Cancer Association of South Africa (CANSA)

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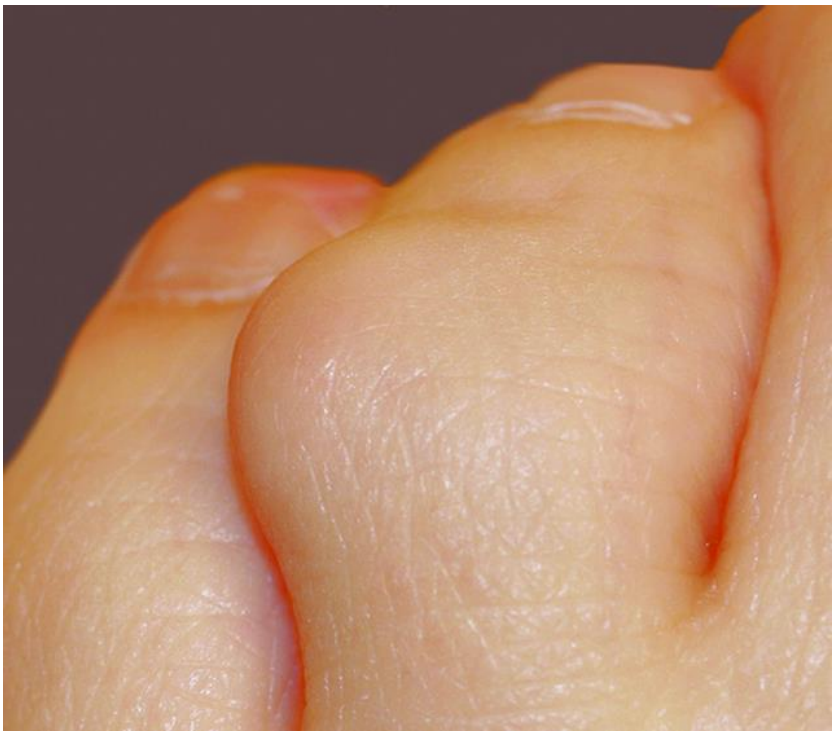
Fact Sheet
on
Myxoinflammatory Fibroblastic Sarcoma

Introduction

Myxoinflammatory Fibroblastic Sarcoma (MFS) is a soft tissue sarcoma. Like other soft tissue sarcomas, it arises in connective tissue - specifically, the connective tissue that surrounds muscles and separates muscles from each other and from skin. An MFS may lie just below the skin or deeper in muscle tissue.



[**Picture Credit**: Myxoinflammatory Fibroblastic Sarcoma of the toe]

MFS is not as well-known or understood as many other types of cancer, partly because the features distinguishing it from another soft tissue sarcoma came into focus only recently. Also, an MFS is often mistaken for a benign tumour and treated as such, by removing only the visible growth. This delays accurate diagnosis and complicates further treatment.

There is generally an equal sex distribution, with some small series showing a very slight male predilection

Myxoinflammatory Fibroblastic Sarcoma

Myxoinflammatory fibroblastic sarcoma is a low grade sarcoma that is composed of a mixed inflammatory infiltrate along with spindled, epithelioid and bizarre appearing cells in a background of hyaline and myxoid zones. Seen affecting the distal extremities commonly, with an equal sex predilection, these tumors are rare and require an extensive immunohistochemical work up for proper diagnosis. They have a tendency to recur.

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Synonyms may include:

- Atypical Myxoinflammatory Fibroblastic Tumour
- Inflammatory Myxohyaline Tumour of the Distal Extremities with Virocyte or Reed-Sternberg-Like Cells
- Inflammatory Myxoid Tumour of the Soft Parts with Bizarre Giant Cells

Myxoinflammatory Fibroblastic Sarcoma (MIFS) is a rare, malignant, soft tissue tumour that is found to be locally aggressive. In a majority of cases, Myxoinflammatory Fibroblastic Sarcoma is found in middle-aged adults. MIFS is known to grow very slowly over several years that it is often mistakenly considered as a benign tumour. Commonly the tumour involves the hands and feet (mostly the fingers). The joints, muscles, and bones may also be affected resulting in associated signs and symptoms. Tumour recurrence is commonly noted. The prognosis of Myxoinflammatory Fibroblastic Sarcoma depends upon several factors including the size and stage of the tumour. Small-sized tumours that are detected early and can be completely removed have a good prognosis

It mainly affects middle-aged persons, and is usually located in the extremities (fingers and hands, for 75% of cases). Clinically, the lesion is infiltrating, pain-free and of slow evolution.

Differential diagnosis:

- Epithelioid Sarcoma
- Hodgkin Lymphoma
- Myxofibrosarcoma
- Pleomoarphic Liposarcoma
- Rosai-Dorfman Disease
- Tenosynovitis

Arbajian, E., Hofvander, J., Magnusson, L. & Mertens, F. 2020.
"Myxoinflammatory fibroblastic sarcoma (MIFS) has recurrent genetic features in the form of a translocation t(1;10)(p22-31;q24-25), BRAF gene fusions, and/or an amplicon in 3p11-12 including the VGLL3 gene. The breakpoints on chromosomes 1 and 10 in the t(1;10) cluster in or near the TGFBR3 and OGA genes, respectively. We here used a combination of deep sequencing of the genome (WGS), captured sequences (Cap-seq), and transcriptome (RNA-seq) and genomic arrays to investigate the molecular outcome of the t(1;10) and the VGLL3 amplicon, as well as to assess the spectrum of other recurrent genomic features in MIFS. Apart from a ROBO1-BRAF chimera in a t(1;10)-negative MIFS-like tumor, no fusion gene was found at RNA-seq. This was in line with WGS and Cap-seq results, revealing variable breakpoints in chromosomes 1 and 10 and genomic breakpoints that should not yield functional fusion transcripts. The most common genomic rearrangements were breakpoints in or around the OGA, NPM3, and FGF8 genes in chromosome band 10q24, and loss of 1p11-p21 and 10q26-qter (all simultaneously present in 6/7 MIFS); a breakpoint in or near TGFBR3 in chromosome 1 was found in four of these tumors. Amplification and overexpression of VGLL3 was a consistent feature in MIFS and MIFS-like tumors with amplicons in 3p11-12. The significant molecular genetic outcome of the recurrent t(1;10) could be loss of genetic material from 1p and 10q. Other recurrent genomic imbalances in MIFS, such as homozygous loss of CDKN2A and 3p- and 13q-deletions, are shared with other sarcomas, suggesting overlapping pathogenetic pathways."

Suster, D., Michal, M., Huang, H., Ronen, S., Springborn, S., Debiec-Rychter, M., Billings, S.D., Goldblum, J.R., Rubin, B.P., Michal, M., Suster, S. & Mackinnon, A.C. 2020.
"Myxoinflammatory fibroblastic sarcoma (MIFS) is a rare, low-grade soft tissue neoplasm preferentially arising in the extremities of young to middle-aged adults characterized histologically by a variegated appearance and absence of a distinctive immunophenotype. Herein we have evaluated a series of 73 cases

of MIFS to define potential features and markers that may facilitate diagnosis. An immunohistochemical study with a large panel of antibodies showed strong positivity of the tumor cells for bcl-1 (94.5%), FXIIIa (89%), CD10 (80%), and D2-40 (56%). FISH and array comparative genomic hybridization (aCGH) were performed in a large subset of cases to investigate the utility for detecting the TGFBR3 and OGA t(1;10) rearrangement and BRAF abnormalities. Using a combination of FISH and/or aCGH, t(1;10) was detected in only 3 of 54 cases (5.5%). The aCGH study also demonstrated amplification of VGLL3 on chromosome 3 that was detected in 8 of 20 cases (40%). BRAF alterations were observed by FISH in 4 of 70 cases (5.7%) and correlated with gain of chromosome 3p12 (VGLL3). A novel fusion transcript involving exon 6 of ZNF335 and exon 10 of BRAF was identified in one case. Demonstration of amplification of VGLL3 on chromosome 3 in combination with expression of bcl-1 and FXIIIa may help support the diagnosis, however, due to their low specificity these markers are not sufficient for a definitive diagnosis in the absence of the appropriate clinical-pathological context. Until a more robust genetic or immunohistochemical signature is identified, the diagnosis of MIFS rests on its characteristic clinicopathological features."

Incidence of Myxoinflammatory Fibroblastic Sarcoma

The National Cancer Registry does not provide any information on the incidence of Myxoinflammatory Fibroblastic Sarcoma in South Africa.

Signs and Symptoms of Myxoinflammatory Fibroblastic Sarcoma

Signs and symptoms may include:

- Painless swelling of affected area
- Swollen area may be nodular in appearance
- Usually cutaneous lesions appearing a plaques

Diagnosis of Myxoinflammatory Fibroblastic Sarcoma

Myxoinflammatory Fibroblastic Sarcomas are low-grade sarcomas with a protracted clinical course, a high rate of local recurrence and a low rate of metastasis. They are rare, painless, low-grade neoplasm which commonly occurs in the extremities. It has a distinctive morphology and can be a diagnostic challenge, simulating inflammatory conditions as well as neoplastic conditions.

An MRI scan may be helpful in reaching a diagnosis.

Wangsiricharoen, S., Ali, S.Z. & Wakely, P.E. Jr. 2021.

Introduction: Myxoinflammatory fibroblastic sarcoma (MIFS) is a rare low-grade sarcoma presenting as a slow-growing mass that occurs mainly in the distal extremities of adults. Relatively little is known about the cytopathology of MIFS. We evaluated cytologic characteristics of MIFS on fine-needle aspiration (FNA).

Materials and methods: A search was made of our cytopathology and surgical pathology databases for cases diagnosed as MIFS. FNA biopsy smears and cell-block were performed and examined using standard technique.

Results: Eight cases were retrieved from patients aged 22-90 years (mean, 56 years), and M:F ratio of 1:1. Six tumors (75%) were primary, and 2 (25%) locally recurrent. Distal lower limb was involved in all but one case (88%). One (13%) recurrent case was correctly diagnosed cytologically as MIFS; remaining single diagnoses were varied: myxofibrosarcoma, low-grade sarcoma, malignant neoplasm, myxoid neoplasm, atypical

fibrohistiocytic neoplasm, atypical cells with chronic inflammation, and spindle cells with atypia. Among 7 cases with available cytologic slides for review, common features were spindle cells with variable atypia (100%), rare virocyte/Reed-Sternberg -like cells (86%), background mixed inflammation (71%), and variable myxoid stroma (57%). Pseudolipoblasts and multinucleated giant cells were rare. Hemosiderin and branching capillaries were largely absent. Immunohistochemistry was non-specific.
Conclusion: MIFS was accurately interpreted in only 13% of cases; remaining cases were diagnosed as atypical or malignant, which would lead to proper management. A specific cytologic diagnosis of MIFS using FNA is extremely difficult in our experience due to an absence of distinctive cytomorphology and specific immunophenotype.

Treatment of Myxoinflammatory Fibroblastic Sarcoma
Therapy may include:

- Excision of lesion
- Amputation
- Limited use of radiotherapy
- Limited use of chemotherapy.

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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Myxoinflammatory Fibroblastic Sarcoma
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