhance prognostic accuracy and therapeutic planning.

CRediT author statement

Conceptualization: J. Alburqueque-Melgarejo and B. Beltrán-Gárate. Data curation: H.M. Virú-Flores and J. Alburqueque-Melgarejo. Formal analysis: J. Alburqueque-Melgarejo and J.C. Roque-Quezada. Investigation: J. Alburqueque-Melgarejo, J.C. Roque-Quezada, and H.M. Virú-Flores. Methodology: J.C. Roque-Quezada and H.M. Virú-Flores. Project administration: H.M. Virú-Flores and B. Beltrán-Gárate. Resources: C.J. León-Peña and J.C. Roque-Quezada. Software: J. Alburqueque-Melgarejo and J.C. Roque-Quezada. Supervision: B. Beltrán-Gárate and J.C. Roque-Quezada. Validation: B. Beltrán-Gárate and H.M. Virú-Flores. Visualization: C.J. León-Peña and H.M.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical considerations

Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval. The authors have followed their institution's confidentiality protocols, obtained informed consent from all patients, and secured approval from the Ethics Committee. SAGER guidelines have been followed as applicable to the nature of the study.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing or creation of the content of this manuscript.

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