

# Hidradenitis Suppurativa and Concomitant Pyoderma Gangrenosum Treated With Infliximab

Patricia F. Groleau, MD; Anna L. Grossberg, MD; Anthony A. Gaspari, MD

## Practice Points

- Pyoderma gangrenosum (PG) and hidradenitis suppurativa (HS) are rare chronic inflammatory dermatoses that may coexist in the same patient.
- Infliximab may represent an effective therapeutic option for the treatment of concurrent PG and HS that is refractory to conventional therapies.

*Pyoderma gangrenosum (PG) and hidradenitis suppurativa (HS) are rare chronic inflammatory dermatoses of unknown etiologies that often are refractory to conventional treatments. The therapeutic benefits of tumor necrosis factor  $\alpha$  (TNF- $\alpha$ ) inhibitors have been reported in patients with refractory PG or HS. The copresentation of these 2 diseases has previously been described in several cases in the literature and may present a therapeutic challenge. We present the case of a 51-year-old man who developed widespread inflammatory ulcers affecting approximately 50% of the body surface area and subsequent chronic debilitation from severe pain. He was ultimately diagnosed with concurrent PG and HS. Both diseases remitted in response to treatment with infliximab, which resulted in complete restoration of skin integrity and resolution of his chronic severe pain.*

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From the Department of Dermatology, University of Maryland School of Medicine, Baltimore.

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Correspondence: Anna L. Grossberg, MD, 419 W Redwood St, Ste 240, Baltimore, MD 21201 (agrossberg@som.umaryland.edu).

**P**oderma gangrenosum (PG) and hidradenitis suppurativa (HS) are rare chronic inflammatory dermatoses of unknown etiologies that often are refractory to conventional treatments. Multiple case reports have described the coexistence of these 2 diseases in the same patient.<sup>1-11</sup> The diagnosis of PG commonly followed the diagnosis of HS by 5 months to 30 years in several of these cases, suggesting that HS may have triggered a possible underlying inflammatory process that resulted in subsequent development of PG. When presenting in the setting of preexisting HS, PG lesions have occurred both in the same sites of the body affected by HS as well as in distinct sites such as the legs.<sup>1</sup>

Although the treatment of either PG or HS alone can be difficult, the combination of these 2 diseases presents a further therapeutic challenge. Tumor necrosis factor  $\alpha$  (TNF- $\alpha$ ) has been implicated in the pathogenesis of both of these diseases, and several cases have demonstrated great potential for the use of TNF- $\alpha$  inhibitors, particularly infliximab, in the treatment of resistant cases of each of these conditions.<sup>2,12</sup> We report a case of severe concurrent PG and HS in a 51-year-old man that was refractory to other treatments but clinically remitted in response to infliximab therapy.

## Case Report

A 51-year-old man was transferred to our institution from an outside hospital where he had presented

with fevers and a worsening rash that had prevented him from ambulating for several days secondary to severe pain. At the outside facility, he was noted to have extensive ulcerations with granulation tissue on the scalp, face, sacrum, buttocks, and bilateral legs. A skin biopsy performed at the outside facility revealed a neutrophilic dermal infiltrate with abscesses and granulation tissue consistent with PG. He was transferred to our institution for continued local wound care, corticosteroid administration, and hyperbaric oxygen therapy.

On presentation at our institution, continued ulcerative skin lesions were noted in the previously

mentioned areas (Figures 1A and 1B), and deeper purulent sinus tracts were noted in the axillae and extending onto the chest (Figure 1C). A biopsy from the chest showed folliculitis with a prominent plasmacytic infiltrate consistent with HS. Cultures from the sinus tracts showed abundant growth of *Enterobacter aerogenes*, *Klebsiella pneumoniae*, *Enterobacter cloacae*, and *Proteus mirabilis*. The patient was subsequently treated with intravenous ampicillin-sulbactam and vancomycin as well as oral prednisone 80 mg daily for 2 weeks with only mild improvement of the lesions. The prednisone was gradually tapered to



**Figure 1.** On initial presentation, extensive areas of ulceration with variable amounts of granulation tissue and rusting were noted on the scalp (A) and legs (B). Sinus tract formation also was evident in the neck (A) and axilla (C).

a dose of 10 mg daily in preparation for a trial of infliximab. During the early course of his therapy, subsequent cultures from draining sinus tracts grew *Pseudomonas aeruginosa* and *Acinetobacter baumannii*, requiring concomitant treatment with oral antimicrobials including doxycycline, sulfamethoxazole-trimethoprim, ciprofloxacin, and amoxicillin-clavulanic acid for control of the superinfection.

The patient received 3 induction infusions of infliximab at a dosage of 5 mg/kg per treatment at weeks 0, 2, and 6. At the time of the first treatment, he was noted to have numerous crusted draining

erosions on the head, neck, and chest. The patient reported no adverse effects during or after each treatment. Following completion of the 3 infliximab infusions, the skin lesions showed considerable improvement, with only 1 draining lesion remaining on the left temple and only erythematous plaques remaining on the scalp, upper back, and axillae. Maintenance infusions were continued every 8 weeks with an increased infliximab dose of 7.5 mg/kg.

After 1 year of treatment, the lesions had healed to form cicatrices with no evidence of erythema, drainage, or infection (Figure 2). Doxycycline and prednisone were discontinued, and the infliximab



**Figure 2.** After 11 infusions with infliximab (dose range, 5–7.5 mg/kg), all previously affected areas showed resolution with cicatrices and postinflammatory hyperpigmentation (A–C), with no evidence of ulceration or active sinus tract formation.

dose was decreased to 5 mg/kg per infusion every 8 weeks. Following sustained improvement after 2 infusions at this lower dose, infliximab was successfully tapered to 2.5 mg/kg every 8 weeks for 2 doses and then was subsequently discontinued; however, the patient's disease relapsed approximately 7 months after discontinuation of the infliximab and was immediately resumed at a dose of 5 mg/kg per infusion every 8 weeks. He has remained disease free on this dose to date.

### Comment

Pyoderma gangrenosum is a chronic inflammatory ulcerative skin condition that most commonly occurs on the lower legs.<sup>3</sup> In its most common form, PG lesions typically begin as tender erythematous nodules or pustules that evolve into enlarging painful ulcers with raised, undermined, violaceous borders.<sup>13</sup> Biopsy specimens taken from the edges of the lesions typically show a diffuse neutrophilic infiltrate, and pseudoepitheliomatous hyperplasia also may be seen. Lesions tend to persist for months to years, ultimately healing as cribriform scars. The etiology of PG is unknown and its pathogenesis is poorly understood.<sup>13</sup> Pyoderma gangrenosum is associated with an underlying systemic disease in approximately 50% of cases, most commonly inflammatory bowel disease, hematologic malignancies, and inflammatory arthritis.<sup>3</sup> An underlying immunologic abnormality is therefore postulated to contribute to the pathogenesis of PG, as it is frequently associated with these immune-mediated systemic diseases.

There is no specific and uniformly effective treatment of PG, but the main therapeutic goals include the reduction of inflammation to promote wound healing, pain reduction, and the treatment of any comorbid diseases that may contribute to the severity of PG, all while minimizing adverse side effects. Systemic corticosteroids and cyclosporine have been reported to produce the most effective results,<sup>13</sup> but due to the side effects and toxicities of these drugs, they are often reserved for severe cases in which the benefits of their use outweigh the risks for other comorbidities. Other reported treatments include antimicrobial agents, topical and intralesional corticosteroids, steroid-sparing immunosuppressive agents, colchicine, hyperbaric oxygen therapy, and more recently drugs that function via immune modulation such as TNF- $\alpha$  inhibitors.

Hidradenitis suppurativa is a chronic suppurative inflammatory disease of follicular occlusion in apocrine gland-bearing areas of the skin such as the groin, axillae, and anogenital region.

Hidradenitis suppurativa is characterized by recurrent skin abscesses, sinus tract and fistula formation, and subsequent fibrosis with bacterial overgrowth as a common secondary process.<sup>14</sup> The pathogenesis of HS remains poorly understood, but histology typically shows a nonspecific inflammatory process with or without concomitant infection.<sup>15</sup> Treatment of HS is complex and usually is transiently effective at best.<sup>14</sup> In 2012, Rambhatla et al<sup>16</sup> discussed the efficacy of various treatments of HS, including systemic and topical antimicrobial agents (eg, clindamycin-rifampicin combination treatment, tetracycline, topical clindamycin phosphate, isotretinoin, dapsone), antiandrogenic agents, biologic agents (eg, infliximab, etanercept, adalimumab, efalizumab), laser surgery (CO<sub>2</sub> laser, Nd:YAG laser), and excisional surgery of sinus tracts. Other therapies include cryotherapy, photodynamic therapy, finasteride, zinc gluconate, topical resorcinol, and acitretin.<sup>16</sup>

Both PG and HS are categorized as chronic inflammatory disorders with nonspecific histopathologic findings. Although the etiologies of these 2 disorders remain poorly understood, several case reports have suggested an association between PG and HS.<sup>14</sup> In many of the reported cases of concurrent HS and PG, HS preceded the diagnosis of PG by several years and no correlation in disease activity was observed between the 2 conditions.<sup>1,4,6-8</sup> Additionally, the clinical triad of PG, acne, and suppurative hidradenitis, known as PASH syndrome, has been described, which may represent a new entity within the spectrum of autoinflammatory syndromes.<sup>5</sup> It is not uncommon for either PG or HS to be refractory to conventional therapies, and therefore the management of concomitant PG and HS presents an even further therapeutic challenge.

Recently, biologic agents such as TNF- $\alpha$  inhibitors have been used with increased frequency as novel treatments for severe dermatologic diseases including psoriasis and pemphigus vulgaris, among others.<sup>17</sup> Furthermore, several reports have presented convincing results in the off-label use of TNF- $\alpha$  inhibitors in the treatment of isolated PG as well as in the treatment of HS.<sup>12,14,17-22</sup> Infliximab, a chimeric anti-TNF- $\alpha$  monoclonal antibody, has been used with particular success in recalcitrant cases of these conditions.<sup>12,17,19-21</sup>

In a double-blind, placebo-controlled, crossover trial analyzing 38 patients with moderate to severe refractory HS, Grant et al<sup>19</sup> found that treatment with infliximab was associated with a significantly greater improvement in pain intensity ( $P < .001$ ), disease severity ( $P < .001$ ), and quality of life ( $P = .003$ ), with



concomitant reduction in clinical markers of inflammation compared to placebo. Similarly, a randomized, double-blind, placebo-controlled trial by Brooklyn et al<sup>12</sup> evaluated 30 patients with refractory PG. In this study, infliximab was shown to be superior to placebo for rapid clinical response in patients with PG irrespective of the existence of concomitant inflammatory bowel disease.<sup>12</sup>

On the contrary, lack of efficacy and/or adverse reactions associated with infliximab and other TNF- $\alpha$  inhibitors in the treatment of PG and HS also have been reported in the literature. Fardet et al<sup>20</sup> reported that 2 of 7 (28.6%) HS patients treated with at least 3 infusions of infliximab (5 mg/kg) at weeks 0, 2, and 6 had minimal or nonexistent improvement by week 6. Additionally, adverse events occurred in 3 of 7 (42.9%) HS patients, including abdominal pain caused by colon cancer, multifocal motor neuropathy with conduction block, and a severe allergic reaction.<sup>20</sup> Usmani et al<sup>21</sup> described 1 HS patient who developed an infliximab-induced lupus reaction, 1 who experienced a hypersensitivity reaction to infliximab, and 2 who had poor response to treatment despite 3 infusions. Kleinpenning et al<sup>22</sup> reported a case of PG that failed consecutive trials of etanercept and adalimumab. Wolbing et al<sup>23</sup> reported a case of septic shock after treatment of PG with infliximab. Shareef et al<sup>24</sup> reported progression of IgA gammopathy to myeloma following infliximab treatment for PG in 1 patient.

Of the reported cases of concurrent HS and PG, 3 were treated with TNF- $\alpha$  inhibitors, both alone and in conjunction with other treatment modalities, with varying results. One patient demonstrated a partial response to treatment with etanercept followed by infliximab, 1 was resistant to treatment with infliximab as well as adalimumab, and 1 exhibited clinical improvement following treatment with infliximab.<sup>1,2</sup>

## Conclusion

In our patient with concurrent PG and HS, both conditions showed dramatic improvement with infliximab therapy, and this response has been sustained on 5-mg/kg infliximab maintenance therapy every 8 weeks for the last 3 years. Our case suggests that infliximab may represent an effective therapeutic option for the treatment of concurrent PG and HS that is refractory to conventional therapies. It is yet to be seen whether our patient will continue to experience sustained remission in both his PG and HS permitting the discontinuation of infliximab. Continued study of infliximab and other TNF- $\alpha$  inhibitors is necessary to establish their long-term

safety and efficacy for use in patients affected by both HS and PG.

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