Mycosis Fungoides and Sezary Syndrome

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KEYWORDS

• Mycosis fungoides • Sezary syndrome • T-cell lymphoma • Immunotherapy
• Allogeneic stem cell transplantation

KEY POINTS

- Mycosis fungoides (MF) and the Sezary syndrome represent a heterogenous group of presentations and is incurable for the majority of patients.
- The disease can be difficult to diagnose in its earliest stages because it may mimic a number of benign skin disorders.
- The International Society of Cutaneous Lymphoma has established criteria for diagnosis of early stage MF.
- In its advanced stages the disease is in incurable and patients are often treated with a multimodality approach with skin-directed and systemic agents.

Mycosis fungoides (MF) and the Sezary syndrome (SS) are the most common forms of cutaneous T-cell lymphoma. The World Health Organization and European Organization for Research and Treatment of Cancer classification of primary cutaneous lymphomas distinguishes MF and SS from other types of cutaneous T-cell lymphomas[1] (**Box 1**). The overall incidence of MF/SS according to the Surveillance, Epidemiology, and End Results registry is approximately 4 per 1 million. According to a recent review of Surveillance, Epidemiology, and End Results data, 1713 patients were diagnosed with MF from 2004 to 2008.[2] The mean age for patients at the time of diagnosis is between 40 and 60 years of age, but the disease has been reported in children. MF is more common in males, and is seen more frequently in African Americans relative to Caucasians. The disease presents at a younger age in non-Caucasians and is more likely to present in an advanced stage in African Americans.[2]

The etiology of MF/SS is not well-understood, but there has been consideration of a potential association with conditions leading to chronic antigenic stimulation or

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Box 1
World Health Organization–European Organization for Research and Treatment of Cancer classification of cutaneous lymphomas with primary cutaneous manifestations

Cutaneous T-cell and NK cell lymphomas
- MF
- MF variants and subtypes
  - Folliculotropic MF
  - Pagetoid reticulosis
  - Granulomatous slack skin
- Sezary syndrome
- Adult T-cell leukemia/lymphoma
- Primary cutaneous $CD30^+$ lymphoproliferative disorders
  - Primary cutaneous anaplastic large cell lymphoma
  - Lymphomatoid papulosis
- Subcutaneous panniculitis-like T-cell lymphoma
- Extranodal NK/T-cell lymphoma, nasal type
- Primary cutaneous peripheral T-cell lymphoma, unspecified
  - Primary cutaneous aggressive epidermotropic $CD8^+$ T-cell lymphoma (provisional)
- Cutaneous γ/δ T-cell lymphoma (provisional)
- Primary cutaneous $CD4^+$ small/medium-sized pleomorphic T-cell lymphoma (provisional)

Cutaneous B-cell lymphomas
- Primary cutaneous marginal zone B-cell lymphoma
- Primary cutaneous follicle center lymphoma
- Primary cutaneous diffuse large B-cell lymphoma, leg type
- Primary cutaneous diffuse large B-cell lymphoma, other
  - Intravascular large B-cell lymphoma

Precursor hematologic neoplasm
- $CD4^+/CD56^+$ hematodermic neoplasm (blastic NK-cell lymphoma)

Abbreviations: MF, mycosis fungoides; NK, natural killer.
Data from Willemze R, Jaffe ES, Burg G, et al. WHO-EORTC classification for cutaneous lymphomas. Blood 2005;105:3768–85.

pesticide and chemical exposure.[3] Although there is no known geographic clustering and no evidence of maternal transmission of the disease, MF/SS has been reported in a small number of families.

ETIOLOGY AND BIOLOGY OF MYCOSIS FUNGOIDES AND THE SEZARY SYNDROME

The malignant T cell in MF/SS is derived from a mature $CD4^+$ $CD45RO^+$ memory T cells that express adhesion molecules such as CCR4 and CLA. The circulating malignant Sezary cells have a different phenotype in that they express CCR7 and L-selectin.[4] Skin homing is characteristic of Sezary cells and epidermotropism, is a characteristic feature of the disease, along with Pautrier's microabscesses, which are intraepidermal collections of malignant cells. Immunohistochemistry of the infiltrating malignant T lymphocytes often shows diminished expression or loss of common T-cell antigens, such as CD7, CD5, CD26, or CD2 and dim expression of CD3. Immunosuppression with aberrant T-cell presentation, cutaneous anergy, and increased susceptibility to bacterial and opportunistic infections is a characteristic of the disease.[5,6]

Although there is not a classic chromosomal translocation in MF and SS, significant chromosomal instability has been noted. Losses on 1p, 10q, 13q, and 17p and gains of 4, 17q, and 18 have been identified.[7,8] Genetic instability has been characterized