A mutilating, persistent lip ulcer as a presenting sign of oral mycosis fungoides with large cell transformation

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INTRODUCTION

Mycosis fungoides (MF), the most common type of cutaneous T-cell lymphoma, manifests a spectrum of cutaneous patches, plaques, and tumors, but only rarely involves the oral mucosa.[1,2] $CD30^+$ large cell transformation (LCT) of MF generally heralds poor prognosis and occurs occasionally.[3,4] LCT of MF occurring in the oral mucosa is exceptional.[5] Here, we describe an extraordinary case of MF with $CD30^+$ LCT presenting as a mutilating, persistent upper lip ulcer, posing a challenge to diagnosis.

Abbreviation used:

LCT: large cell transformation
MF: mycosis fungoides

CASE DESCRIPTION

A man in his 60's with a history of alcoholism presented with 4-month history of an expanding, non-healing, necrotic, ulcerated plaque on the upper cutaneous and mucosal lip (Fig 1). Initial biopsy revealed ulcerated and crusted folliculitis, and bacterial culture grew methicillin-sensitive *Staphylococcus aureus*. Over the course of the next 1.5 months, his ulcer grew despite the administration of numerous antibiotics, including cephalexin, rifampin, minocycline, linezolid, trimethoprim-sulfamethoxazole, and oritavancin.

The severity and recalcitrance of the ulcer prompted dermatology consultation. Culture of the ulcer grew *Staphylococcus epidermidis*, *Finegoldia magna*, and *Pseudomonas putida*; however, piperacillin-tazobactam and ciprofloxacin failed to improve the lesion. Biopsy demonstrated extensive neutrophilic infiltration, initially interpreted as consistent with pyoderma gangrenosum. However, the lesion did not respond to prednisone and intralesional triamcinolone. A repeat biopsy of the ulcer margins revealed scattered $CD30^+$ and anaplastic lymphoma kinase 1-negative large atypical lymphoid infiltrates with mixed acute and chronic inflammation and necroinflammatory debris, suggesting a $CD30^+$ lymphoproliferative disorder (Fig 2). A positron emission tomography/computed tomography scan highlighted the ulcerated lip tumor and a small scaly, erythematous plaque over his left eyebrow. One month after completing prednisone treatment, examination revealed red scaly patches and thin plaques affecting 40%-50% of the total body surface area (Fig 1). Biopsy of the left eyebrow plaque showed atypical dermal and pannicular T-lymphocytic infiltrate with epidermotropism, folliculotropism, and syringotropism with a CD4:CD8 ratio of approximately 10:1, including scattered $CD30^+$ large atypical cells (approximately 5%). Biopsy of the right thigh plaque revealed an atypical epidermotropic and adenexotropic lymphocytic infiltrate with a CD4:CD8 ratio of 4:1 and scattered $CD30^+$ cells (approximately 30%). The clinicopathologic picture appeared most compatible with adenexotropic MF with $CD30^+$ LCT. Staging, including peripheral blood flow cytometry, positron emission

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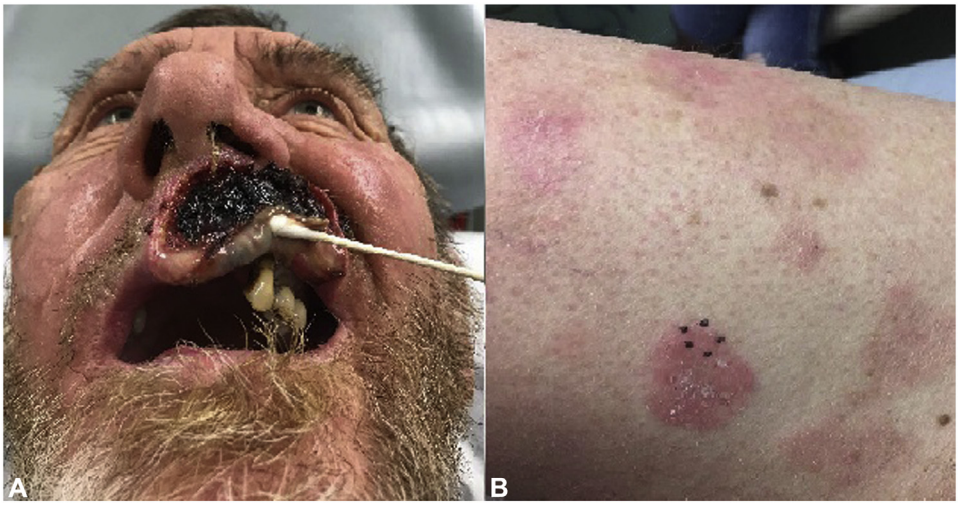

Fig 1. Clinical appearance of characteristic lesions. **A,** Wide and penetrating ulceration with yellow-black necrotic tissue at the base of the left upper cutaneous and mucosal lip with destruction and distortion of both the mucosal and cutaneous lip outlined by an erythematous rolling serpiginous plaque. **B,** Disseminated pink, scaly, thin, nummular plaques and patches, here depicted over the right thigh.

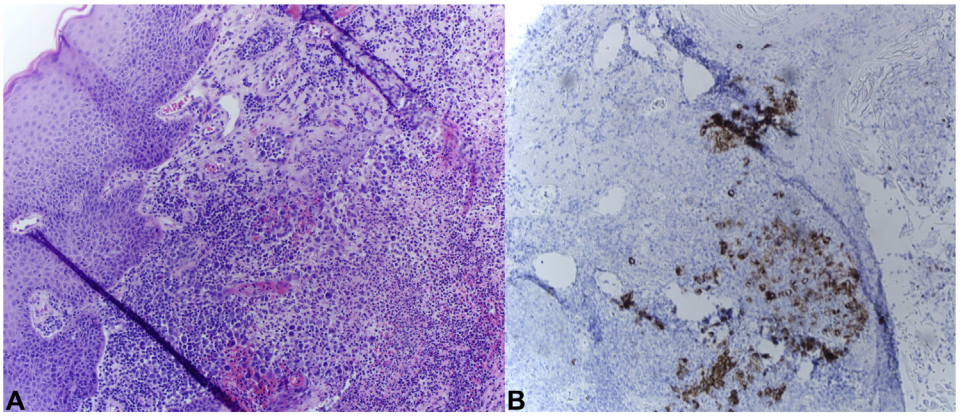

Fig 2. Histopathology of lip ulcer. **A,** Scattered CD30-positive and ALK1-negative large atypical lymphoid infiltrates with associated mixed acute and chronic inflammation and necroinflammatory debris (Hematoxylin-eosin–stain; original magnification: ×20.) **B,** CD30-positive cells are highlighted. (CD30 immunostain; original magnification: ×20.)

tomography/computed tomography, CBC, and SPEP, showed no evidence of systemic involvement.

Radiation therapy rapidly improved the ulcerated lip tumor with a total dose of 4,250 cGy in 25 fractions over a 5-week course. For the remaining involved skin, topical mechloramine gel was prescribed, supplemented by clobetasol ointment for plaques and triamcinolone ointment for patches. Following completion of radiation therapy, significant clinical improvement was observed, with skin involvement decreasing from 40%-50% to 10%-15%, featuring marked reduction in the size of individual patches/plaques and healing with contraction of the lip ulcer.

DISCUSSION

As a "great mimicker," MF is notorious for the spectrum of guises it can assume. While classically presenting with patches, plaques, and tumors of the skin, accentuated in sun-protected regions, the protean variants of MF can manifest a range of morphologies.[6] Involvement of the oral mucosa by MF, however, is highly uncommon, with an estimated <60 cases reported in the literature.[2] When it does affect the oral mucosa, MF appears to preferentially localize to the tongue, palate, and gingiva, with only rare involvement of the upper lip.[5,7] Recognition of MF of the oral mucosa is significant not only for its unique burden on quality of life and management

Table I. Summary of literature documenting oral mycosis fungoides (MF) with large cell transformation (LCT)

Case	Reference	Age at MF diagnosis (Dx)	Age at oral MF Dx	Sex	Oral mucosa involved	Cutaneous involvement	Treatment for oral MF	Treatment for cutaneous disease	Outcome
1	Kunishige et al. (2006)	70	72	M	Tongue	Erythroderma, keratoderma, and well-circumscribed, dome-shaped tumors on scalp, chin, and chest. Baseline-involved body surface area (BSA) was 27.15% (22% patches, 3.5% plaques, 1.65% tumors)	Local radiation therapy	Denileukin diftitox (for chronic lymphocytic leukemia), suberoylanilide hydroxamic acid, gemcitabine, local radiation therapy	Not provided
2	Kunishige et al. (2006)	55	56	F	Tongue	Hyperpigmented patches, evolving into plaques and tumors (86% BSA: 2% patches, 80% plaques, 6.4% tumors)	Boost radiation	Cyclophosphamide, methotrexate, etoposide, dexamethasone, gemcitabine, TSEB radiation	Death (4 months after appearance of tongue lesion)
3	Bittencourt et al. (2015)	48	48	M	Not specified	Plaques; oral large cell lymphoma presented simultaneously with skin lesions	Local radiation therapy, IFN	IFN	Alive with disease (at 9 months) (as of 2015)
4	Bassuner et al. (2016)	63	67	M	Tongue	Exfoliative erythroderma (90% BSA with 3:1 ratio of plaques to patches)	Electron beam radiation, bexarotene	Vorinostat; forodesine with minor partial response; combined modality with IFN-alpha plus bexarotene and extracorporeal photophoresis; TSEB radiation; alemtuzumab.	Alive, disease-free (as of 7 years after appearance of oral lesion)
5	Sultan et al. (2017)	Not provided	68	M	Tongue, buccal mucosa, hard palate	Sezary syndrome; multiple well-demarcated erythematous macules on the bilateral upper and lower distal extremities	Excisional biopsy, PUVA photochemotherapy	Ultraviolet light-B phototherapy, PUVA	Alive with disease (as of 2017)
6	Goggins et al. (2018)	40	65	M	Tongue	Patches, plaques > tumors (15% BSA)	Brentuximab vedotin	Brentuximab vedotin	Complete resolution of oral lesions, improvement of skin lesions
7	Robinson et al. (2020) (current case)	61	61	M	Upper lip	Patches, plaques > tumors (35% BSA)	Local radiation therapy	Topical mechloramine gel, clobetasol ointment, triamcinolone ointment	Resolution of lip lesion, slow progression of skin lesions

BSA, Body surface area; *Dx,* diagnosis; *IFN,* interferon; *PUVA,* psoralen ultraviolet-A; *TSEB,* total skin electron beam.

challenges, but also because oral MF is generally associated with poor prognosis.[2]

Another adverse prognostic feature of MF is LCT, defined as development of tumors in the setting of pre-existing patch- or plaque-stage MF, which frequently harbors CD30-positive large atypical cells. On histopathology, LCT is defined as large cells comprising >25% of the total lymphoid infiltrate or forming microscopic nodules.[3-5] An uncommon occurrence, LCT is estimated to occur in 6%-32% of MF cases, with a prognosis of <20% survival in 5 years.[1,4]

The combination of LCT and oral involvement by MF is exceedingly rare, with only six cases reported to date (Table I), when restricted to those with detailed characterization.[1] While one article alludes to three cases of oral MF, only one case is highlighted in detail as qualifying as LCT.[8] Moreover, involvement of the upper lip by MF with LCT to our knowledge has not been previously documented.[5]

Our case adds to the literature an extraordinary presentation on the oral mucosa of MF with LCT, and highlights how MF should be considered in the differential diagnosis for any persistent, non-healing ulcer.

Conflicts of interest

None declared.

REFERENCES

1. Goggins CA, Gocke MT, Jang S, DeSimone JA. Oral mycosis fungoides with CD30^{+} large cell transformation successfully treated with brentuximab vedotin. *JAAD Case Rep*. 2019;5(2):180-183.
2. Rosebush MS, Allen CM, Accurso BT, Baiocchi RA, Cordell KG. Oral mycosis fungoides: a report of three cases and review of the literature. *Head Neck Pathol*. 2019;13(3):492-499.
3. Arulogun SO, Prince HM, Ng J, et al. Long-term outcomes of patients with advanced-stage cutaneous T-cell lymphoma and large cell transformation. *Blood*. 2008;112:3082-3087.
4. Bittencourt AL, Oliveira PD, Carvalho-Andrade A, Araújo I. Correlations between clinical and pathological features in 17 cases of mycosis fungoides before and after transformation. *Int J Dermatol*. 2015;54:e327-e331.
5. Sultan AS, Mostoufi B, Papadimitriou JC, Koka R, Basile J, Younis RH. Large cell transformation of oral mycosis fungoides. *Head Neck Pathol*. 2018;12:247-251.
6. Hodak E, Amitay-Laish I. Mycosis fungoides: a great imitator. *Clin Dermatol*. 2019;37(3):255-267.
7. Kunishige J, Harriott Fisher A, Holsinger F, Feasel A, Duvic M. Mycosis fungoides of the tongue. *Internet J Dermatol*. 2006;5(1):1-4.
8. Bassuner J, Miranda RN, Emge DA, DiCicco BA, Lewis DJ, Duvic M. Mycosis fungoides of the oral cavity: fungating tumor successfully treated with electron beam radiation and maintenance bexarotene. *Case Rep Dermatol Med*. 2016;2016:5857935.