

Pemphigus Vulgaris Successfully Treated With Doxycycline Monotherapy

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PRACTICE POINTS

- The treatment of pemphigus vulgaris (PV) is challenging given the side-effect profile of commonly used systemic medications, including steroids, especially in elderly patients.
- Tetracyclines have an advantageous side-effect profile and may be efficacious in treating PV.

To the Editor:

Pemphigus vulgaris (PV) is an acquired autoimmune bullous disease with notable morbidity and mortality if not treated appropriately due to loss of epidermal barrier function and subsequent infection and loss of body fluids. Although the use of systemic corticosteroids and immunosuppressive agents has improved the prognosis, these drugs also may have severe adverse effects, especially in elderly patients. Hence, alternative and safer therapies with anti-inflammatory and immunomodulatory agents such as tetracyclines and nicotinamide have been used with variable results. We report a case of PV that was successfully treated with doxycycline.

An 81-year-old man presented with well-demarcated erosions with overlying yellow crust as well as vesicles and pustules on the scalp (Figure 1A), forehead, bilateral cheeks, and upper back (Figure 1B) of 6 months' duration. He used topical fluorouracil in the month prior to presentation for suspected actinic keratosis but had stopped its use after 2 weeks. At the first visit, a diagnosis of a reaction to topical fluorouracil with secondary bacterial infection was made and he was prescribed doxycycline hyclate 100 mg twice daily. The patient returned 4 weeks later for follow-up and reported initial notable improvement with subsequent worsening of lesions after he

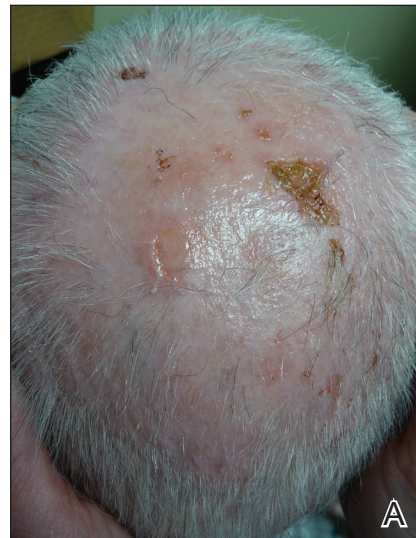


Figure 1. Initial presentation showed well-demarcated erosions with overlying yellow crust as well as vesicles and pustules on the scalp (A) and upper back (B).

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ran out of doxycycline. On physical examination the lesions had considerably improved from the last visit, but he still had a few erosions on the scalp and a few in the oral mucosa. A 1-cm shallow erosion with minimal surrounding erythema on the forehead was present, along with fewer scattered, edematous, erythematous plaques on the back and chest. Pemphigus vulgaris was suspected and 2 shave biopsies from the lesions on the back and cheek were obtained for confirmation. Histopathologic examination revealed epidermal hyperplasia and suprabasal acantholysis as well as moderate perivascular and perifollicular lymphocytic infiltrate with several eosinophils and plasma cells, characteristic of PV (Figure 2). Direct immunofluorescence showed moderate intercellular deposition of IgG within the basal layer and to a lesser extent within suprabasal layers as well as moderate intercellular deposition of C3 within the basal layer, characteristic of PV. IgA and IgM were not present. Indirect immunofluorescence using monkey esophagus revealed no antibodies against the intercellular space of the basement membrane zone. Due to the dramatic response, he continued on doxycycline 100 mg twice daily and remained in complete remission. Ten months after initiating treatment he discontinued doxycycline for 2 days and developed a 1-cm lesion on the left cheek. He resumed treatment with clearing of lesions and was slowly tapered to 50 mg of doxycycline once daily, remaining in complete remission (Figure 3). Doxycycline was discontinued 16 months after initiation; he has remained clear at 13 weeks.

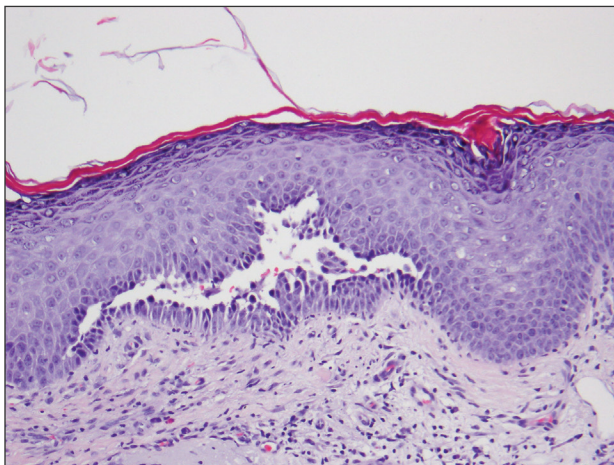


Figure 2. Histopathology showed epidermal hyperplasia and suprabasal acantholysis (H&E, original magnification $\times 40$).

The treatment of PV is challenging given the multiple side effects of steroids, especially in elderly patients. Tetracyclines have an advantageous side-effect profile and they have been shown to be efficacious in treating PV when combined with nicotinamide or when used as adjuvant therapy to steroids.¹⁻³ Our case shows a patient who was treated exclusively with doxycycline and achieved complete remission.

Tetracyclines have multiple biological activities in addition to their antimicrobial function that may provide a therapeutic benefit in PV. They possess immunomodulatory and anti-inflammatory effects by inhibiting leukocyte chemotaxis and activation⁴⁻⁸ and inhibiting cytokine release. They inhibit matrix metalloproteinases, which are the major enzymes responsible for breakdown of the extracellular matrix,⁹ and they indirectly inhibit neutrophil elastase by protecting α_1 -protease inhibitor from matrix metalloproteinase degradation.¹⁰ Additionally,



Figure 3. Treatment with doxycycline resulted in complete remission of the lesions on the scalp (A) and upper back (B).

tetracyclines increase the cohesion of the dermo-epidermal junction¹¹; whether they increase the adhesion between epidermal cells is unknown. It has been determined that CD4⁺ T cells play an essential role in the pathogenesis of PV by promoting anti-desmoglein 3 antibody production.¹² Szeto et al¹³ reported that minocycline, a member of the tetracycline family, has suppressive effects on CD4⁺ T-cell activation by hindering the activation of nuclear factor of activated T cells (NFAT), a key regulatory factor in T-cell activation. We hypothesize that doxycycline exerted what appears to be immunomodulatory properties in our patient by suppressing CD4⁺ T-cell activity.

In conclusion, tetracyclines can be an effective and promising therapy for PV given their relatively few side effects and immunomodulating properties. However, further randomized controlled trials will be important to support our conclusion.

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