

# Cutaneous squamous cell carcinoma arising within a mycosis fungoides patch: Case report and review of the literature



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**Key words:** cutaneous squamous cell carcinoma; cutaneous T-cell lymphoma; mycosis fungoides.

## INTRODUCTION

Mycosis fungoides (MF) is the most common type of primary cutaneous T-cell lymphoma (CTCL) and is defined as clonal proliferation of skin-infiltrating atypical T lymphocytes. Patients with MF have increased risk for both primary hematologic malignancies and secondary solid tumors.<sup>1</sup> However, the development of squamous cell carcinoma (SCC) in skin that is affected by MF is extremely rare. The majority of previously reported cases of SCC in patients with MF have been described following treatment with skin-directed therapies, including topical nitrogen mustard, total skin electron beam radiation, psoralen and ultraviolet A treatment, and narrow-band ultraviolet B therapy.<sup>2</sup>

Here, we present a patient who developed an SCC within a patch of long-standing MF with no prior local or systemic therapy.

## CASE REPORT

A 70-year-old man with a 24-year-long history of stage Ia (T1N0M0B0; TNMB staging by the European Organization of Research and Treatment of Cancer and International Society of Cutaneous Lymphomas) MF presented to our clinic with multiple poikilodermatous patches over his buttocks and thighs affecting 4.25% of the body surface area and a hyperkeratotic nodule on one of the patches that was located inferior to the left gluteal fold (Fig 1). The lesion had appeared 6 months prior to presentation, and there was no history of trauma, bleeding, or pruritus. No lymphadenopathy was noted on examination. Past medical history was

### Abbreviations used:

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

significant for multiple basal cell carcinomas of the face. Although topical treatment was recommended at the time of diagnosis, approximately 24 years ago, the patient had opted for observation.

Histologic examination of the nodule within the patch revealed well-differentiated, superficially invasive SCC. Surrounding the nests of the invasive squamous cells was a heavy infiltrate of atypical large lymphocytes. On immunohistochemical staining, the atypical lymphocytes expressed CD3 and predominantly CD4, with partial loss of CD7. CD30 was present in less than 1% of the lymphoid infiltrate, and the CD4:CD8 ratio was 4:1 (Fig 2). Flow cytometry demonstrated atypical CD4<sup>+</sup> T cells with aberrant loss of both CD7 and CD26, consistent with the patient's known history of MF. Peripheral blood flow cytometry results were negative for blood involvement. Given the immunohistochemical findings and the known history of MF, the patient was diagnosed with SCC arising within an active MF patch. Treatment consisted of surgical excision of the SCC, followed by radiation therapy.

## DISCUSSION

Increased risks for both cutaneous and internal malignancies in patients with CTCL have been reported, with the greatest incidence within the

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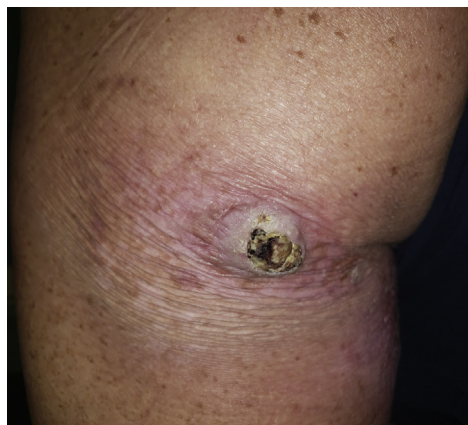
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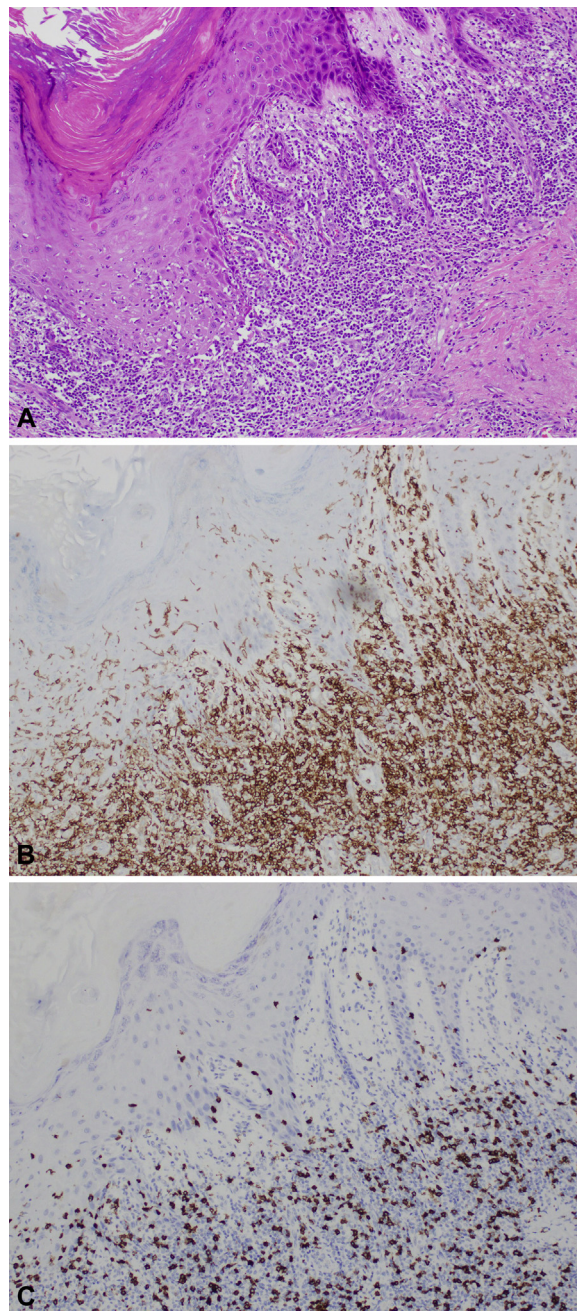
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**Fig 1.** Clinical appearance of cutaneous squamous cell carcinoma arising in an erythematous mycosis fungoides patch inferior to the left gluteal fold.

first year of diagnosis.<sup>1</sup> Concomitant MF and SCC within the same lesion have rarely been described. Development of SCCs in patients with MF on systemic therapy with INF- $\alpha$ , phototherapy (ultraviolet A, narrow-band ultraviolet B), and extracorporeal photopheresis has been previously reported.<sup>3,4</sup> In these reports, the authors suggested that the carcinogenic properties of ultraviolet irradiation could have contributed to the development of SCC in these patients. SCC development in an active, untreated MF lesion is even rarer.<sup>5,6</sup> Terada<sup>5</sup> reported a case of poorly differentiated SCC cells infiltrating an MF patch on the face of an 86-year-old patient, shortly after the diagnosis of MF. Le et al<sup>6</sup> described multiple, moderately differentiated SCCs in the MF-affected skin of the leg, arm, shoulder, chest, and neck of a 51-year-old male patient within several weeks of CTCL diagnosis. The three patients whose cases have been reported in the literature, which includes our patient, had low-grade disease at the time of SCC diagnosis without prior carcinogenic MF treatments, suggesting that potential alterations in the early tumor microenvironment predispose patients to the development of secondary SCC. However, in the present case, we cannot exclude the possibility that the patient's advanced age and lifestyle factors may have contributed to the development of SCC.

Topical phototherapies and systemic immunosuppressive therapies used to treat CTCL are well-established carcinogens. However, the reason for increased risk of developing a secondary malignancy in an active CTCL lesion is unknown, especially in patients without prior anticancer treatments. These patients may be predisposed to the development of other primary cutaneous malignancies because of



**Fig 2.** Histologic and immunohistochemical findings. **A**, Specimens from the erythematous patch demonstrate heavy infiltrate of atypical lymphocytes surrounding the keratinizing squamous cell neoplasm and marked epidermotropism. **B** and **C**, Immunohistochemical studies of atypical lymphocytes show stronger CD4 positivity as compared with that of CD8. (Hematoxylin-eosin and other indicated stains; original magnifications: **A**,  $\times 20$ ; **B** and **C**,  $\times 10$ .)

underlying reduced cutaneous immunosurveillance.<sup>7</sup> Heald et al<sup>8</sup> demonstrated that patients with erythrodermic CTCL have a markedly decreased number of normal circulating CD4<sup>+</sup> T cells, similar

to what is seen in patients with advanced acquired immunodeficiency syndrome. Lee et al<sup>9</sup> found a significant decrease in the ability to synthesize interferon gamma by Th1 cells in patients with CTCL when compared with that of healthy individuals, and Hwang et al<sup>10</sup> reported the loss of T cell diversity and narrowed CD8<sup>+</sup> repertoire in even early disease stages. Therefore, both reduced number of T lymphocytes and ineffective antitumor cytotoxic T lymphocyte activity can be seen in patients with CTCL and may contribute to the development of secondary malignancies, internally and locally. Additionally, advanced MF stages have been associated with severe and recurrent bacterial and viral cutaneous infections, suggesting weakened immune defense mechanisms in the skin. More studies investigating the potential role of T lymphocyte dysregulation in the pathogenesis of secondary cutaneous malignancies in CTCL are needed.

In conclusion, our case adds to the literature regarding increased risk of secondary malignancies in patients with MF and suggests that careful screening for possible signs of cutaneous malignancy in active and changing CTCL lesions in patients with both long-standing and newly diagnosed MF is necessary.

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