

# Gamma-delta mycosis fungoides in a posttransplant patient



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**Key words:** cutaneous oncology; cutaneous T-cell lymphoma; gamma-delta mycosis fungoides; immunosuppression; transplant.

## INTRODUCTION

Mycosis fungoides (MF) is a clonal T-cell lymphoproliferative disorder of the skin that accounts for an estimated 50% to 60% of cutaneous T cell lymphoma (CTCL) cases.<sup>1,2</sup> The gamma-delta ( $\gamma\delta$ ) subtype of MF (GD-MF) is a rare variant, with only a few cases reported in the literature and only 1 in a patient after solid organ transplant.<sup>3</sup> Here we present a case of GD-MF developing after liver transplantation in an older man.

## CASE

A 63-year-old man was seen for many years by a dermatologist for xerotic eczema. He initially presented in April 2014, just prior to orthotopic liver transplantation in June 2014 for a history of hepatitis C, alcohol-induced cirrhosis, and hepatocellular carcinoma. He underwent dual-agent immunosuppression with everolimus and tacrolimus over the ensuing years with periodic evaluation by a dermatologist for an ongoing eczematous rash. Because of worsening skin disease and infections poorly controlled with topical or oral antibiotics, he represented to dermatology for progressive disease in February 2019. The rash was pruritic, tender, and weeping, and he believed it was spreading. On examination, large plaques, eroded tumors, and indurated pink-to-violaceous nodules were seen on all 4 extremities, head, neck, chest, back, abdomen, and buttocks (Fig 1, A and B).

The patient was started on an 18-day prednisone taper and biopsies of 2 lesions were obtained from his left lower cutaneous lip and left dorsal forearm. The histopathology of both biopsy sites showed

### Abbreviations used:

|           |   |
|-----------|---|
| CTCL:     | cutaneous T-cell lymphoma                     |
| GD-MF:    | gamma-delta mycosis fungoides                 |
| MF:       | mycosis fungoides                             |
| PCGD-TCL: | primary cutaneous gamma-delta T-cell lymphoma |

T-cell infiltrates extending to dermis and patchy band-like atypical lymphoid infiltrate with epidermotropism. The epidermotropic component stained positive for CD3, CD8, and  $\gamma\delta$  T-cell receptor and negative for TIA-1, CD4, CD56, and CD30, consistent with  $\gamma\delta$  subset of CD8<sup>+</sup> disease (Fig 2). Positron-emission tomography/computed tomography and peripheral blood flow cytometry found no obvious evidence of visceral disease and less than 5% burden in the peripheral blood. His disease was staged IIB (T3, N1, M0, B0) by World Health Organization/European Organisation for Research and Treatment of Cancer criteria.

At 1-month follow-up visit, the patient had progression of disease with thickening of his skin lesions. After discussion with the hematology/oncology department, the patient was started on bexarotene, was given an additional short course of prednisone, and was instructed to begin dilute bleach baths several times per week. Despite these measures, he had progressive disease over the ensuing 2 months and was planned to switch therapy to romidepsin after palliative radiotherapy to symptomatic tumors on the left face and left thigh. He, however, had worsening clinical decline and blood infection to which he succumbed in August 2019.

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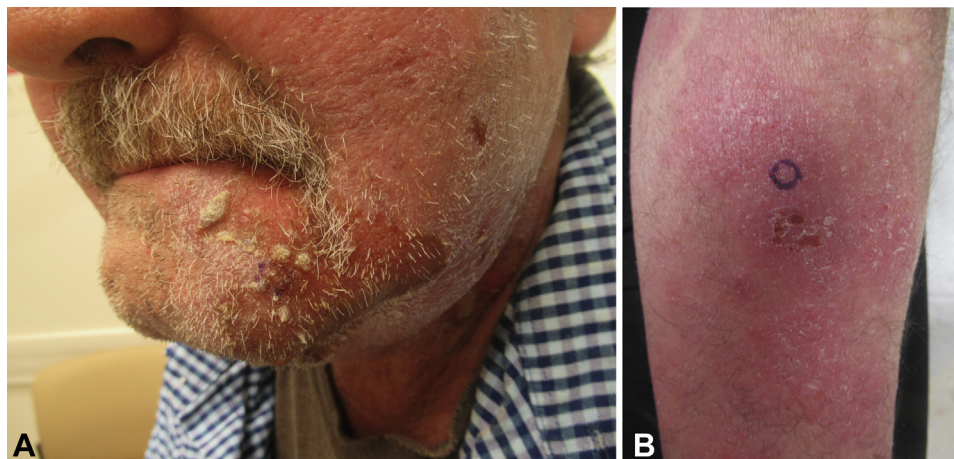
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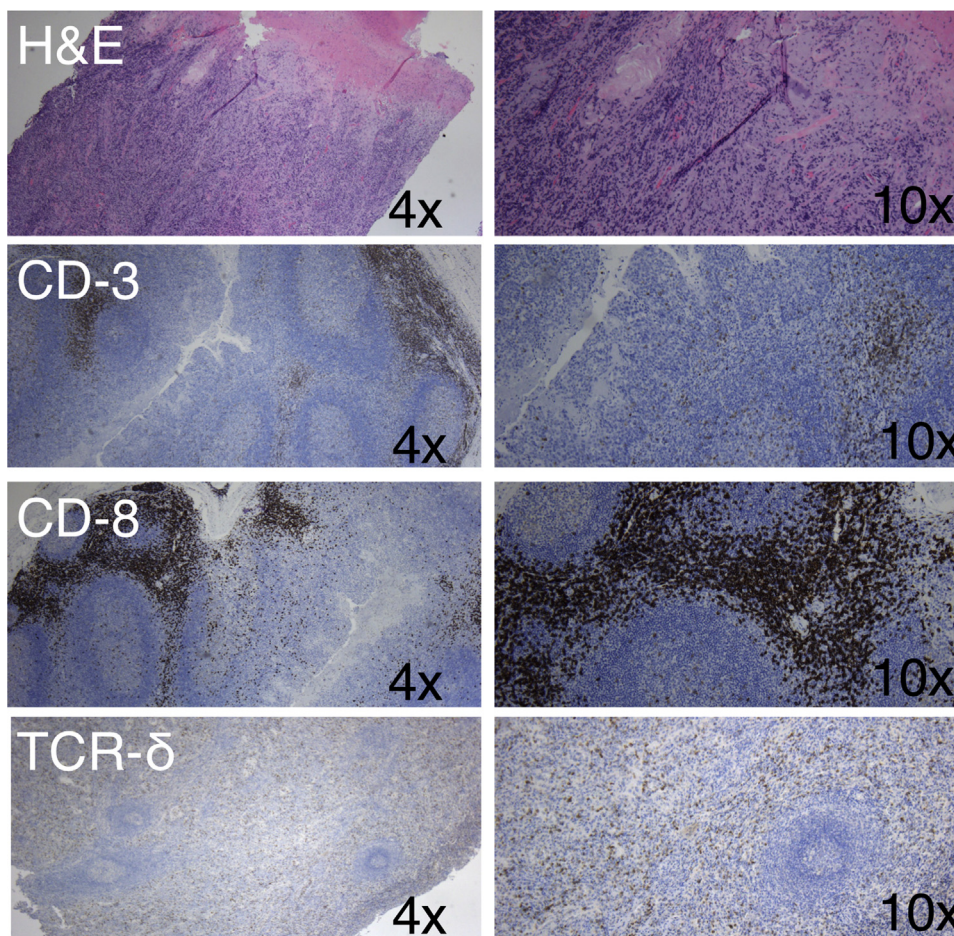
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**Fig 1.** **A**, Large erythematous plaque with erosion-draining serous yellow fluid on the left mandible. **B**, Well-defined pink-to-violaceous plaque on the arm.



**Fig 2.** Immunohistochemistry shows CD3, CD8, and TCR-gamma receptor positivity and band like lymphocytic proliferation with epidermotropism.

## DISCUSSION

Of the various forms of CTCL, MF is the most common, presenting as erythematous patches, plaques or tumors on the skin.<sup>2</sup> MF typically has an

indolent growth phase with an estimated 88% 5-year survival rate.<sup>4</sup> The World Health Organization/European Organisation for Research and Treatment of Cancer classification for primary cutaneous

lymphomas defines multiple subtypes of MF, including classic plaque-stage MF, folliculotropic MF, pagetoid reticulosis, and granulomatous slack skin. The  $\gamma\delta$  subtype is a rare subtype of MF and is characterized by the expression of the  $\gamma\delta$  T-cell receptor (TCR $\gamma\delta$ ).

It can be difficult to distinguish this condition from primary cutaneous  $\gamma\delta$  T-cell lymphoma (PCGD-TCL), which also expresses TCR $\gamma\delta$ .<sup>3</sup> PCGD-TCL is a rare (<1% of cases), aggressive variant of CTCL, with 5-year survival rate estimated between 11% and 33%.<sup>5,6</sup> The disease usually presents with multiple deep plaques, nodules, or tumors with or without epidermal ulceration that may resemble panniculitis. Most patients will also present with systemic “B” symptoms (fever, weight loss, night sweats).<sup>2,5</sup> In contrast, GD-MF behaves similarly to classical MF with an indolent course and without systemic symptoms or panniculitis-like features.<sup>1,7</sup> The extant literature suggests that TCR clonality does not affect the prognosis of early MF.<sup>7,8</sup> Despite the *TCR* gene phenotype, TCR $\gamma\delta$ <sup>+</sup> neoplasms with clinical features consistent with that of typical MF should be classified as GD-MF rather than PCGD-TCL.

Few cases of GD-MF are reported in the literature. Furthermore, primary cutaneous posttransplant lymphoproliferative disorders of any type are also rare, with an estimated incidence of 0.07% in solid organ transplant recipients.<sup>9</sup> To date, there has been only 1 reported case of GD-MF in a transplant patient.<sup>3</sup> However, in that case, the patient had pre-existing indolent MF for 27 years before undergoing renal transplantation. To our knowledge, our case represents the first case of GD-MF development after solid organ transplantation.

Because of its rarity, there are limited data to guide therapy on GD-MF. Given its similarity to classic MF, patients with MF found to have TCR $\gamma\delta$  clonality should likely be treated with similar modalities. However, careful history taking and physical examination is warranted to rule out the signs/symptoms of PCGD-TCL. Further study will elucidate the effects of solid organ transplant on this patient population.

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