Cancer Association of South Africa (CANSA)

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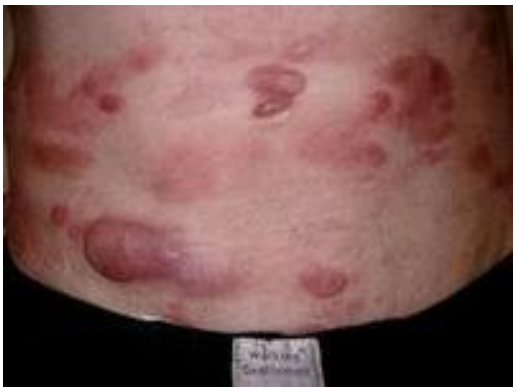
Fact Sheet
on
Mycosis Fungoides

Introduction

Mycosis fungoides, also known as Alibert-Bazin syndrome or granuloma fungoides, is the most common form of cutaneous T-cell lymphoma. It generally affects the skin, but may progress internally over time. Symptoms include rash, tumours, skin lesions, and itchy skin. While the cause remains unclear, most cases are not genetic or hereditary. It occurs mostly in people over 20 years of age, and it is more common in men than women.



[Picture Credit: Mycosis Fungoides]

Mycosis Fungoides (MF)

Mycosis Fungoides is a type of T-cell Lymphoma. Lymphoma is the most common type of blood cancer. The two main forms of lymphoma are Hodgkin's lymphoma and non-Hodgkin's lymphoma (NHL). Lymphoma occurs when cells of the immune system called lymphocytes, a type of white blood cell, grow and multiply uncontrollably. Cancerous lymphocytes can travel to many parts of the body, including the lymph nodes, spleen, bone marrow, blood, or other organs, and form a mass called a tumour. The body has two main types of lymphocytes that can develop into lymphomas: B-lymphocytes (B-cells) and T-lymphocytes (T-cells).

T-cell lymphomas account for approximately 15 percent of all NHLs. There are many different forms of T-cell lymphomas, some of which are extremely rare. Most T-cell lymphomas can be classified into two broad categories: aggressive (fast-growing) or indolent (slow-growing). One of the most common forms of T-cell lymphoma is cutaneous T-cell lymphoma (CTCL), a general term for T-cell lymphomas that involve the skin. CTCL also can involve the blood, the lymph nodes, and other internal organs. Symptoms can include dry skin, itching (which can be severe), a red rash, and enlarged lymph nodes. The disease affects men more often than women and usually occurs in men in their 50s and 60s – usually after the age of 20 although children have been diagnosed with the condition.

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Early in the course of disease, skin lesions may be non-specific, so confusion with benign (non-cancerous) conditions is common. Over time, Mycosis Fungoides becomes more aggressive, and in about 20 per cent of patients the disease will undergo a transformation to highly malignant lymphoma with widespread dissemination into various organs of the body. Late-stage disease is associated with the decline of the immune system. Death often results from systemic infection, especially with *Staphylococcus aureus* or *Pseudomonas aeruginosa*, and other organisms.

Signs and Symptoms of Mycosis Fungoides (MF)

Mycosis fungoides is the most common form of cutaneous T-cell lymphoma (CTCL). It does not look the same for all patients. This form of CTCL may present itself as patches, plaques or tumours.

Mycosis fungoides - typically presents with flat, red, scaly patches that are often mistaken for eczema, psoriasis or non-specific dermatitis. Plaques are thicker, raised lesions. Tumours are raised bumps, which may or may not ulcerate (break down). A common characteristic is itching, although some patients do not experience itching. It is possible to have one or all three types of presentations.

Sezary syndrome - is another common form of CTCL, and is considered an advanced, variant of mycosis fungoides, which distinguishes itself by the presence of malignant lymphocytes in the blood.

Incidence of Mycosis Fungoides (MF) in South Africa

The National Cancer Registry (2014) does not provide any information on the incidence of Mycosis Fungoides.

According to the National Cancer Registry (2014) the following number of Non-Hodgkin's Lymphoma cases were histologically diagnosed in South Africa during 2014:

Group - Males 2014	Actual No of Cases	Estimated Lifetime Risk	Percentage of All Cancers
All males	932	1:221	2,53%
Asian males	36	1:182	3,84%
Black males	533	1:331	4,81%
Coloured males	89	1:189	2,11%
White males	274	1:113	1,33%

Group - Females 2014	Actual No of Cases	Estimated Lifetime Risk	Percentage of All Cancers
All females	870	1:296	2,30%
Asian females	39	1:206	3,28%
Black females	492	1:448	3,06%
Coloured females	91	1:205	2,22%
White females	249	1:156	1,52%

Geller, S., Lebowitz, E., Pulitzer, M. & Myskowski, P.L. 2019.
"Incidence rates of cutaneous T-cell lymphomas (CTCL) and mycosis fungoides (MF) are higher among African American (AA) than white individuals in the United States of America. Population-based registries and single center retrospective studies have shown that AAs present with earlier onset and more advanced disease in comparison to white patients."

Diagnosis of Mycosis Fungoides (MF)
Mycosis fungoides (MF), the most common cutaneous T-cell lymphoma, is a low-grade cutaneous lymphoma characterised by skin-homing CD4+ T cells. It is notable for highly symptomatic progressive skin lesions, including patches, plaques, tumours, and erytheroderma, and has a poorer prognosis at later stages. Diagnosis remains difficult owing to MF's nonspecific skin presentation and identification of the optimal treatment strategy is challenging given the paucity of controlled trials and numerous and emerging treatment options (Galper, *et al*.).

In most cases of mycosis fungoides, the diagnosis is reached owing to its clinical features, disease history, and histomorphologic and cytomorphologic findings. An additional diagnostic criterion to distinguish CTCL from inflammatory skin conditions is demonstration of a dominant T-cell clone in skin biopsy specimens by a molecular assay (i.e., Southern blot, polymerase chain reaction [PCR]). Genetic testing may also be considered.

The following laboratory tests may be included in the diagnostic workup:
- Complete blood count with differential; review the buffy coat smear for Sézary cells
- Liver function tests: Look for liver-associated enzyme abnormalities
- Uric acid and lactate dehydrogenase levels: These are markers of bulky and/or biologically aggressive disease
- Flow cytometric study of the blood (include available T-cell–related antibodies): To detect a circulating malignant clone and to assess immunocompetence by quantifying the level of CD8-expressing lymphocytes
- Human immunodeficiency virus (HIV) and human T-lymphotropic virus type 1 (HTLV-I) testing
- Imaging studies
  - Chest radiography: To determine whether there is lung involvement
  - Abdominal/pelvic computed tomography (CT) scanning: In patients with advanced mycosis fungoides (stage IIB to IVB) or those with clinically suspected visceral disease
  - Positron emission tomography (PET) scanning: To determine visceral involvement

Staging of Mycosis Fungoides (MF)
Staging describes the severity of a person's cancer based on the size and/or extent (reach) of the original (primary) tumour and whether or not cancer has spread in the body. Staging helps the doctor plan the appropriate treatment.

Treatment of Mycosis Fungoides (MF)
Although one may be managed by a general dermatologist, MF is such a rare disease that treatment by a team of specialists is more appropriate.

The treatment team ideally should consist of physicians from different medical specialties:

- dermatologist who specialises in lymphoma
- medical oncologist
- radiation oncologist
- dermatopathologist

The simplest way to think about the multiple treatments available for MF is by dividing them into two categories: skin-directed therapies versus systemic therapies.

Skin-directed therapies are aimed at the skin primarily. The major treatments in this category include topical chemotherapy agents (nitrogen mustard or Mustargen), topical corticosteroids, topical retinoids (Targretin gel), phototherapy (PUVA, UVB), and electron beam radiation.

Lovgren, M.L. & Scarisbrick, J.J. 2018.
"Mycosis fungoides (MF) represents the majority of the primary cutaneous T-cell lymphomas (CTCL). Most have early stage MF with localised patches and plaques, which has a favourable survival outcome, but nearly a quarter progress to late stage with tumours, erythroderma, and systemic involvement. Management is based on stage directed treatment with early stage MF (IA-IIA) using skin directed therapies (SDTs), including topical corticosteroids (TCS), chlormethine or retinoids, phototherapy, and radiotherapy (localised or total skin electron beam therapy). Advanced stages (IIB-IVB) or refractory MF often requires systemic treatments which may be used in combination with SDTs. These are primarily employed as a palliative approach, aiming to provide symptomatic relief. For advanced patients achieving a complete or near complete response (CR) with a good performance status may be considered for allogeneic bone marrow transplantation."

Systemic therapies are administered by mouth or injection and are aimed at treating the skin and/or internal organs affected or at risk. These include chemotherapy agents and biologic response modifiers (oral retinoids, interferons, fusion proteins, or extracorporal photopheresis).

Commonly, multiple treatments may be used together, which is called Combined Modality Therapy (CMT).

For each treatment option, the following paragraphs include information on treatment indications, practical use of the therapy, and potential side effects.

Whole Body Radiation and Local Radiation - mycosis fungoides is very sensitive to radiation.

Johnson, W.T., Mukherji, R., Kartan, S., Nikbakht, N., Porcu, P. & Alpdogan, O. 2018.
"Mycosis fungoides and Sézary syndrome encompass over 70% of all cases of cutaneous T-cell lymphoma (CTCL). While early stage disease has excellent long-term survival rates, advanced stage disease (IIB-IV) carries a poor prognosis with a median 5-year overall survival rate of approximately 50%. Early stage and advanced stage disease have different treatment algorithms with systemic therapy being indicated upfront in the later. The role of allogeneic hematopoietic stem cell transplant (HSCT) has gained considerable interest in recent years as a treatment option for CTCL given the increasingly promising long-term outcomes in an otherwise incurable disease."

Oral retinoids - retinoids are a class of drugs that are derivatives of vitamin A. These medications are effective in MF because they can change the growth and maturation pattern of MF cells.

Systemic chemotherapy agents - systemic chemotherapy agents are usually reserved for MF that have failed skin-directed or systemic biologic therapies or have disease that extended to lymph nodes or other internal organs.

Stem Cell Transplant

Foss, F.M. & Girardi, M. 2017.

"Mycosis fungoides and the Sezary syndrome (SS) are rare lymphomas of $CD4^+$ helper T cells. There is stagewise progression from patch/plaques to thicker tumor lesions/diffuse erythroderma. Blood involvement is a characteristic of SS. Outcomes are related to the extent of skin, blood, lymph node, and visceral organ involvement. Patients with limited patch and plaque disease are treated with skin-directed therapies. More advanced/refractory disease is treated with skin-directed therapies and oral or systemic immunomodulatory agents. Single-agent chemotherapies are used against tumors, refractory plaques, and lymph node and visceral involvement. Allogeneic stem cell transplantation is a potentially curative strategy for advanced/resistant disease."

Larocca, C. & Kupper, T. 2019.

"Cutaneous T-cell lymphomas are a heterogeneous collection of non-Hodgkin lymphomas that arise from skin-tropic memory T lymphocytes. Among them, mycosis fungoides (MF) and Sézary syndrome (SS) are the most common malignancies. Diagnosis requires the combination of clinical, pathologic, and molecular features. Significant advances have been made in understanding the genetic and epigenetic aberrations in SS and to some extent in MF. Several prognostic factors have been identified. The goal of treatment is to minimize morbidity and limit disease progression. However, hematopoietic stem cell transplantation, considered for patients with advanced stages, is the only therapy with curative intent."

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/

Medical Disclaimer

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