Bullous pemphigoid: Rituximab to the rescue?

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It is not my imagination—the incidence of bullous pemphigoid (BP) is increasing in my practice. This is a function of an aging population in concert with more drug-induced cases, notably with dipeptidyl peptidase IV inhibitors and anti–PD-1/PD-L1 agents. Treating BP is challenging—although corticosteroids are the bedrock of therapy, every effort is made to administer steroid-sparing medications. Options include dapsone, doxycycline, niacinamide, immunosuppressive agents (mycophenolate mofetil, azathioprine, others), and biologics (omalizumab, dupilumab, and rituximab [RTX]). Research suggests that anti–interleukin 17 and anti–interleukin 23 monoclonal antibodies may be potentially effective agents for BP.[1] Sutimlimab, which provides highly selective inhibition of the classical complement pathway, may become a valuable therapeutic option.[2]

Diagnosing BP is based on routine histology, direct or indirect immunofluorescence assays, and quantification of circulating autoantibodies against BP180 and/or BP230 with enzyme-linked immunosorbent assay. The pathogenesis of BP is based on a dysregulated T-cell immune response and synthesis of immunoglobulin G and E autoantibodies against hemidesmosomal proteins, resulting in neutrophil chemotaxis and degradation of the basement membrane zone.[3]

RTX, a chimeric anti-CD20 monoclonal antibody, is approved by the US Food and Drug Administration (FDA) for treating pemphigus vulgaris. Should it also be approved for BP?

Polansky et al[4] performed a retrospective study of 20 patients who received at least 1 dose of RTX therapy, either as initial therapy for severe BP or as therapy for recalcitrant disease. They found that 75% of patients (n = 15) achieved remission an average of 169 days after RTX therapy. Of the 5 patients who did not respond to RTX, 3 had persistent disease requiring prednisone, 1 had no response to the first RTX course but attained remission 306 days after a second course, and 1 was lost to follow-up. There were no RTX-related deaths and significantly fewer adverse events after RTX.

Abbreviations used:

BP: bullous pemphigoid
CR: complete response
FDA: US Food and Drug Administration
RTX: rituximab

In this issue of the *Journal of the American Academy of Dermatology,* Tovanabutra and Payne[5] performed a retrospective case series (N = 38) of patients with pemphigoid (including BP, mucous membrane pemphigoid, and epidermolysis bullosa acquisita EBA). The primary endpoint was complete remission (CR). Overall, 29 of 38 (76%) patients with pemphigoid achieved CR after a median of 1 RTX cycle, with a median time to CR of 14.3 months. With the more rigorous endpoint of complete remission off therapy (CROT), 15 of 38 (39%) patients achieved CROT after a median of 2 RTX cycles. No substantive difference in CR/CROT rates was observed among pemphigoid subtypes. A statistically significant decrease in BP 180 titers was noted (in the 13 patients with BP tested) 12 months after RTX therapy. Of 7 infectious serious adverse events in 5 patients (13%), 5 occurred in patients receiving concomitant prednisone at a dosage of at least 7.5 mg/d and/or adjunctive immunosuppressives. Two deaths (primary central nervous system lymphoma, heart failure) were deemed unrelated to RTX.

Although RTX is clearly promising, further studies will determine if it should become an FDA-approved

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first-line treatment for BP. I asked my patient Zana, a 74-year-old woman with recalcitrant BP who had partial remission with RTX and still required low-dose prednisone, what she would tell the FDA committee. Her response was straightforward: "RTX changed my life. Please approve it to help others like me."

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