

## Cutaneous T-Cell Lymphoma: Establishing a Diagnosis in a Patient with a Dramatic Tumor

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### Abstract

Mycosis fungoides is the most common subset of cutaneous T-cell lymphoma. We discuss a rare case of advanced mycosis fungoides that presented as a dramatic tumoral stage lymphoma. Early lesions can often mimic other dermatologic conditions and while the patient was unable to provide a history on early lesions initial diagnosis and mis-treatment for psoriasis may have contributed to a late presentation. In attempting to confirm our suspected diagnosis multiple biopsies and immunohistochemical analysis were required to reach a verdict. This paper emphasizes the importance of compiling a comprehensive picture and the need for persistence when there is inconclusive evidence to establish a diagnosis of mycosis fungoides.

**Keywords:** Mycosis fungoides; T-cell lymphoproliferative disorder; T-cell lymphoma; Cutaneous lymphoma

**Abbreviations:** MF: Mycosis Fungoides; CTCL: Cutaneous T-cell Lymphoma; BSA: Body Surface Area

### Introduction

Mycosis fungoides (MF), the most common subset of cutaneous T-cell lymphoma (CTCL) [1], is one of the great masqueraders in medicine. Despite this, however, the clinical picture can be striking, and persistence is often needed in confirming the diagnosis [1,2]. We present a case of dramatic tumor stage mycosis fungoides. Prior to our encounter with the patient, he had been evaluated and been diagnosed, incorrectly, with psoriasis. Despite various (erroneous) treatment attempts, his cutaneous lesions continued to progress until clearly his clinical manifestations were not psoriatic in nature. Our evaluation required multiple biopsies, including excisional biopsies and repeat immunohistochemistry and immunophenotyping. This eventually confirmed the suspected diagnosis of mycosis fungoides. Although mycosis fungoides may be difficult to diagnose in early stages, multiple factors correlated to this patient's late stage of diagnosis. As early diagnosis is paramount in improving patient survival, this paper demonstrates the need for communication and relentless workups when reconciling clinical with histopathologic findings [2].

### Case Report

Dermatology was consulted on a 62-year-old man for a "flare of psoriasis." The patient was released from prison one-month prior and was currently living in a halfway house. He reported that during his incarceration he was evaluated by many physicians (including dermatologists); he underwent several biopsies and was ultimately diagnosed with psoriasis. The patient was treated with multiple oral prednisone tapers (inconsistent with his stated diagnosis of psoriasis), completing his most recent course one-month prior to admission. Other treatments included methotrexate (discontinued due to leukopenia) and apremilast, initiated by his primary care physician just prior to this admission. His medical history was otherwise unremarkable.

Physical examination revealed an erythrodermic man with multiple grossly apparent erythematous, soft, non-tender nodules, plaques, and tumors involving the chin, upper lip, cheek, and forehead (Figure 1). Trunk and extremities were involved as well (Figure 2). The occipital scalp was involved with similar larger lesions, some with a central eschar



**Figure 1:** Mucinous, erythematous, non-tender tumors and plaques involving the face, scalp, and ears bilaterally.



**Figure 2:** Large confluent erythematous plaques with some overlying scale and crust extensively involving the patients back.

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**Figure 3:** Multiple large soft tumors of the occipital scalp.



**Figure 4:** Erythematous tumor of the distal left dorsal forearm with slight overlying scale that had significantly increased in size.



**Figure 5:** Large non-tender ulceration with serous discharge over right medial thigh. Surrounding vivid erythema from adhesive for occlusive dressing.

(Figure 3). Smaller erythematous plaques with micaceous scale were also noted on the extremities. Lymphadenopathy was not appreciated on physical examination. Upon further questioning, the patient acknowledged a 30-pound unintentional weight loss and drenching night sweats. Human immunodeficiency virus testing and purified protein derivative were negative within the last year, and a complete blood count with differential was entirely within normal limits.

One punch biopsy from the leg confirmed psoriasiform dermatitis. However, a second punch biopsy of tumoral skin on the cheek showed intraepidermal pustular dermatitis and follicular hyperplasia with minimal mucin. Two more biopsies, from the scalp and forehead obtained one week later, showed similar findings. Periodic acid-Schiff, Grocott methanamine silver, Acid-Fast bacilli, and Warthin-Starry stains were negative for microorganisms. Initial immunohistochemistry revealed only scattered dermal T cells without epidermotropism,

further immunophenotyping was not done on the initial specimen. Colloidal iron and Alcian blue stains confirmed minimal mucin. These findings were felt to be non-diagnostic, though clinical findings were highly suspicious for tumor stage mycosis fungoides.

The patient returned two months after discharge with worsening clinical findings, including a 7 cm erythematous firm nodule on the left forearm (Figure 4) and enlargement of the head and neck tumors with increased serous drainage. He also developed an ulcer on the right thigh (Figure 5), and more indurated plaques on the trunk and extremities.

Two excisional biopsies from the left abdomen and right thigh revealed numerous abnormal lymphocytes with irregular hyperchromatic nuclei infiltrating the epidermis. Immunostaining revealed predominantly T-cells being CD3, CD4, CD7, and CD45 positive, while CD5 and CD8 negative. Additionally molecular genetic analysis revealed a positive T-cell gene rearrangement. This, combined with the clinical picture yielded a diagnosis of epidermotropic T-cell lymphoma, finally confirming the suspected tumor stage mycosis fungoides. T-cell gene rearrangement also confirmed a clonal T-cell population. Surprisingly, a third specimen from the right arm sent for flow cytometry revealed a Kappa-restricted B-cell lymphoproliferative disorder with no T-cell abnormality.

The patient was subsequently referred to an oncologist, who agreed with the diagnosis of cutaneous T-cell lymphoma. Full body computed tomography scans showed no lymphadenopathy. He began treatment with vincristine, cyclophosphamide, and prednisone. He remains in treatment at the time of publication.

## Discussion

Primary cutaneous lymphomas have an incidence of 1 per 100,000 in the United States with primary cutaneous T-cell lymphomas outnumbering B-Cell lymphomas at a rate of three to one [1]. Males are affected more commonly with average age of onset after 50 years. Mycosis fungoides, also known as Alibert-Bazin syndrome, is the most prevalent of the CTCLs, accounting for up to 50% of cases [1]. Although the etiology is unknown, multiple possible triggers, including genetic, environmental, and infectious, have been postulated. One hypothesis is that of persistent antigen stimulation, suggesting that various exogenous sources including *Staphylococcus aureus* super toxin or even glass exposure may induce a malignant T-cell clone through chronic stimulation. Additionally, viral induction has been observed to stimulate malignant T-cell populations, particularly human T-cell lymphotropic virus type 1 [2].

Diagnosis of MF relies on histopathologic and immunohistochemical findings. However, MF can be difficult to diagnose in early stages as clinical manifestations and biopsy findings can be subtle and similar to other benign skin conditions including psoriasis and atopic dermatitis [2]. Classic histopathologic findings include lymphocytes infiltrating the epidermis (epidermotropism), atypical lymphocytes with cerebriform nuclei [2], small aggregates of atypical lymphocytes in association with Langerhans cells (*Pautrier microabscesses*) [2,3], and increasing size of lymphocytes as they migrate towards the granular layer of the epidermis [2]. Pautrier microabscesses are seen in less than a quarter of patients with early MF and atypical lymphocytes are seen in less than 10% [4].

Clinical findings include progressive patches and thin plaques, distribution on photoprotected areas, variable size and shape, and poikiloderma [5]. Arcuate lesions, plaques with atrophy, and associated alopecia are commonly seen as well. Involvement of the palms and soles

is rare and can contribute to misdiagnosis, particularly of psoriasis (as in our patient) [6]. Neoplastic T-cells in MF are most often CD4+, with an increased CD4 to CD8 ratio. Loss of CD7 and/or CD5 also occurs commonly [3]. Cellular and molecular markers can be variable, and dual expression of CD3 and CD20 can highlight a rare CD20+ T-cell [7]. T-cell receptor gene rearrangement studies showing a clonal T-cell population have also been useful in diagnosing MF [8], but benign dermatoses and spongiotic dermatitis can show similar rearrangements [4]. The finding of a concomitant B-cell lymphocyte population can be seen in some patients with MF. This finding, although occasionally seen in non-transformed MF, is more commonly seen after transformation of MF to large cell lymphoma, which by definition requires large cells to exceed 25% of the infiltrate seen on histopathology [9,10]. In addition, immunophenotyping of a B-cell population in one patient with MF has also revealed underlying B-cell chronic lymphocytic leukemia [11].

Classic MF progresses clinically from patch, to plaque, to tumor stages; in reality, this clear progression is not always observed [3]. The patch stage presents as asymmetric scaly erythematous patches involving the buttocks, breast and flexural areas (the “bathing suit distribution”). Lesions are often asymptomatic and transitory with non-scarring, spontaneous resolution [4]. Fewer than 10% of patients with patch stage disease have been reported to progress to more advanced stages, and long term survival was similar to a matched control population [12]. In the plaque stage, lesions are infiltrative, scaly, sharply-demarcated red-brown plaques which may coalesce and involve much of the body. The tumor stage is characterized by tremendous vertical growth and can be dramatic in appearance. Lesions are often large brown to blue-red nodules and tumors that may ulcerate. The leukemic phase of CTCL, Sezary syndrome, is an aggressive variant with a poor prognosis. Classically, it manifests as a triad of erythroderma, lymphadenopathy, and clonal neoplastic T-cells with cerebriform nuclei (Sezary cells) in the peripheral circulation. Diagnosis requires an absolute Sezary cell count of at least 1000 cells/microliter with a CD4 to CD8 ratio greater than 10 to 1 [3,6]. Multiple other subtypes have been described including (but not limited to) folliculotropic MF, granulomatous slack skin, and pagetoid reticulosis [2].

Treatment of CTCL is determined based on the stage of presentation. While patch/plaque stage involving less than 10% of body surface area (BSA) may theoretically be closely observed, topical therapies (corticosteroids, BCNU/carmustine, or mechlorethamine) and phototherapy (narrowband UVB or PUVA) are necessitated when involvement is greater than 10% BSA or if there is associated lymphadenopathy. Topical and systemic retinoids (i.e., tazarotene, bexarotene) are another option at the patch and plaque stage. Options for tumor stage MF include total skin electron beam therapy, systemic chemotherapy, alpha-interferon, or newer agents including vorinostat, a histone deacetylase inhibitor. PUVA or extracorporeal photopheresis, either with alpha-interferon or methotrexate, are options for cases of Sezary syndrome. Any visceral involvement requires both radiotherapy and chemotherapy [6,13].

Prognosis is directly related to subtype and tumor stage [6]. With classic MF, survival is inversely related to the stage of the disease [1,3]. Five-year survival for classical MF is up to 97.3% when <10% of the BSA is affected by patches and plaques, but declines to 27.6% if tumorous lesions exist [1]. Granulomatous slack skin disease has an excellent prognosis, in contrast to folliculotropic MF, which portends to the worst prognosis with 5-year survival rates between 60% and 70% [3].

## Conclusion

This case demonstrates the importance of clinical, histologic, and

immunophenotypical findings in a patient with mycosis fungoides. Multiple biopsies were obtained from our patient over the course of months and required a second immunohistochemical analysis to confirm a diagnosis of cutaneous T-cell lymphoma even with an impressive and advanced clinical presentation. Immunophenotyping on the initial specimen could have led to earlier diagnosis. His unfortunate social situation, prior misdiagnosis, improper treatment, and poor follow-up likely also contributed to his delay. While his workup and clinical picture prior to our care is unclear it is important to emphasize that any lesion suspicious for mycosis fungoides should undergo biopsy and immunohistochemistry to establish diagnosis as early as possible. As the prognosis for patients with MF is inversely related to the stage of disease, identifying early lesions is paramount. In any case where the initial pathology report does not fit the suspected clinical diagnosis, or in cases of benign spongiotic or psoriasiform eruptions that do not respond to typical therapy, the astute dermatologist must be persistent in communicating with the dermatopathologist, repeating biopsies, and obtaining appropriate tissue samples for further investigation.

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