

# Cutaneous Lymphomas: Types, Diagnosis, And Treatment

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## Introduction

Cutaneous lymphomas represent a varied spectrum of malignant lymphocytes predominantly affecting the skin, often presenting with symptoms that can mimic benign dermatological conditions, potentially leading to diagnostic delays [1]. Mycosis fungoides (MF) and Sézary syndrome (SS) are recognized as the most common forms of primary cutaneous T-cell lymphomas (CTCLs), with early MF stages manifesting as eczematous or psoriatic patches and advanced stages presenting as plaques, tumors, or erythroderma [1]. Sézary syndrome is notably characterized by generalized erythroderma, lymphadenopathy, and the presence of circulating atypical T-cells known as Sézary cells [1].

Mycosis fungoides is the most prevalent type of primary cutaneous T-cell lymphoma and can present in a deceptively benign manner, often resembling common inflammatory dermatoses like eczema or psoriasis [2]. Key diagnostic indicators include persistent, pruritic skin lesions with morphologies such as patches, plaques, and eventually tumors, with the 'three Ps'—patches, plaques, and pruritus—being suggestive, though not definitive [2].

Sézary syndrome, a leukemic variant of CTCL, is distinguished by a triad of generalized erythroderma, persistent lymphadenopathy, and circulating neoplastic T-cells (Sézary cells) with a specific abnormal phenotype (CD4+/CD26-) [3]. The erythroderma in SS is frequently intense and pruritic, significantly impairing the skin barrier and causing substantial discomfort [3].

Dermatopathology plays a fundamental role in the diagnosis of cutaneous lymphomas, with biopsies providing essential tissue for histopathological examination and immunophenotyping [4]. Early MF can exhibit non-specific inflammatory changes, necessitating meticulous evaluation for epidermotropism, Pautrier microabscesses, and dermal lymphocytic infiltration [4].

Phototherapy, particularly narrowband ultraviolet B (NB-UVB) and psoralen plus ultraviolet A (PUVA), serves as a primary treatment modality for early to intermediate-stage mycosis fungoides [5]. NB-UVB is often favored due to its superior tolerability and safety profile compared to PUVA, with both methods demonstrating effectiveness in achieving remission [5].

Systemic therapies are crucial for managing advanced or refractory cutaneous lymphomas, with agents like bexarotene, interferons, and histone deacetylase inhibitors being employed for MF and SS [6]. Bexarotene has shown efficacy in inducing remission, while interferons offer antiproliferative and immunomodulatory benefits [6].

Cutaneous B-cell lymphomas (CBCLs), which originate from B-lymphocytes, differ from CTCLs and commonly include primary cutaneous follicle center lymphoma (PCFCL) and primary cutaneous marginal zone lymphoma (PCMZL) [7]. PCFCL typically appears as papules, plaques, or nodules, often on the head and neck,

while PCMZL usually presents as multiple papules or plaques on the trunk and extremities [7].

Allogeneic stem cell transplantation (allo-SCT) is a therapeutic option for advanced-stage cutaneous lymphomas that are refractory to conventional treatments, offering a potential cure through graft-versus-lymphoma (GvL) effects [8]. However, allo-SCT carries significant risks, including graft-versus-host disease (GVHD), infections, and treatment-related mortality [8].

Ongoing research in cutaneous lymphoma is crucial for improving patient outcomes, with recent advancements focusing on targeted therapies and immunotherapies [9]. Novel agents targeting specific molecular pathways and immunotherapies like checkpoint inhibitors are being investigated for their potential in certain subtypes [9].

The prognosis for cutaneous lymphomas is highly variable, depending critically on the specific subtype, stage at diagnosis, and response to treatment, with early-stage MF generally having an excellent outlook, whereas advanced disease and SS carry a poorer prognosis [10].

## Description

Cutaneous lymphomas encompass a diverse array of malignant neoplasms originating from lymphocytes that predominantly infiltrate the skin. Their clinical presentations can be highly varied, frequently mimicking benign dermatological conditions, which can unfortunately lead to delays in diagnosis [1]. Mycosis fungoides (MF) and Sézary syndrome (SS) stand out as the most prevalent types of primary cutaneous T-cell lymphomas (CTCLs). In its early stages, MF often presents as patches with an eczematous or psoriatic appearance, while more advanced disease can manifest as plaques, tumors, or generalized erythroderma. SS, on the other hand, is characterized by generalized erythroderma, lymphadenopathy, and the presence of circulating atypical T-cells, known as Sézary cells [1].

Mycosis fungoides is indeed the most common form of primary cutaneous T-cell lymphoma and can present in a deceptively benign manner, often masquerading as common inflammatory dermatoses such as eczema or psoriasis [2]. The hallmark diagnostic features include persistent, pruritic skin lesions with characteristic morphology including patches, plaques, and eventually tumors. The combination of 'patches, plaques, and pruritus' is often indicative, although not pathognomonic for the condition [2].

Sézary syndrome, recognized as a leukemic variant of CTCL, is clinically defined by a distinct triad: generalized erythroderma, persistent lymphadenopathy, and the presence of circulating neoplastic T-cells (Sézary cells) exhibiting an abnormal CD4+/CD26- phenotype [3]. The erythroderma associated with SS is typically intense and profoundly pruritic, leading to significant patient discomfort and com-

promised skin barrier function [3].

The role of dermatopathology in the accurate diagnosis of cutaneous lymphomas is paramount, with biopsies, especially serial or excisional ones, providing critical tissue for detailed histopathological examination and immunophenotyping [4]. Early stages of MF may reveal non-specific inflammatory changes, thus requiring careful assessment of epidermal and dermal infiltrates, including the distribution and presence of atypical lymphocytes [4].

Phototherapy, specifically narrowband ultraviolet B (NB-UVB) and psoralen plus ultraviolet A (PUVA), is considered a cornerstone in the management of mycosis fungoides in its early to intermediate stages [5]. NB-UVB is frequently preferred due to its better tolerability and safety profile when compared to PUVA, although both modalities have demonstrated significant efficacy in inducing remission [5].

Systemic therapies play a crucial role in the treatment of advanced or refractory cutaneous lymphomas. For conditions like mycosis fungoides and Sézary syndrome, a variety of agents are utilized, including bexarotene, a retinoid X receptor agonist, interferons (IFN- $\alpha$ ), and histone deacetylase inhibitors (e.g., vorinostat, romidepsin) [6]. Bexarotene has the capacity to induce remission in a notable proportion of patients, while interferons exert antiproliferative and immunomodulatory effects [6].

Cutaneous B-cell lymphomas (CBCLs) are a distinct group of lymphomas arising from B-lymphocytes and are differentiated from CTCLs. The most frequently encountered forms include primary cutaneous follicle center lymphoma (PCFCL) and primary cutaneous marginal zone lymphoma (PCMZL) [7]. PCFCL characteristically presents as solitary or grouped papules, plaques, or nodules, often situated on the head and neck region [7].

The management of advanced-stage cutaneous lymphomas, particularly those that are refractory to conventional therapeutic approaches, may involve allogeneic stem cell transplantation (allo-SCT) [8]. This intensive treatment modality offers the potential for cure by replacing the patient's diseased marrow with healthy donor stem cells and importantly, by harnessing graft-versus-lymphoma (GvL) effects [8].

Understanding the evolving landscape of research in cutaneous lymphomas is essential for achieving improvements in patient outcomes. Recent advancements include the development of targeted therapies and immunotherapies, with novel agents designed to target specific molecular pathways within lymphoma cells currently under investigation [9].

The prognosis associated with cutaneous lymphomas is notably variable and is significantly influenced by the specific subtype, the stage at which the diagnosis is made, and the patient's response to treatment [10]. Early-stage mycosis fungoides, for instance, generally carries an excellent prognosis with long-term survival expected [10].

## Conclusion

Cutaneous lymphomas are a diverse group of skin cancers originating from lymphocytes. Mycosis fungoides (MF) and Sézary syndrome (SS) are the most common types of cutaneous T-cell lymphomas (CTCLs). MF often starts as patches resembling eczema or psoriasis, progressing to plaques or tumors. SS presents with widespread red skin, swollen lymph nodes, and abnormal T-cells in the blood.

Diagnosis relies on clinical assessment, skin biopsies, and immunophenotyping. Early MF is treated with topical therapies and phototherapy. Advanced disease and SS may require systemic agents like retinoids, interferons, or chemotherapy. Allogeneic stem cell transplantation is a treatment option for refractory cases. Cutaneous B-cell lymphomas are a separate category with different presentations and management. Prognosis varies greatly depending on the lymphoma type and stage.

## Acknowledgement

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## Conflict of Interest

None.

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