Cancer Association of South Africa (CANSA)

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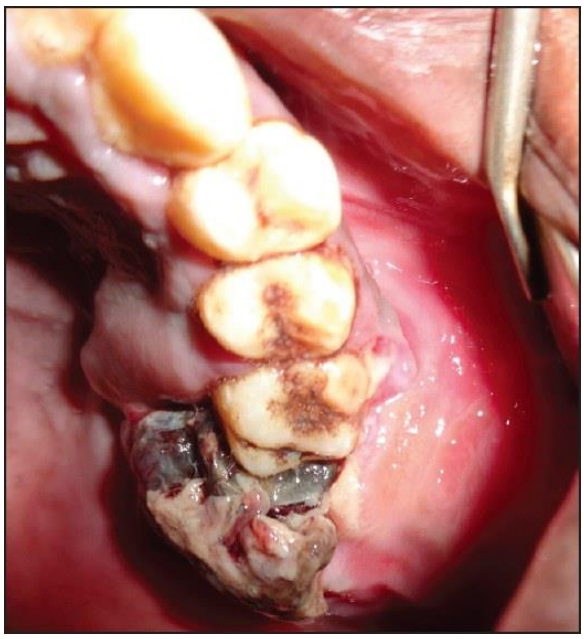
Fact Sheet on Myxofibrosarcoma

Introduction

Cancerous (malignant) tumours of the connective tissues are called "sarcomas". Sarcoma arises in the connective tissue of the body.

Normal connective tissue includes, fat, blood vessels, nerves, bones, muscles, deep skin tissues, and cartilage. Sarcomas are divided into two main groups, bone sarcomas and soft tissue sarcomas. They are further sub-classified based on the type of presumed cell of origin found in the tumour. They all share certain microscopic characteristics and have similar symptoms. Sarcomas can develop in children and adults. For children under 20 approximately 15 percent of cancer diagnosis are sarcomas. In general sarcomas are divided into the large groups of soft tissue sarcoma and bone sarcomas.



[Picture Credit: Myxofibrosarcoma]

The picture above shows myxofibrosarcoma of the jaw (a typical case of head-and-neck myxofibrosarcoma).

Myxofibrosarcoma (MFS)

Myxofibrosarcoma (MFS) is one of the most common sarcomas in the extremities of the adult, especially elderly patients. It may also arise in the head and neck region. Myxofibrosarcoma (MFS) forms a group of malignant soft tissue tumours that are commonly observed in older adults. It is also referred to as Myxoid Malignant Fibrous Histiocytoma. Morphologically, these tumours may be classified as high grade, intermediate-grade, or low-grade. The cause of Myxofibrosarcoma occurrence is unknown and no risk factors have been reported.

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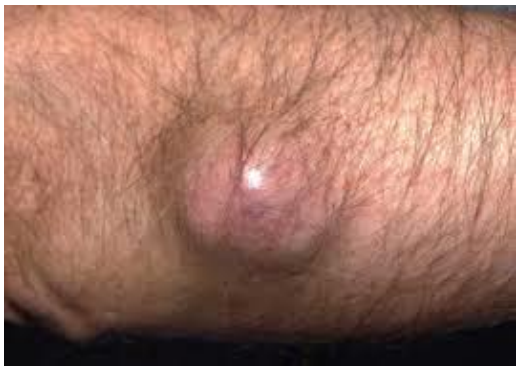
It has distinct features under the microscope. It commonly grows in a nodular pattern. Tumour cells are round and without distinct cell margins. According to the number of cells involved and appearance of cells under the microscope, myxofibrosarcoma can be divided into different grades. Low-grade myxofibrosarcoma has lower tendency for distant spread (metastasis). However, it tends to become progressively higher grade in recurrences.

High-grade, advanced or malignant soft tissue sarcomas are aggressive diseases with poor prognosis and are usually invasive and metastasise.

Tjarks, B.J., Ko, J.S. & Billings, S.D. 2018.
BACKGROUND: Myxofibrosarcoma classically presents as a painless mass in the proximal extremities. Cutaneous myxofibrosarcomas arising in the head and neck and distal extremities are extremely uncommon. We present a series of 6 cases of myxofibrosarcoma presenting in the head and neck and acral locations.
METHODS: Archives were searched using the term "myxofibrosarcoma" over a 6-year period (2009-2015). The clinicopathologic features of myxofibrosarcoma were recorded. Cases in the head and neck or acral locations were retrieved. When available, the patient's medical records were reviewed.
RESULTS: Ninety-five cases of myxofibrosarcoma were identified over a 6-year period. Six patients were identified with myxofibrosarcoma arising in the head (n = 4, M:F 3:1), hand (n = 1, F) and foot (n = 1, F). Each had typical features of myxofibrosarcoma. Two of the tumors on the head were high-grade and had multiple recurrences, while the remaining 2 were intermediate grade. Both acral tumors were intermediate grade and 1 recurred locally within a year of diagnosis.
CONCLUSIONS: Myxofibrosarcoma may rarely involve the head and neck and acral locations, and presentation in these sites is a potential source of diagnostic difficulty. Recognition of the characteristic histologic features of myxofibrosarcoma in conjunction with judicial use of immunohistochemical stains should allow for accurate diagnosis.

Incidence of Myxofibrosarcoma
The National Cancer Registry (2017) makes no reference to Myxofibrosarcoma.

Age and Sex Distribution of Myxofibrosarcoma
Myxofibrosarcoma mainly affects older adults in the 50-80 year age range (average age 66 years). However, adults of a wide age range may be affected. It is very difficult to observe Myxofibrosarcomas in individuals below 20 years of age i.e., in children and very young adults. Both males and females are affected, though a slight male predominance is sometimes seen. There is no known ethnic or racial preference noted



[Picture Credit: Myxofibrosarcoma on Limb]

Diagnosis of Myxofibrosarcoma (MFS)

Myxofibrosarcoma (MFS) is a variant of the group of malignant fibrous histiocytomas. It is one of the most aggressive types of soft tissue neoplasms. The clinical presentation is not pathognomonic and the histological aspects are highly heterogenous, frequently delaying the diagnosis or leading to misdiagnosis. (Castronovo, *et al*., 2013).

Li, H., Xie, L., Wang, Q., Dang, Y., Sun, X., Zhang, L., Han, Y., Yan, Z., Dong, H., Zheng, H., Li, Y., Zhu, W. & Guo, X. 2020.

"Myxofibrosarcoma is a complex genetic disease with poor prognosis. However, more effective biomarkers that forebode poor prognosis in Myxofibrosarcoma remain to be determined. Herein, utilizing gene expression profiling data and clinical follow-up data of Myxofibrosarcoma cases in three independent cohorts with a total of 128 Myxofibrosarcoma samples from The Cancer Genome Atlas (TCGA) and Gene Expression Omnibus (GEO) databases, we constructed an easy-to-use web tool, named Online consensus Survival analysis for Myxofibrosarcoma (OSmfs) to analyze the prognostic value of certain genes. Through retrieving the database, users generate a Kaplan-Meier plot with log-rank test and hazard ratio (HR) to assess prognostic-related genes or discover novel Myxofibrosarcoma prognostic biomarkers. The effectiveness and availability of OSmfs were validated using genes in ever reports predicting the prognosis of Myxofibrosarcoma patients. Furthermore, utilizing the cox analysis data and transcriptome data establishing OSmfs, seven genes were selected and considered as more potentially prognostic biomarkers through overlapping and ROC analysis. In conclusion, OSmfs is a promising web tool to evaluate the prognostic potency and reliability of genes in Myxofibrosarcoma, which may significantly contribute to the enrichment of novelly potential prognostic biomarkers and therapeutic targets for Myxofibrosarcoma."

Wakely Jr, P.E.2020.

Introduction: Myxofibrosarcoma is one of the more common sarcomas encountered in adults.

Materials and methods: A search was made of our cytopathology and surgical pathology databases for cases diagnosed as myxofibrosarcoma (MyxoFS). FNA biopsy smears and cell block were performed and examined using standard techniques.

Results: Sixty-six cases were retrieved from patients aged 40 to 94 years (mean: 67 years), with a male:female ratio of 1.4:1. Forty-seven (71%) were primary neoplasms, 13 (20%) locally recurrent, and 6 (9%) metastasis. Lower extremity was the most common site 38 (58%) cases, followed by upper extremity and trunk (each 13 [20%] cases), 1 head/neck, and 1 pleural-based mass. Forty-two (64%) cases were specifically/correctly diagnosed as MyxoFS. Thirteen (20%) were diagnosed as undifferentiated pleomorphic sarcoma (UPS), 3 (4.5%) as myxoid neoplasm, 2 (3%) as myxoid sarcoma, and 1 (1.5%) sarcoma, not otherwise specified. As most were examples of high-grade (HG) MyxoFS, cytomorphology contained pleomorphic and spindled cells set in a variable amount of myxoid stroma. Arborizing capillaries were common, and pseudolipoblasts were uncommon. All cases interpreted as UPS were HG MyxoFS histologically. Five (7.5%) cases-pleomorphic liposarcoma (3), solitary fibrous tumor (1), and atypical lipoma (1)-were mistakenly diagnosed. Ancillary immunohistochemistry played a minor role in diagnostic assessment.

Conclusion: MyxoFS was accurately interpreted using FNA biopsy in about two thirds of cases. One fifth were misinterpreted as UPS due to the absence/near absence of myxoid stroma, which varies considerably in the definition of this neoplasm.

Treatment of Myxofibrosarcoma (MFS)
Treatment usually aims to prolong survival, prevent local recurrence, maximise function and minimise morbidity. Radical, limb salvage surgery with clear margins is often essential and adjuvant treatment involving radiotherapy is sometimes advised. In order to obtain a radical excision, tissue reconstruction may be required following resection rather than direct wound closure, hence the level of soft tissue resection needs to be carefully planned. Where local control is not achieved, amputation may be recommended.

Surgery, radiation therapy and chemotherapy, often a combination of two or more regimens may be used in the treatment of myxofibrosarcoma.

Surgical resection is often the mainstay of therapy for soft tissue sarcomas. When feasible, wide-margin function–sparing surgical excision is the cornerstone of effective treatment for extremity tumours.

Tumour size may affect the development of metastatic disease and the management of primary disease. Neoadjuvant radiotherapy may have a potential role in the routine management of myxofibrosarcoma. The use of chemotherapy after surgical removal of the original tumour to try and destroy microscopic undetected metastatic disease to other parts of the body (adjuvant chemotherapy) remains controversial.

There is presently no specific "targeted" therapy against fibrosarcoma because scientists have not identified proteins unique to fibrosarcomas that could be used as targets for such treatment. However, it is expected that new drugs available for other soft tissue sarcomas may be used for fibrosarcomas as well. (Look Hong, *et al*., 2012).

Song, L., Pan, D. & Zhou, R. 2020.
"The main therapeutic strategy for metastatic Myxofibrosarcoma (MFS) is palliative chemotherapy. A number of studies have demonstrated that anti-angiogenic therapy and immunotherapy could improve the survival rate of patients with metastases. However, the effectiveness of the combination of anti-angiogenic therapy and immunotherapy for the therapy of MFS is undetermined. The current study reports a case of metastatic myxofibrosarcoma that was treated with combination Nivolumab (monoclonal antibody, PD-1 inhibitor) and Bevacizumab (monoclonal antibody, anti-VEGF) after progression from the single use of Nivolumab. The aim of the current study is to assess the efficacy and safety of Nivolumab and Bevacizumab for metastatic myxofibrosarcoma and to review the literature. Up to the termination of the follow-up, the patient achieved a partial response for 16 months, had an overall survival for over 29 months since the metastasis and demonstrated a sustained benefit from treatment. The most frequent adverse events were fatigue, abnormality of Alanine aminotransferase (ALT), hypertension and proteinuria. Nivolumab and Bevacizumab treatment indicate beneficial clinical effects and are indicated to be safe to use in patients with metastatic myxofibrosarcoma."

About Clinical Trials
Clinical trials are research studies that involve people. They are conducted under controlled conditions. Only about 10% of all drugs started in human clinical trials become an approved drug.

Clinical trials include:

- Trials to test effectiveness of new treatments
- Trials to test new ways of using current treatments
- Tests new interventions that may lower the risk of developing certain types of cancers
- Tests to find new ways of screening for cancer

The South African National Clinical Trials Register provides the public with updated information on clinical trials on human participants being conducted in South Africa. The Register provides information on the purpose of the clinical trial; who can participate, where the trial is located, and contact details.

For additional information, please visit: www.sanctr.gov.za/

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