

Eruptive squamous cell carcinomas in an erythrodermic patient



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INTRODUCTION

The erythrodermic patient presents a diagnostic challenge to dermatologists as the differential diagnosis is broad, and numerous biopsies are often required before a diagnosis is made. The greatest concern is that such erythroderma could represent an evolving cutaneous T-cell lymphoma (CTCL) (Mycosis fungoides [MF] or Sézary Syndrome) or a paraneoplastic finding indicative of another underlying malignancy. MF is the most common CTCL, affecting approximately 6.6/100,000 people in the United States.¹ The global incidence of CTCL is rising, with men having a two-fold increased risk for disease when compared with women.² The clinical manifestations of MF are heterogeneous, usually with a prolonged, persistent course, with treatments aimed at control rather than cure.³

CASE DESCRIPTION

An 80-year-old male presented with a 6-month history of a pruritic, scaly, erythematous eruption, which previously failed to respond to triamcinolone. His past medical history included prostate cancer, non-melanoma skin cancer, gout, and atopic dermatitis. On examination, widespread erythroderma was present along with hyperkeratotic palmar and pedal surfaces (Fig 1). Initial biopsies of the involved areas showed spongiotic dermatitis with eosinophils, with similar findings upon several repeat biopsies. Initial flow cytometry studies of peripheral blood and thoraco-abdominal computed tomography scan were unremarkable. He was started on methotrexate, which he received for 7 months without notable improvement in his symptoms.

At this point, our patient began developing numerous biopsy-proven invasive and superficial squamous cell carcinomas (SCCs) (Fig 2). The

Abbreviations used:

CTCL: cutaneous T-cell lymphoma
 MF: mycosis fungoides
 SCC: squamous cell carcinoma

suspicious lesions presented as hyperkeratotic, erosive, crusty papules, including on the mucosa (Fig 3). None of the lesions presented as keratoacanthoma-type lesions. While he had a prior history of non-melanoma skin cancer, the rapidity and number of newly arising SCCs was a new observation. Over the next 2 years, our patient developed 3 SCCs per month on average, necessitating multiple excisional and destructive procedures to reduce his cutaneous cancer load. 5-fluorouracil topically was tried briefly but was too uncomfortable for the patient in the setting of his erythroderma. Acitretin was initiated in an attempt to both treat the erythroderma as well as for chemoprevention of the developing SCCs; however, he continued to develop 2-3 SCCs per month.

Two years after initial presentation, our patient's pruritic and erythrodermic symptoms were still unresolved, with the added burden of the onset of numerous SCCs requiring therapy. Repeat biopsies were collected, which showed an epidermotropic proliferation of atypical lymphocytes (Fig 4). The cellular infiltrate was predominantly CD3⁺/CD4⁺ with loss of CD7. C-C chemokine receptor type 4 staining was not performed. Molecular studies from this skin biopsy revealed the presence of a T-cell receptor clone. Other than a slight eosinophilia, peripheral blood analysis, including flow cytometry, did not demonstrate any notable abnormalities. Flow cytometric studies were not performed on the tissue

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Fig 1. Clinical presentation with widespread scaling and erythroderma. Biopsy at this stage showed eosinophilic spongiotic dermatitis.

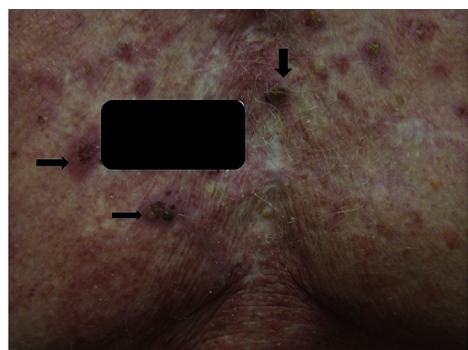


Fig 2. Hyperkeratotic, erosive papules on the chest (arrows) showing moderately differentiated invasive SCC upon biopsy. Background erythroderma is evident on the chest. SCC, Squamous cell carcinoma.

from skin biopsies. Repeat thoraco-abdominal CT scans were unremarkable.

Based on the persistent erythroderma and the atypical T-cell infiltrate with demonstrable clonality, it was determined that our patient had MF, stage III. Treatment options were limited, as many modalities would exacerbate his SCC tumor burden. He finished 2 cycles of mogamulizumab without improvement in his erythroderma, while continuing to develop numerous squamous cell neoplasms. He and his family have elected to forego any further therapy other than topical steroids at this time.

DISCUSSION

Our patient presented with erythroderma with an eventual diagnosis of MF. Prior to the detection of an atypical T-cell infiltrate in his skin, he began developing numerous moderately-to-poorly differentiated, invasive SCCs, as if he were functionally immunosuppressed. Patients with MF/Sézary syndrome regularly develop severe immunodeficiency during disease progression, and often die of infection rather than tumor burden.⁴ The identification



Fig 3. A poorly differentiated SCC on the lower lip, with confluent erythroderma visible on the face and neck. SCC, Squamous cell carcinoma.

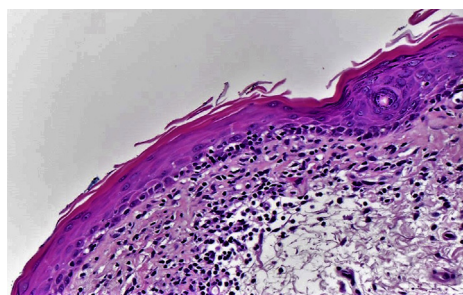


Fig 4. A representative biopsy from our patient 2 years after onset of erythroderma now showing a band-like infiltrate of atypical lymphocytes abutting the dermal-epidermal junction with evidence of epidermotropism. The lymphocytes were CD3⁺/CD4⁺ and CD7⁻. Molecular studies from this section demonstrated T-cell receptor clonality. (Original magnification: $\times 20$.)

of immunosuppressive regulatory T cells in some cases of MF spurred a number of studies, but results were discordant. The normal T cells in patients with erythrodermic CTCL have been shown to be markedly suppressed, being displaced by the malignant T cells, which can be difficult to identify with routine techniques.⁵ SCCs arising subsequent to certain treatments of MF, such as topical nitrogen mustard, total skin electron beam therapy, psoralen UVA light, or X-ray irradiation are well-recognized, but usually occur many years post-therapy.^{6,7}

Thus far, only one case in the literature demonstrates the concomitant appearance of MF and SCCs without the cause and effect relationship of MF treatment followed by SCC development. This case differs from ours in that the patient was a middle-aged man with type IV skin who had no documented history of skin cancers and no apparent risk factors pre-disposing him toward developing SCCs prior to his MF diagnosis.⁸ Both MF and Sézary Syndrome have been considered to be T-helper cell type 2 diseases which may

contribute to the infectious disease susceptibility of these patients.⁹

We postulate that the eruptive SCCs occurring in conjunction with erythroderma in this patient were an early paraneoplastic clue to his functional immunosuppression and eventual diagnosis of MF. Our case further suggests that additional study is required to determine the extent to which immunosuppression affects patients diagnosed with MF.

Conflicts of interest

None disclosed.

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