Successful Treatment of Refractory Epidermolysis Bullosa Acquisita With Intravenous Immunoglobulin and Dapsone

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PRACTICE **POINTS**

- Treatment of epidermolysis bullosa acquisita (EBA) is difficult, and most treatment regimens are based on anecdotal reports.
- Systemic corticosteroids have been the mainstay of therapy for severe or extensive disease but impose an increased risk for postoperative complications including surgical site infections.
- A steroid-sparing regimen of intravenous immunoglobulin and systemic dapsone may be used when rapid clearance of EBA is needed prior to elective surgery.

To the Editor:

Evidence-based recommendations for optimal medical management of patients with immunobullous diseases prior to elective surgery are sparse.[1,2] There is an uncertain balance between the use of immunomodulators and immunosuppressants, and implementation of these agents is heavily weighted against an increased infection risk from both active disease with denuded skin and suboptimal wound healing due to iatrogenic immunosuppression.[1-5] Historically, clinical management of epidermolysis bullosa acquisita (EBA) seldomly has resulted in substantial disease resolution.[1,3,4] Herein, we describe a case of recalcitrant EBA that was treated with a combination of intravenous immunoglobulin (IVIG) and dapsone, which resulted in a favorable clinical response and successful hip arthroplasty without cutaneous complications.

A 66-year-old man presented to an outside clinic with nonhealing ulcers on the oral mucosa, hands, groin, and feet. He was treated with systemic steroids after a histologic examination suggested bullous pemphigoid, but the lesions did not exhibit any appreciable improvement after several months of treatment. Despite the lack of improvement, the patient was continued on systemic steroids with a waxing and waning disease course.

Within a year, the patient presented to an orthopedist at our institution with severe left hip pain that had been limiting his mobility and had become unresponsive to conservative therapy. Radiologic investigations suggested advanced osteoarthritis and avascular necrosis of the left hip. Surgical intervention was delayed, as his orthopedist expressed concern that the extent of the body surface area affected by cutaneous denudation placed him at an unacceptable risk for infection. The orthopedic surgeon then referred the patient to our clinic for evaluation of the lesions. Physical examination revealed numerous crusted erosions in various stages of healing on the oral mucosa, palms, groin, and soles. Repeat biopsy of a denuded ulcer on the patient's arm was obtained by our providers (nearly 1 year after the first biopsy by the outside physician). Histologic examination showed a pauci-immune subepidermal blister without acantholysis, which in combination with the clinical presentation of tense bullae on trauma-prone surfaces led to a favored diagnosis of EBA.

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The authors report no conflict of interest.

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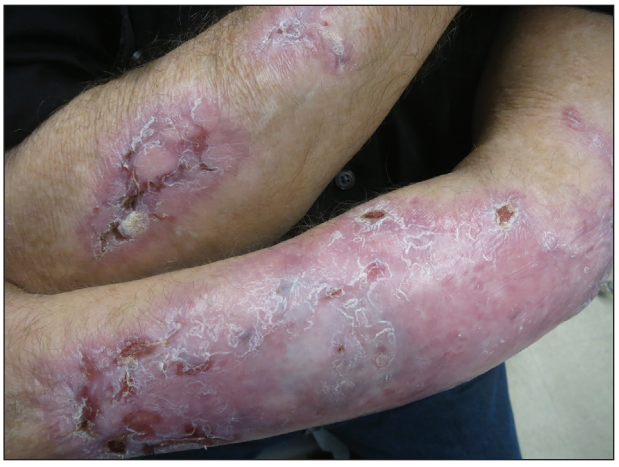

FIGURE 1. Multiple well-healed, pink to violaceous ulcers with a few peripheral crusted erosions distributed on the dorsal aspects of the forearms 1 week after the patient underwent his final intravenous immunoglobulin infusion.

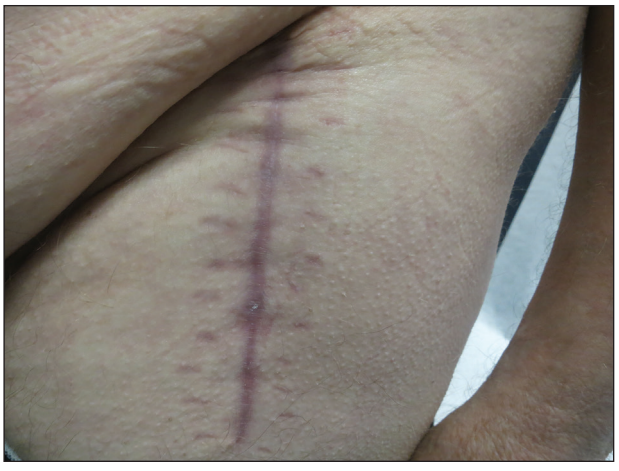

FIGURE 2. Well-healed vertical scar 1 month following left hip arthroplasty.

The patient began trials of several immunomodulatory and immunosuppressive agents, both in isolation and in combination, including systemic steroids, mycophenolate mofetil, four 1000-mg infusions of rituximab, and dapsone. Although results were suboptimal, dapsone 150 mg once daily for 3 months yielded the greatest clinical improvement with subsequent granulation and/or re-epithelialization of the chronic ulcers. After discussion during our department's Grand Rounds, it was determined that the patient should undergo a trial of IVIG infusions, which were initiated with a loading dose of 2000 mg/kg over 5 consecutive days, followed by once-monthly maintenance infusion doses of 1200 mg/kg for 4 consecutive months. While receiving IVIG, he was maintained on a once-daily dose of dapsone 150 mg. This dual approach was designed to suppress both the humoral and cellular-mediated disease mechanisms so that his treatment would obviate the need for systemic corticosteroids.

Following this treatment regimen, he was noted to have marked improvement with only few scattered healing erosions. Upon completion of his last IVIG infusion, his cutaneous and mucosal manifestations of EBA were greatly minimized, demonstrating the best level of control that had been achieved during the disease course (Figure 1). This therapy completely cleared the cutaneous and mucosal ulcerations, thus permitting the patient to undergo a total left hip arthroplasty without complications (Figure 2).

Our report is novel in that it supports a combination of IVIG and dapsone as a viable presurgical therapy for patients with EBA, and this treatment also may be applicable for other primary immunobullous disorders.[2,5] Our case was particularly challenging in that the severity of the patient's bullous disease precluded him from an elective orthopedic joint replacement due to the risk for wound dehiscence and surgical site infection.[2] We determined that IVIG and dapsone would be the most optimal combination therapy to facilitate superior disease control and concurrently allow for appropriate wound healing without impairing the host immune response. This report is unique from a clinical perspective in that a balance was successfully achieved between immune suppression, with avoidance of associated side effects, and disease activity.

REFERENCES

1. Ahmed AR, Gürcan HM. Treatment of epidermolysis bullosa acquisita with intravenous immunoglobulin in patients non-responsive to conventional therapy: clinical outcome and post-treatment long-term follow-up [published online August 8, 2011]. *J Eur Acad Dermatol Venereol*. 2012;26:1074-1083.
2. Rubin J, Touloei K, Favreau T, et al. Mohs surgery in patients immunobullous diseases: should prednisone be increased prior to surgery? *J Clin Aesthet Dermatol*. 2014;7:45-46.
3. Ishii N, Hamada T, Dainichi T, et al. Epidermolysis bullosa acquisita: what's new? *J Dermatol*. 2010;37:220-230.
4. Mosqueira CB, Furlani Lde A, Xavier AF, et al. Intravenous immunoglobulin for treatment of severe acquired bullous epidermolysis refractory to conventional immunosuppressive therapy. *An Bras Dermatol*. 2010;85:521-524.
5. Ludwig RJ. Clinical presentation, pathogenesis, diagnosis, and treatment of EBA. *ISRN Dermatology*. 2013;2013:812029.