Treatment of Pyoderma Gangrenosum

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KEYWORDS

• Pyoderma gangrenosum • Ulcer • Therapy • Treatment • Review • Neutrophil

KEY POINTS

- Pyoderma gangrenosum (PG) is a rare neutrophilic dermatosis that results in painful cutaneous ulcers and is frequently associated with underlying hematologic disorders, inflammatory bowel disease, or other autoimmune conditions.
- The pathogenesis involves dysregulation of both innate and adaptive immunity, with imbalance between proinflammatory and anti-inflammatory mediators, leading to neutrophilic inflammation and tissue damage.
- First-line treatment options with the best evidence are systemic corticosteroids, cyclosporine, and tumor necrosis factor alpha inhibitors. Topical corticosteroids, intralesional corticosteroids, and calcineurin inhibitors are often used as adjuncts and are well tolerated.
- Other steroid-sparing therapies include dapsone, mycophenolate mofetil, intravenous immunoglobulin, and targeted biologic or small molecule inhibitors.
- Patients without associated comorbidities respond better to treatment and suffered fewer adverse events. Wound care and management of underlying disorders are also critical parts of care.

INTRODUCTION

Pyoderma gangrenosum (PG) is a rare neutrophilic dermatosis that results in painful cutaneous ulcers. The classic lesion of PG begins as a tender pustule that rapidly enlarges into a painful, irregularly shaped ulcer with purulent base and gunmetal gray-violaceous undermined borders, and perilesional erythema. The ulcers typically heal with atrophic cribriform scars and dyspigmentation. Besides the ulcerative form of PG, other possible variants include bullous, pustular, vegetative, and peristomal presentation. PG most commonly affects the lower extremities but can occur anywhere including the genitalia.

The cause of PG remains unclear but approximately half of all patients presenting with PG have a concomitant underlying hematologic disorder, inflammatory bowel disease or other autoimmune disorders, or malignancy (**Box 1**). Certain medications have also been implicated in PG, including isotretinoin, propylthiouracil, and sunitinib. The diagnosis of PG requires clinicopathologic correlation and the exclusion of other potential causes of cutaneous ulceration. The diagnostic criteria of PG have been listed in **Table 1**.[1–7]

The pathogenesis of PG is complex and thought to be due to immune dysregulation in both the innate and adaptive immune pathways. PG lesions or serums of patients with PG have shown to contain elevated levels of proinflammatory molecules and cytokines C5a, interleukin (IL)-1, IL-4, IL-5 IL-8, IL-12, IL-15, IL-17, IL-23, IL-36, tumor necrosis factor alpha (TNF-α), Janus Kinase (JAK)-1,

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Box 1
Systemic diseases associated with pyoderma gangrenosum[75]

Hematologic disorders

- Monoclonal gammopathy (especially immunoglobulin A)
- Polycythemia vera
- Acute myelogenous leukemia
- Chronic myelogenous leukemia
- Hairy cell leukemia
- Lymphoma
- Myelodysplasia

Autoimmune disorders

- Inflammatory bowel disease
- Rheumatoid arthritis
- Sjogren syndrome
- Systemic lupus erythematosus
- Granulomatosis with polyangiitis

Medications

- Cocaine laced with levamisole
- Isotretinoin
- Propylthiouracil
- Sunitinib

Others

- Neutrophilic disorder
  - Behçet disease
  - Subcorneal pustular dermatosis
  - Sweet syndrome
  - Bowel-associated dermatosis arthritis syndrome
- Autoinflammatory disorders
  - PAPA syndrome (pyogenic arthritis, pyoderma gangrenosum, acne)
  - PASH syndrome (pyogenic arthritis, hidradenitis suppurativa)
  - PAPASH syndrome (Pyogenic arthritis, pyoderma gangrenosum, acne, hidradenitis suppurativa)
- Solid tumor malignancies

JAK-2, JAK-3, interferon (IFN)-γ, chemokine receptors, and reduced levels of anti-inflammatory cytokines IL-10, transforming growth factor beta (TGF-β), Foxhead box P3 (FOXP3), and regulatory T-cells (T-reg).[8] This imbalance leads to a predominant neutrophilic inflammation, tissue necrosis, and ulceration. Skin trauma results in the release of IL-8 and IL-36 inflammatory cytokines by keratinocytes. Hence, PG may be triggered or aggravated by minor trauma (ie, pathergy).

Since the discovery of novel therapies, the treatment of PG has evolved from a blanket immunosuppression to a more targeted immunomodulation. The goals of therapy should be to reduce inflammation to allow healing to place, pain control, and management of underlying comorbidities. Multidisciplinary management involving dermatology, wound care, pain, plastic surgery, rheumatology, gastroenterology, hematology, and oncology are often required to achieve disease control and prevent recurrence. Herein, we discuss various treatment options stratified by level of evidence (**Box 2**) and propose an algorithm to approach PG (**Fig. 1**).

DISCUSSION

Level 1 Evidence (Randomized Controlled Trials)

Systematic corticosteroids

Corticosteroids (CS) asserts its immunosuppressive effects by binding to glucocorticoid receptors and affecting transcription factors, leading to a reduction in proinflammatory cytokines such as IL-1 and TNF-α, while increasing anti-inflammatory mediators such as T-reg and IL-10. CS has a rapid onset of action, making it an excellent first-line treatment option for PG.

Prednisolone 0.75 mg/kg/d resulted in resolution in 47% of PG by 6 months.[9] Patients with milder disease and without underlying PG-associated disorders had better response to CS. Steroid-sparing agents should be initiated concurrently with CS to allow tapering once disease remission is achieved. Serious adverse events (AEs) associated with CS included hyperglycemia, diabetes mellitus, serious infections, and bowel perforation. Patient characteristics discouraging the use of prednisone include obesity, impaired fasting glucose, osteoporosis, gastrointestinal ulcers, and mental illness.

Calcineurin inhibitors (cyclosporine and tacrolimus)

Cyclosporine and tacrolimus are calcineurin inhibitors that predominantly reduce IL-2, IFN-γ, and T-cells proliferation.

Cyclosporine 4 mg/kg/d resulted in complete resolution in 47% of PG lesions by 6 months.[9] Serious AEs associated with cyclosporine included abdominal aortic aneurysm rupture and renal dysfunction. Patient characteristics discouraging the use of cyclosporine include hypertension, renal insufficiency, and malignancy. Compared with prednisolone, cyclosporine showed similar treatment

Table 1
Diagnostic criteria for pyoderma gangrenosum[1–4]

Criteria by Su *et al* (2004)	Delphi Consensus Criteria (2018)	Paracelsus Score (2019)
Diagnosis requires 2 major and ≥2 minor criteria	*Diagnosis requires 1 major and ≥4 minor criteria*	*Diagnosis (highly likely) requires a score of ≥10 points*
Major Criteria	*Major Criterion*	*3 points each*
• Rapidly developing painful, necrolytic ulcer with an irregular, violaceous, and undermined border • Ruled out other causes of ulcers	• Biopsy of ulcer edge demonstrates neutrophilic infiltrate	• Progressive disease • Excluded other potential causes • Red-violet wound border
Minor Criteria	*Minor Criteria*	*2 points each*
• History suggestive of pathergy or cribriform scarring on examination • Underlying systemic disease with known association to PG • Histopathology consistent with PG (sterile neutrophilic dermal infiltrate, ± mixed infiltrates, ± lymphocytic vasculitis) • Rapid response to systemic CS	• Infection excluded on histology (with appropriate stains and tissue culture) • Pathergy • Underlying inflammatory bowel disease or inflammatory arthritis • Papule, pustule, or vesicle that rapidly evolves into an ulcer within 4 d • Ulcer with undermined borders and peripheral erythema • Multiple ulcers including ≥1 on anterior lower leg • Cribriform atrophic scarring after ulcer heals • Ulcer decreases in size within 1 mo of starting immunosuppressive medication	• Ameliorates with immunosuppressive medications • Irregularly shaped (bizarre) ulcer • Pathergy • Significant pain (>4/10 on the visual analog scale)
		1 point each
		• Suppurative inflammation on histopathology • Undermined wound edge • Associated systemic disease

efficacy while having fewer serious AEs.[9] Cyclosporine was also found to be a more cost-effective treatment option, especially for larger lesions (20 cm^2 or greater).[10]

Oral tacrolimus is more potent than cyclosporine. Oral tacrolimus has been used in the management of PG.[11–13] Four patients with PG refractory to conventional immunosuppressive medications developed significant clinical improvements within 1 week of initiating oral tacrolimus, and 3 of them had complete resolution by 8 weeks.[11] Potential AEs were similar to that of cyclosporine.

Tumor necrosis factor alpha inhibitors

TNF-α is a proinflammatory cytokine that leads to the downstream production of IL-17, IL-23, and further TNF-α cytokines, which propagates the proinflammatory state. TNF-α inhibitors used in the treatment of PG have included adalimumab, certolizumab pegol, etanercept, infliximab, and golimumab.

Clinical improvement and complete resolution of PG was seen in 87% and 67% of lesions treated with TNF-α inhibitors.[14,15] Complete resolution was seen in 87% of PG with disease duration less than 12 weeks, compared with 69% of PG with disease duration greater than 12 weeks.[14] Infliximab had the greatest evidence supporting its use in PG, followed by adalimumab and then by etanercept. Infliximab and adalimumab trended toward greater clinical improvements compared with etanercept but this difference was not statistically significant.[14] Certolizumab pegol and golimumab had the fewest evidence in PG.

Box 2
Systemic treatment options stratified by available level of evidence

Level 1 (Randomized controlled trials)

- Systemic corticosteroids[9]
- Calcineurin inhibitors (cyclosporine and tacrolimus)[9]
- TNF-α inhibitors[15]

Level 2 (cohort studies)

- Topical corticosteroids[16]
- Topical calcineurin inhibitors[18]
- Dapsone[23]
- Mycophenolate mofetil
- IL-1 inhibitors[26]
- IL-17 inhibitors[28]

Level 3 (case-control studies)

- Intravenous immunoglobulin (IVIG)[36]
- IL-12/23[14]

Level 4 (case series or case reports)

- Azathioprine[38]
- Colchicine[41]
- Methotrexate[62]
- Thalidomide[50]
- IL-23 inhibitors[57]
- IL-36R inhibitor[62]
- JAK inhibitors[64]
- PDE-4 inhibitors[68]

Highest (Level 1) to lowest.

Level 2 Evidence (Cohort Studies)

Topical corticosteroids and intralesional corticosteroids

High-potency topical corticosteroids (TCSs) have been evaluated in the treatment of PG.[16] Clobetasol propionate 0.05% resulted in complete resolution in 43% of PG lesions within 6 months.[16] Intralesional CS have also been successfully used for the treatment of PG lesions.[17] Lesion size at time of presentation was an important prognostic factor because smaller lesions resolved more quickly.[16]

Topical calcineurin inhibitors

Topical calcineurin inhibitors (TCIs) work via a similar mechanism to cyclosporine and reduce IL-2, IFN-γ, and T-cells proliferation. Topical tacrolimus 0.1% ointment resulted in complete resolution in 50% to 100% of PG lesions within 2 to 6 months.[16,18] Caution should be paid when using TCI in extensive PG because one patient experienced acute renal dysfunction with elevated serum levels of tacrolimus after applying topical tacrolimus repeatedly to PG.[19] Topical pimecrolimus has less systemic absorption compared with topical tacrolimus and may be a safer choice in extensive PG.[20–22]

Dapsone

Dapsone is an antineutrophilic medication that works by inhibiting myeloperoxidase in neutrophils and preventing cellular damage from reactive oxygen species. Dapsone has been evaluated as an adjunct to other first-line immunosuppressive therapies.[23] When used as an adjuvant to systemic CS, antibiotics, intralesional CS, or TNF-α inhibitors, dapsone at 50 to 100 mg/d resulted in clinical improvements in 96.9% patients with PG, of which 81.3% had partial response and 15.6% had complete resolution of PG after a mean therapy duration of 14.3 months.[23] AEs included hemolytic anemia and methemoglobinemia in 9.4% and 3.7% of patients, respectively.

Mycophenolate mofetil

Mycophenolate mofetil (MMF) is an immunosuppressive agent that inhibits inosine monophosphate dehydrogenase, a key enzyme preferentially expressed in activated lymphocytes but not in nonactivated lymphocytes or other inflammatory cells. MMF also inhibits antibody production by B cells, tissue fibrosis by fibroblast, and recruitment of inflammatory cells. MMF was evaluated as a steroid-sparing agent and used concomitantly with systemic CS to reduce the overall dose of CS necessary to achieve clinical improvement.[24,25] When used alongside systemic CS, MMF at starting doses of 1 to 2 g/d and increasing to maintenance doses of 2 to 3 g/d resulted in clinical improvements in 85% to 93% of patients with PG, with 36% to 50% having complete resolution of PG lesions within 12 months.[24,25] Adding MMF to the treatment regimen allowed patients to reduce their mean doses of systemic CS from 35 to 40 mg/d to 9 to 18 mg/d.[24] MMF was overall tolerable, with minor GI discomfort being the most commonly reported SE.

Interleukin-1 inhibitors

IL-1 is an inflammatory cytokine that recruits and activates neutrophils, in addition to its involvement in inflammasome formation. Anakinra, an IL-1 receptor antagonist, and canakinumab, IL-1β inhibitor, have been successfully used for the treatment of PG. Among 12 patients treated with anakinra, clinical improvements or complete resolution was

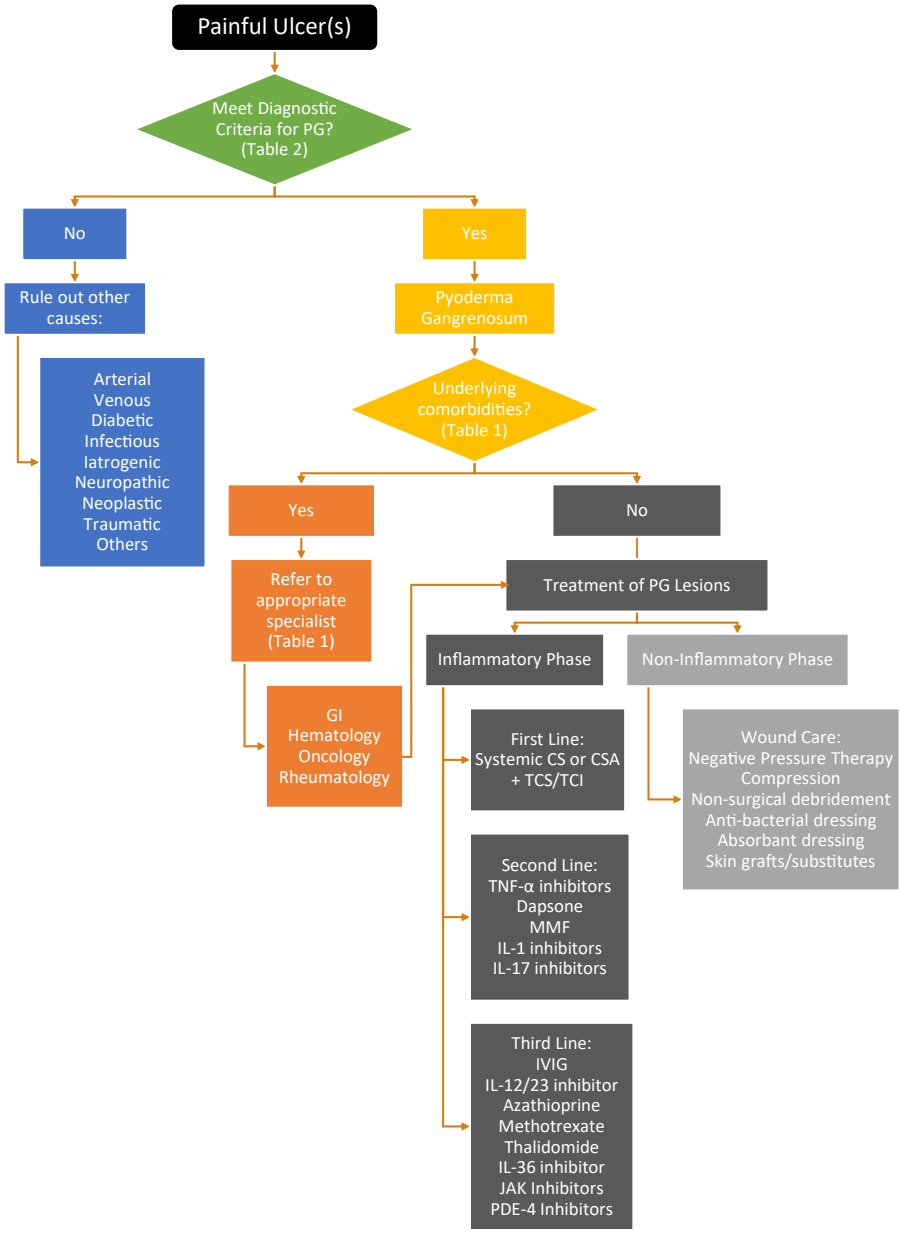

Fig. 1. Management algorithm for PG. CS, corticosteroids; CSA, cyclosporine; GI, gastroenterology; IL, interleukin; IVIG, intravenous immunoglobulin; MMF, mycophenolate mofetil; PDE-4, phosphodiesterase-4; TCI, topical calcineurin inhibitors; TCSs, topical corticosteroids.

observed in 10 patients (83.3%).[26] Among 10 patients with PG, treatment with canakinumab resulted in complete resolution of PG in 6 patients and clinical improvements in 1 patient.[26] In a separate case series of 5 patients with steroid-resistant PG, canakinumab resulted in clinical improvements in 4 patients (80%) after 16 weeks.[27]

Interleukin-17 inhibitors

IL-17 inhibitors secukinumab, brodalumab, and ixekizumab have all been successfully used for the treatment of PG. A small phase I-II investigator-initiated trial found that secukinumab reduced pain significantly in all 7 patients, and resulted in significant clinical improvements in 2 patients after 32 weeks (28%).[28] Secukinumab resulted in complete resolution of PG in 1 patient within 3 months.[29] Brodalumab resulted in complete resolution of PG in 3 patients within 12 weeks, including one that had been previously refractory to secukinumab.[30,31] It was postulated that brodalumab but not secukinumab inhibited IL-17E, which is responsible for the

recruitment of neutrophils by activated macrophages.[31] Ixekizumab resulted in complete resolution of PG in 4 patients within 3 months.[32] Interestingly, IL-17 inhibitors have also been implicated in triggering PG.[33] It is postulated that the inhibition of IL-17 leads to a paradoxic increase in IL-23, thereby inducing PG. Hence, clinicians need to be cautious when choosing IL-17 inhibitors for PG.

Level 3 Evidence (Case-Control Studies)

Intravenous immunoglobulin

Intravenous immunoglobulin (IVIG) is derived from purified plasma pooled from more than 1000 healthy donors and contains supraphysiologic amounts of immunoglobulin G primarily. IVIG has been shown to neutralize pathogenic antibodies in circulation, inhibit antibody production, inhibit complement activation, induce selective apoptosis of autoreactive T cells, and prevent adhesion and migration of inflammatory cells. IVIG is not an immunosuppressive agent, thereby making it an excellent choice in those with concomitant infections or sepsis or steroid-sparing agent.

IVIG has been evaluated as an adjunct treatment of refractory PG.[34–36] Among 50 patients with refractory PG, IVIG as an adjunct to systemic CS or cyclosporine resulted in clinical improvements in 44 patients (88%), with 27 patients (54%) having complete resolution of PG by 6 months.[34,35] No major AEs occurred.

Interleukin-12/23 inhibitors

Ustekinumab targets the common p40 subunit of IL-12 and IL-23 cytokines. IL-12 and IL-23 are proinflammatory cytokines released by antigen-presenting cells that result in the activation of T-helper 1 (Th1) and T-helper 17 (Th17) cellular pathway respectively that lead to downstream inflammatory cytokines that were found to be elevated in PG lesions. Th1 cells produce proinflammatory cytokines IL-2, TNF-α, and IFN-γ, whereas Th17 cells produce proinflammatory cytokines IL-17, IL-22, and TNF-α.

Ustekinumab has been used for the treatment of PG.[14,37] Among 34 patients with PG who received ustekinumab, clinical improvement and complete resolution were seen in 79% and 71% of patients, respectively.[14] Ustekinumab was effective in all types of PG but patients without associated comorbidities had better response to ustekinumab.[37] No major AEs were reported.

Level 4 Evidence (Case Series or Case Reports)

Azathioprine

Azathioprine works by inhibiting purine metabolism and cell division, thereby selectively affecting lymphocyte activation and antibody production. Azathioprine has been used as a steroid-sparing agent in combination with prednisolone, infliximab, and topical tacrolimus for the successful treatment of PG.[38,39]

Colchicine

Colchicine has antimitotic and anti-inflammatory properties. It prevents the proliferation of lymphocytes, reduces recruitment and activation of inflammatory cells including neutrophils, and inhibits inflammasome-mediated IL-1β.[40]

Colchicine has been successful in the management of PG.[41,42] Low-dose colchicine monotherapy was used as a maintenance therapy in 3 patients and allowed for the tapering of traditional immunosuppressive medications without disease recurrence.[41,42]

Methotrexate

Methotrexate is an immunosuppressant that inhibits cellular division through the inhibition of nucleotides necessary for DNA synthesis. Methotrexate has been reported to be successful in the management of PG primarily as a steroid-sparing agent and in combination with adalimumab, infliximab, cyclosporine, dapsone, and systemic CS.[43–47]

Intralesional methotrexate was used as an adjuvant to oral CS.[48] The patient had a lack of response to oral methotrexate, so intralesional methotrexate was instead administered to the borders of PG lesions weekly and the patient had almost complete resolution after 7 weeks.[48] Low-dose methotrexate was also used as an adjuvant to reduce neutralizing antidrug antibodies to infliximab (ADA-I).[46] Among 6 patients with PG who initially responded well to infliximab but subsequently developed ADA-I and lost clinical response, adding low-dose methotrexate resulted in restoration of infliximab's efficacy and complete resolution of PG in 4 patients.[46]

Thalidomide

Thalidomide inhibits neutrophil chemotaxis and phagocytosis and inhibits the production of proinflammatory mediators IL-12, TNF-α, and IFN-γ, whereas it upregulates anti-inflammatory mediators IL-4 and IL-5. Major AEs associated with thalidomide include irreversible peripheral neuropathy and teratogenicity. Thalidomide should be strictly avoided in women of childbearing potential due to the almost 100% incidence of birth defects.[49]

Thalidomide has been successful in the management of numerous neutrophilic disorders including PG. Thalidomide was added as one of the last resorts after patients had failed numerous

conventional immunosuppressants and antibiotics.[50–55] A 49-year-old patient with 27-year history of recalcitrant PG developed significant improvement after 6 months of thalidomide.[50] Thalidomide resulted in complete resolution of lesions in 2 patients with PG involving their penis.[52,56] Thalidomide has also been successful for PG in the pediatric population.[55,56]

Interleukin-23 inhibitors

In contrast to ustekinumab, the IL-23 inhibitors guselkumab, risankizumab, and tildrakizumab target the p19 subunit of IL-23 only and have no effect on IL-12. All 3 IL-23 inhibitors have been used in the treatment of PG. Significant clinical improvements or complete resolution of PG lesions were observed within 3 to 4 months of initiating guselkumab, risankizumab, or tildrakizumab.[57–61]

Interleukin-36R inhibitor

IL-36 is a proinflammatory cytokine released by keratinocytes in response to cutaneous injury that plays a key role in the unrelenting inflammation in PG. Activated IL-36 causes downstream release of neutrophil-recruiting cytokines IL-6, IL-8, IL-17A, and TNF-α, to drive the innate immune response. IL-36 also upregulates the adaptive immunity by skewing Th1 differentiation and reducing T-reg differentiation.

Spesolimab, an IL-36 receptor inhibitor approved for the treatment of generalized pustular psoriasis, has been used in 2 patients with severe, recalcitrant PG.[62] In the first patient, repeated attempts at tapering prednisone and cyclosporine led to disease flare up. Adding spesolimab to his treatment regimen resulted in significant clinical improvements and allowed the tapering of systemic CS and cyclosporine within 5 weeks.[62] Of note, the first patient developed epididymitis on spesolimab requiring treatment with doxycycline. In the second patient, spesolimab added to a regimen consisting of prednisone, cyclosporine, hydroxychloroquine, and IVIG. The patient experienced dramatic improvement in pain and reduced purulent discharge within 48 hours of spesolimab infusion and complete resolution of PG lesions after several weeks.

Janus kinase inhibitors

JAK is a family of tyrosine kinases that respond to proinflammatory cytokines such as IFN-γ and further propagate the proinflammatory response. JAK inhibitors are a newer class of medications that have been approved for other inflammatory or autoimmune disorders including atopic dermatitis and psoriatic arthritis.

JAK inhibitors, baricitinib, ruxolitinib, tofacitinib, and upadacitinib, have been successful in the treatment of 15 cases of PG.[63–67] Patients without underlying comorbidities responded to JAK inhibitors more quickly and without AEs, as compared with patients with underlying associated inflammatory disorders.[63] Potential AEs of JAK inhibitors include reactivation of latent infections including herpes zoster or tuberculosis, liver or lipid abnormalities, or other infections. There are no reports of topical JAK inhibitor use in PG. Of note, in our opinion, JAK inhibitors will be increasingly used for PG and the level of evidence should improve over time because it has been used effectively in recalcitrant PG.

Phosphodiesterase-4 inhibitors

Phosphodiesterase-4 (PDE-4) is an enzyme present mainly in immune cells and is responsible for the downstream expression of proinflammatory cytokines IL-17, TNF-α, and IFN-γ and downregulation of anti-inflammatory cytokines IL-10. PDE-4 inhibitor apremilast has been approved for the treatment of psoriasis, and oral ulcers in Behçet disease recently.

Apremilast has been used either as a monotherapy or adjuvant steroid-sparing agent in the management of PG.[68–70] Apremilast monotherapy was initiated in a patient with 5-year history of PG without underlying associated disorders and resulted in significant clinical improvements within 4 months, and complete resolution after 3 years.[68] Apremilast was used as a steroid-sparing agent in 2 cases of PG and allowed the tapering of systemic CS.[69,70] Side effects reported include diarrhea, nausea, and weight loss. There are no reports of topical PDE-4 inhibitors crisaborole and roflumilast for PG.

SUMMARY

PG remains an orphan disease that neither has any approved treatments nor has active clinical trials evaluating potential treatments.[71] Management of PG requires a multidisciplinary approach, involving but not limited to dermatology, pain, wound care, plastic surgery, and management of underlying associated disorders.

Systemic CS, cyclosporine, and TNF-α inhibitors have the strongest evidence supporting their efficacy and safety in PG. Although systemic CS is the most popular first-line option, it has been associated with higher incidence of serious AEs compared with cyclosporine and TNF-α inhibitors.[9,72] The choice between systemic CS and cyclosporine should be based on the patient's preexisting comorbidities and lesion size.[9] Ultrapotent TCSs, intralesional CS, or TCI should be used in conjunction with systemic therapies to minimize overall dose required to achieve disease remission.

Once inflammation of PG is in remission, then the focus should be redirected to other factors that may affect wound healing. A useful mnemonic, TIME, has been proposed: tissue, infection, moisture, and epithelization.[73] Although surgical debridement is contraindicated due to the risk of pathergy, the use of nonsurgical debridement, negative pressure wound therapy, and compression, have shown to be safe and effective for PG.[73,74] Patients without underlying associated comorbidities tended to have better response to treatment and suffered fewer treatment-related AEs.

CLINICS CARE POINTS

- PG remains an orphan disease with no approved treatment
- Multidisciplinary approach to PG is necessary for optimal management, especially for wound care and underlying comorbidities
- Systemic CS, cyclosporine, and TNF-α inhibitors have the greatest body of evidence supporting their use in PG
- Patients receiving systemic CS suffered more serious AEs than patients receiving cyclosporine. The choice of medication should be based on the patient's preexisting comorbidities and size of PG lesions. Patient characteristics discouraging the use of prednisone include obesity, impaired fasting glucose, osteoporosis, gastrointestinal ulcers, mental illness, and large lesion size ($\geq$20 cm). Patient characteristics discouraging the use of cyclosporine include hypertension, renal insufficiency, and malignancy
- Topical CS, intralesional CS and/or TCI should be incorporated into most treatment regimen due to low risk of AEs
- Spesolimab, a new IL-36 receptor antagonist, has demonstrated preliminary evidence for treating neutrophilic disorders including PG
- Patients without underlying associated disorders tended to have better response to treatment and suffered fewer incidences of treatment-related AEs

DISCLOSURE

The authors have nothing to disclose.

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