Surgical Science, 2023, 14, 667-672
https://www.scirp.org/journal/ss
ISSN Online: 2157-9415
ISSN Print: 2157-9407

Unexpected Metastatic Recurrent Myxofibrosarcoma: A Scenario That May Be More Common than You Think

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How to cite this paper: Laura, C.-P., Adriana, C.-M., Dioney, U.-G., Alejandro, F.-L. and Ximena, G.-P. (2023) Unexpected Metastatic Recurrent Myxofibrosarcoma: A Scenario That May Be More Common than You Think. *Surgical Science*, **14**, 667-672.
https://doi.org/10.4236/ss.2023.1411072

Received: September 18, 2023
Accepted: November 13, 2023
Published: November 16, 2023

Abstract

Soft tissue sarcomas represent only 1% of all adult cancers; myxofibrosarcoma is the most common type that arises in adult extremities, particularly lower limbs (77%), other less common locations are the trunk (12%) and neck (3%). Usually presenting as a painless, subcutaneous, slow growing mass with tendency for recurrence, they are prone to have higher histological grade and metastatic potential after recurrence; even in optimal multidisciplinary settings patients can have incomplete resections, making metastatic disease more common after misdiagnosis. We present the case of a 69-year-old male patient with a right infraescapular tumor, presenting as a painless 15 × 8 cm, mobile mass, with a slow but progressive growth, history of a previous tumor excised at the same location 5 years prior without histopathological report.

Keywords

Case Report, Myxofibrosarcoma, Metastatic Disease, Misdiagnosis

1. Introduction

Myxofibrosarcoma is an aggressive subtype of soft tissue sarcoma making up to 5% of all malignant soft tissue sarcomas, most commonly found as a painless, slow growing mass on adult lower extremities is characterized by having one of the highest rate of local recurrence among soft tissue sarcomas, up to 60% and a tendency for a higher histological grade with an increased metastatic potential with each recurrence.

Treatment for localized disease is characterized by surgical resection, (neo)-adjuvant radiotherapy or chemotherapy in some settings, however despite early proper diagnosis and optimal resection margins up to 38% of patients have incomplete resections.

2. Case

69 year old male patient with a history of diabetes and hypertension for the last 10 years well controlled with oral medication, surgical history was positive for phacoemulsification and intraocular lens on both eyes 2 and 1 year prior, surgical resection of a "fibromuscular" tumor on the dorsal surface of the right scapula 5 years prior, this time presenting as a painless 15 × 8 cm, mobile mass, with a slow growth; no proper histopathological report was obtained from the previous resection; on simple computed tomography the lesion is described as infraescapular polylobulated/nodular lesion, isodense to the adjacent musculature with regular, well defined borders of approximately 15 × 7.6 × 9 cm and a attenuation value of −4 to 23 hounsfield units (HU) (**Figure 1**); at pulmonary level, focal interstitial thickening is observed on the posterior region of the middle right lobe, a subsolid lateral nodule at the same level and a 3 mm nodule at the anterior region of the inferior left lobe with a pair of calcified granulomas at the inferior basal region. Excisional biopsy is performed (**Figure 2**) with a postoperative pathology report of a Grade 2 well delimitated sarcoma of approximately 12 × 8 × 7 cm based on cytomorphologic features and immunohistochemical profiling,

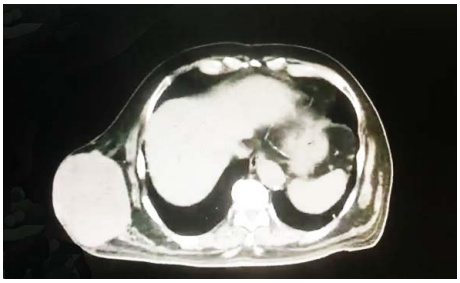

Figure 1. Right infraescapular nodular lesion on simple computed tomography.

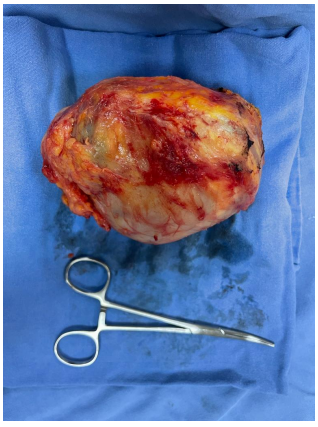

Figure 2. Excsional biopsy specimen.

subclassified as Grade 3 by World Health Organization (WHO) myxofibrosarcoma due to its high mitotic index and 30% necrosis. The patient was later referred to the oncologist for tumor staging and appropriate management with doxorubicin based palliative chemotherapy.

3. Review of Literature

Soft tissue sarcomas represent a group of rare and heterogenous tumors of mesenchymal origin, representing 1% of all adult cancers. Myxofibrosarcoma (MFS) is a rare, aggressive and infiltrative subtype of soft tissue sarcoma (STS) constituting 5% of all malignant soft tissue sarcomas and it's considered the subtype that most commonly affects adult extremities; previously known as the myxoid variant of the malignant fibrous histiocytoma, it was recognized as its own entity in 2002 and confirmed in 2013 by the WHO; it's characterized by its myxoid stroma, pleomorphism, curvilinear vessels and an important tendency for local recurrency and metastases [1] [2] [3] [4].

Usually presenting as a painless, subcutaneous, slow growing mass with tendency for local recurrence after excision, they usually affect the older population between 6th and 7th decades of life with a slight male preponderance; the most affected sites being the lower limbs (77%) and less frequently the trunk (12%) and neck (3%) and rarer still the retroperitoneum and abdominal cavity. They are classified depending on their location as superficial (dermis/ subcutaneous tissue) or deep (intermuscular or subfascial), presenting most commonly as superficial tumors (75%) that infiltrate subcutaneous tissue and fascia extensively, but can also be found as cutaneous or deep circumscribed but infiltrative lesions [2].

The diagnosis of MFS is made by a pathologist, based on cytomorphologic features in relation to the WHO criteria, including the assessment of myxoid and fibrous areas, pleomorphism, curvilinear vessels and immunostaining. Macroscopically often described as multinodular lesions with fibrous septa, curvilinear vessels of variable caliber, gelatinous content, and infiltrative margins; microscopically as a microcellular lesion with a myxoid background or a hypercellular lesions with spindle, pleomorphic or epithelioid cells; the epithelioid subtype is considered the most aggressive [3].

Histological grading is done according to the proportion of myxoid to cellular component with Federation Nationale des Centres de Lutte Contre le Cancer (FNCLCC) grading system in 3 respective grades, depending on the level of tissue differentiation, mitotic activity and necrosis, as low, intermediate, and high-grade tumors. Low grade tumors are characterized by their low mitotic activity, hypocellularity and absence of necrosis; higher grade tumors exhibit a higher level of cellularity, high mitotic activity and necrosis; high grade tumors present all 3 characteristics [4] [5]. Currently, no immunohistochemical specific marker has been identified that supports the diagnosis of myxofibrosarcoma over other soft tissue sarcomas, most of them present with highly complex karyotypes in all

grades, that get even more complex with each recurrence [4] [5].

As previously mentioned, myxofibrosarcoma has the highest rate of recurrence among all STS, ranging from 20% - 60% at 5 years compared to 10% in other subtypes of STS; 15% - 38% of MFS local recurrences evolve to higher histological grade with increased metastatic potential. The overall incidence of distant metastases is estimated to be between 20% and 25% with the most affected sites being the lung, regional lymph nodes, pleura, and bone; less commonly being the adrenals and mesentery [4] [5] [6] [7].

It's estimated that in an appropriate multidisciplinary setting, up to 21% - 38% of patients with optimal resection margins have incomplete resections, this number may be much higher in unspecialized centers where the whole protocol maybe overlooked, such could be the case in overcrowded hospitals and in underdeveloped countries; this is consistent with one of the largest patient cohorts involving patients with MFS [7] where it was seen that primary unplanned resection at non-specialized facilities or centers with low case-volume, were at risk of unclear resection margins, which is considered a factor for poor prognosis; other factors that have been reported to influence overall survival are age ≥ 65 y/o, male sex, cancer medical history, tumor size > 5 cm, deep tumor depth, high histological grade, distant metastases at diagnosis or residual disease after surgery, with an associated five-year overall survival of 68% [7].

Given its variable presentation and most common superficial location, as over half of them arise subcutaneously, in accordance with American College of Radiology (ACR) guidelines ultrasound is an appropriate initial imaging tool for its evaluation as with other superficial or palpable soft tissue masses [8], however given MFS's variable appearance, imaging can be a challenge, for they are often misdiagnosed as a hematomas, intramuscular myxoma or inflammatory processes; so myxofibrosarcoma awareness is important factor at the beginning of its evaluation, and it should always be considered as a differential when evaluating soft tissue masses in the older population, especially in absence of trauma history; on US they are described as hypoechoic lesion of heterogenous appearance and on CT they appear as iso-attenuating masses similar to muscle and since they are often mistake with benign lesions, it's not uncommon after excision to reveal the presence of inadequate tumor margins. US-guided core needle biopsies have not proven to be useful in all cases and its low negative predictive value and low specificity could lead to tumor undegrading [8] [9].

Multidisciplinary preoperative planning with magnetic resonance imaging (MRI) imagining evaluation is key. MRI is considered the imaging modality of choice in determining tumor extension, given its infiltrative nature and tendency to grow along fascial planes, tumor extension is often described as a high "tail-like" signal on T2-weighted MRI imaging with gadolinium enhancement, which is well recognized to contain tumor, though they can be infiltrative even without this appearance [10] [11] [12].

Treatment for localized disease is characterized by surgical resection, (neo)-adjuvant radiotherapy, or chemotherapy in some settings. MFS infiltrative na-

ture requires a careful surgical excision including all potential tissue with a 2 cm surgical margin, usually followed by adjuvant radiotherapy. In the setting of uncertain surgical margins, a two-stage surgical approach allows assessment of margins and further excision before reconstruction that may require multidisciplinary involvement of vascular, reconstructive, and orthopedic surgeons, based on the extent of the resection and potential need for grafts [10] [11] [12] [13]. The presence of distant metastasis indicates a poor prognosis, its mechanism remains unknown; palliative chemotherapy represents the backbone of its treatment, with standardized anthracycline e.g. Doxorubicin, however its role remains controversial as its outcome is very poor [11] [12] [13] [14].

4. Conclusion

Myxofibrosarcoma is the most common subtype of soft tissue sarcoma found in the adult population, particularly lower extremities and trunk, despite having a better overall survival compared to other sarcoma subtypes, its tendency for local recurrence plays an important role in overall morbidity and mortality; large tumor size, recurrence and higher grade at diagnosis are all associated with a worst prognosis, there it lies the importance of tumor awareness with a high level of suspicion in early diagnosis and a multidisciplinary approach in specialize center, as both could improve what is until now an uncertain prognosis.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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