Novel use of apremilast for adjunctive treatment of recalcitrant pyoderma gangrenosum

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INTRODUCTION

Pyoderma gangrenosum (PG) is a rare, neutrophilic, ulcerative dermatosis without a therapeutic gold standard.[1] Vegetative PG is a chronic superficial variant, which is more indolent and typically responds well to treatment.[1,2] Here we describe a patient with a 3-year history of uncharacteristically recalcitrant vegetative PG who responded to apremilast.

Abbreviations used:

PG: pyoderma gangrenosum
TNF: tumor necrosis factor

CASE

A 73-year-old man presented with nonhealing superficial erosions for several months at sites of prior surgical procedures on the back and posterior thigh, which were consistent with vegetative PG on histologic examination. An extensive work-up of systemic associations with PG revealed an IgA kappa monoclonal gammopathy of unknown significance.[3] The patient was initially managed conservatively with intralesional corticosteroids, high-potency topical corticosteroids, topical tacrolimus, and doxycycline without significant improvement. When moving to systemic agents, the patient was not considered to be a candidate for cyclosporine or an anti–tumor necrosis factor (anti-TNF) biologic because of his hematologic abnormalities, and he failed dapsone and colchicine. At the time of introducing apremilast, the patient had been maintained on oral prednisone for 2 years and subcutaneous methotrexate for 1 year, and he continued to have painful erosions.

Apremilast, an oral small-molecule phosphodiesterase-4 inhibitor,[4] was considered an appropriate next option for the patient. Apremilast 30 mg twice daily was added to a regimen of oral prednisone 7.5 mg daily and subcutaneous methotrexate 18 mg weekly. Within 4 months, the patient had complete closure of the back erosion, partial healing of the thigh erosion, and was able to discontinue the methotrexate; by 5 months, he was able to completely taper off the prednisone (Fig 1). The patient did experience moderate nausea and some diarrhea from the apremilast; however, these symptoms were tolerable and did not require any dose adjustments. For wound care, the patient performed once daily dressing changes with sterile cotton gauze and nonadherent dressing.

DISCUSSION

Although the pathogenesis of PG is unclear, immune dysregulation appears to play a major role. PG is associated with other autoimmune disorders, including inflammatory bowel disease and Behçet's disease, and is treated with immunosuppressive therapies including more recently anti-TNF agents.[1] Apremilast is an oral small molecule that inhibits phosphodiesterase-4, increasing intracellular cyclic adenosine monophosphate and, thereby, suppressing numerous inflammatory pathways.[4] Classic PG is associated with the overexpression of key inflammatory mediators such as TNF-α and interleukin (IL) 8, both of which are inhibited by apremilast, providing the rationale for its utility in this case.[4,5] Apremilast is also frequently used in diseases for which anti-TNF agents have demonstrated efficacy

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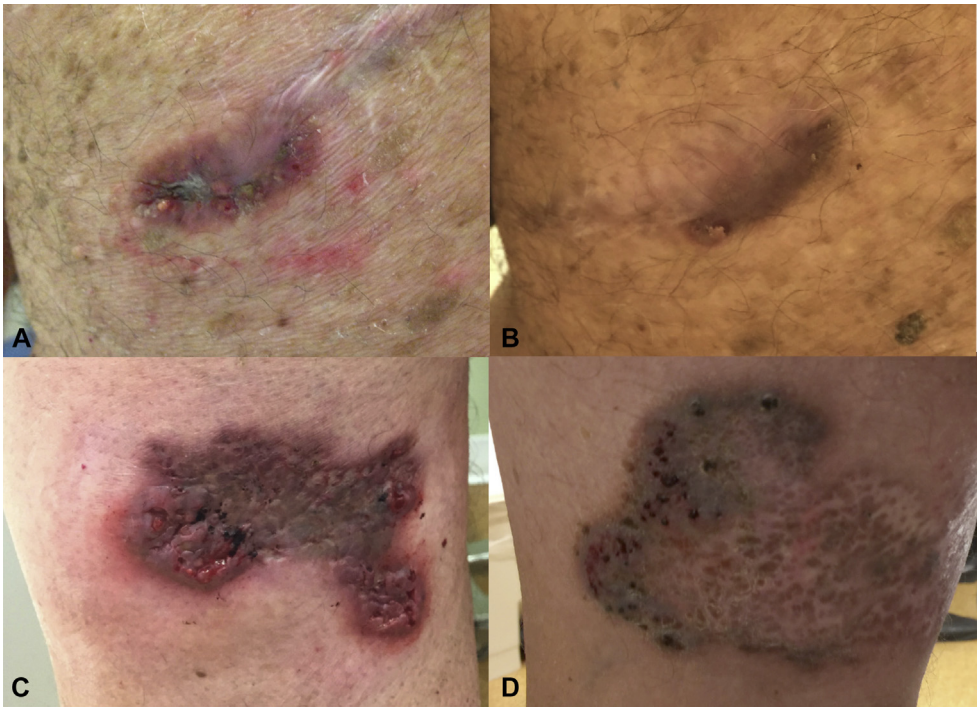

Fig 1. Pyoderma gangrenosum, clinical photographs. Back erosion at baseline (**A**) and after 5 months of apremilast (**B**). Thigh erosion at baseline (**C**) and after 5 months of apremilast (**D**).

and has shown benefit in the treatment of several autoimmune skin disorders including discoid lupus erythematosus and psoriasis, for which the drug is Food and Drug Administration approved.[6-8] Furthermore, apremilast is also under study in PG-associated autoimmune conditions; evidence suggests apremilast has efficacy in the treatment of Behçet's disease,[9] another neutrophilic ulcerative dermatosis, and additional trials are ongoing in inflammatory bowel disease.[10]

Apremilast is an attractive alternative to anti-TNF agents because of its oral dosing, decreased laboratory monitoring requirements, and its lack of black-box lymphoma risk. Diarrhea and nausea, as seen in our patient, are the most common adverse effects and often wane over time; apremilast is overall well-tolerated with low discontinuation rates.[4,7]

In summary, this patient's favorable response to the off-label use of apremilast for vegetative PG refractory to multiple topical and systemic therapies suggests a novel therapeutic option for patients with recalcitrant PG.

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