Lymphoplasmacellular mucositis ameliorated by α4β7 integrin inhibitor vedolizumab in a patient with ulcerative colitis

Doaa Shalabi, BA,[a] Mansha Sethi, MD,[a] Lauren Okon, MD,[a] Gudrun F. Debes, DVM,[b] Jason B. Lee, MD,[a] and Neda Nikbakht, MD, PhD[a]
Philadelphia, Pennsylvania

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INTRODUCTION

Idiopathic lymphoplasmacellular mucositis-dermatitis (ILPMD) is a term that encompasses a group of disorders defined histopathologically by a dense infiltrate predominantly of plasma cells and some lymphocytes in the skin and mucosa.[1] Zoon[2] first described a similar process with dense plasma cell infiltrates in the glans penis that was termed *plasma cell balanitis*. Since then, oral involvement has also been reported and described with multiple terms such as *idiopathic plasmacytosis*, *plasma cell orificial mucositis*, and *mucous membrane plasmacytosis*.[3] However, because all these entities share similar histopathologic features, use of ILPMD as an encompassing diagnosis provides a terminological consolidation.[1] Diagnosis of ILPMD requires exclusion of a wide range of clinical disorders. It exhibits a chronic course and tends to be refractory to treatment.[4] Although several other coincidental autoimmune conditions[3] are reported in patients with ILPMD, an association with inflammatory bowel disease is not established. We report a case of oral ILPMD in a patient with ulcerative colitis (UC). Effectiveness of local treatment of the affected lower lip was significantly enhanced with systemic vedolizumab (Entyvio, Takeda Pharmaceuticals USA, Inc, Deerfield, IL) used to treat UC in this patient.

Abbreviations used:

ILPMD: idiopathic lymphoplasmacellular mucositis-dermatitis
UC: ulcerative colitis

CASE REPORT

A 48-year-old African-American woman with history of UC presented with a crusted lesion on her lower lip that had been waxing and waning for the last 2 years. Examination found a fissured, thickened plaque with yellow-brown hemorrhagic crust covering most of her enlarged, depigmented lower lip (Fig 1, *A*). The remainder of the skin and mucous membrane examination was unremarkable. She was treated previously for cheilitis with topical steroids with minimal improvement, and her flares coincided with worsening of her UC. Past treatments for UC included mesalamine and adalimumab, both of which failed to control her bowel disease.

Punch biopsy found a dense and diffuse inflammatory infiltrate consisting of plasma cells ($CD138^+$), histiocytes ($CD68^+$), T cells ($CD3^+$), B cells ($CD20^+$), and rare $CD30^+$ cells (Figs 2 and 3). No granulomas, keratinocyte atypia, or solar elastosis were observed. Immunohistochemistry showed plasma cells positive for κ and λ light chains as well as IgG4. IgG4-related disease was ruled out because of absence of characteristic histopathologic criteria of storiform fibrosis and venalities in both lip and prior intestinal biopsies.[5] Varicella-zoster and herpes simplex virus tissue polymerase chain reaction tests were negative. Given their association with UC, pyoderma gangrenosum and pyoderma vegetans were considered in

From the Department of Dermatology and Cutaneous Biology[a] and the Department of Microbiology and Immunology, Sidney Kimmel Medical College and Sidney Kimmel Cancer Center,[b] Thomas Jefferson University.
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Correspondence to: Neda Nikbakht, MD, PhD, Assistant Professor of Dermatology, Department of Dermatology and Cutaneous Biology, Thomas Jefferson University, 233 S. 10th Street, Rm 410, Philadelphia, PA 19107. E-mail: neda.nikbakht@jefferson.edu.
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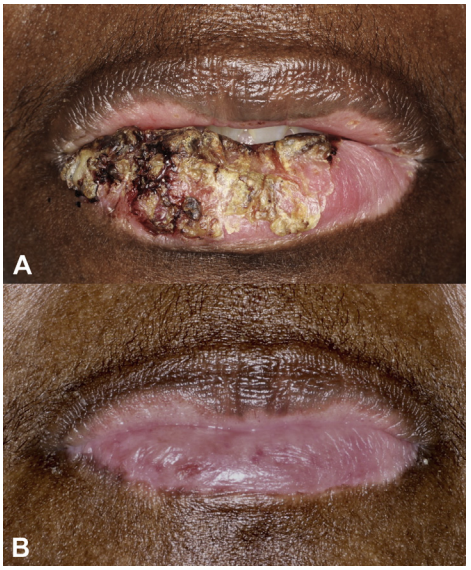

Fig 1. A, A broad eroded lesion with thick purulent hemorrhagic scale-crust on the lower lip. **B**, Complete clearance of the lesion after treatment with vedolizumab.

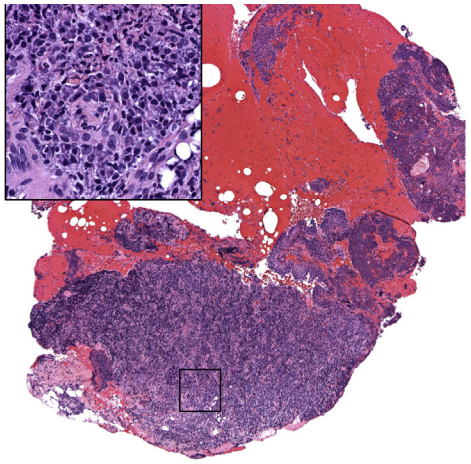

Fig 2. An ulcer with thick hemorrhagic crust accompanied by a dense infiltrate of inflammatory cells consisting of neutrophils, lymphocytes, histiocytes, and numerous plasma cells. (Hematoxylin-eosin stain; original magnification: ×40; inset: ×100.)

the differential diagnoses. However, the lack of a predominantly neutrophilic infiltrate excluded pyoderma gangrenosum and the absence of a pseudocarcinomatous hyperplasia with neutrophilic dermal abscesses ruled out pyoderma vegetans.[6] Given the mucosal ulceration with an underlying dense infiltrate composed predominantly of plasma cells with some neutrophils and lymphocytes, a diagnosis of ILPMD was established.[1]

The patient was treated with three 1-mL doses of 10 mg/mL intralesional triamcinolone acetonide,

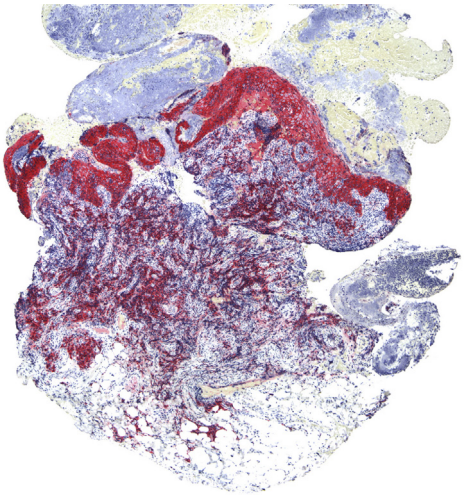

Fig 3. CD138 stain highlighting a dense infiltrate of plasma cells throughout the lesion. (CD138 stain; original magnification: ×40.)

administered every 2 weeks with daily application of triamcinolone acetonide 0.1% dental paste. After 6 weeks of this treatment, she noticed only mild improvement of oral lesions and did not continue with intralesional therapy. At this time, her gastroenterologist started systemic infusions of $\alpha 4\beta 7$ integrin inhibitor vedolizumab to treat her UC. Within 4 weeks of receiving her second dose of monthly infusions, the oral lesions completely resolved and remained in remission (Fig 1, *B*). Treatment also led to resolution of her UC symptoms. However, when vedolizumab was temporarily discontinued because of logistical issues, her oral lesions flared again only to resolve upon the reinstitution of vedolizumab.

DISCUSSION

No defined guidelines exist for the management of ILPMD. Treatment options include topical, intralesional, and systemic corticosteroids; topical and systemic antibiotics or antifungals; topical cyclosporine; topical tacrolimus; dapsone; isotretinoin; and liquid nitrogen cryotherapy.[7] Spontaneous regression over 6 months has also been observed.[7] Our patient's chronic course of ILPMD remained in remission while on vedolizumab and flared when her vedolizumab dosing was delayed. Vedolizumab is a monoclonal antibody that targets gut-homing molecule $\alpha 4\beta 7$ integrin and exerts anti-inflammatory activity in UC.[8] Plasma cells express $\alpha 4\beta 7$ integrin,[9] and $\alpha 4\beta 7$ ligand, MAdCAM-1, is expressed in oral mucosa.[10] Therefore, plasma cell homing to oral mucosa may be inhibited by vedolizumab in ILPMD. Together, these observations suggest a role for vedolizumab in patients

with concurrent ILPMD and inflammatory bowel disease. We conclude that close collaboration between gastroenterologists and dermatologists can lead to selection of a dually effective treatment strategy in these patients.

REFERENCES

1. Brix WK, Nassau SR, Patterson JW, Cousar JB, Wick MR. Idiopathic lymphoplasmacellular mucositis-dermatitis. *J Cutan Pathol*. 2010;37:426-431.
2. Zoon JJ. Chronic benign circumscript plasmocytic balanoposthitis. *Dermatologica*. 1952;105:1-7.
3. Solomon LW, Wein RO, Rosenwald I, Laver N. Plasma cell mucositis of the oral cavity: report of a case and review of the literature. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2008;106:853-860.
4. Gupta SR, Steele EA, Solomon AR. Idiopathic lymphoplasmacellular mucositis-dermatitis of the eyelid. *Ophthalmic Plast Reconstr Surg*. 2014;30:e149-e151.
5. Deshpande V, Zen Y, Chan JK, et al. Consensus statement on the pathology of IgG4-related disease. *Mod Pathol*. 2012;25:1181-1192.
6. Schaumburg-Lever WFLG. *Lever's Histopathology of the Skin*7 ed. J.B. Lippincott Company; 2014.
7. Liu RF, Chen CB, Kuo TT, Chung WH. Idiopathic lymphoplasmacellular mucositis of the lips: a case report and review of the literature. *J Cutan Pathol*. 2017;44:776-780.
8. Smith MA, Mohammad RA. Vedolizumab: an alpha4beta7 integrin inhibitor for inflammatory bowel diseases. *Ann Pharmacother*. 2014;48:1629-1635.
9. Quiding-Jarbrink M, Nordstrom I, Granstrom G, et al. Differential expression of tissue-specific adhesion molecules on human circulating antibody-forming cells after systemic, enteric, and nasal immunizations. A molecular basis for the compartmentalization of effector B cell responses. *J Clin Invest*. 1997;99:1281-1286.
10. Berlin C, Berg EL, Briskin MJ, et al. Alpha 4 beta 7 integrin mediates lymphocyte binding to the mucosal vascular addressin MAdCAM-1. *Cell*. 1993;74:185-195.