CASE REPORT

Generalized pyoderma gangrenosum treated with adalimumab : Case Report

Ali S. Alghamdi, MD

Dermatology consultant, Aseer Central Hospital, Kingdom of Saudi Arabia, Abha

ABSTRACT

I report a case of generalized pyoderma gangrenosum in a 39 year old Saudi female patient treated with adalimumab with complete response and without side effects.

KEY WORDS: Inflammatory bowel disease; Extra-intestinal manifestations; Adalimumab; Pyoderma gangrenosum; Ulcerative colitis

INTRODUCTION

Pyoderma gangrenosum is a rare inflammatory disease of unknown etiology characterized by sterile neutrophilic infiltration of the skin. The diagnosis is usually made by exclusion of other infective causes of cutaneous ulcers. There is no gold standard treatment available, and there is a paucity of clinical trials to support evidence-based therapies.

Many case reports and series mentioned the effectiveness of anti-tumor necrosis factor alfa (Anti- TNF-α) in treating pyoderma gangrenosum.

Here, I report a case of pyoderma gangrenosum in a Saudi female treated successfully with adalimumab therapy and without any side effects.

CASE REPORT

My patient was a 39 year old Saudi female, a known case of diabetes mellitus and hypertension who came to emergency department with multiple disseminated painful skin lesions since more than 3 months. The lesions over the groin, buttocks & axillae were ulcerated and very painful and had enlarged with time. She also complained of abdominal pain and diarrhea on and off since one month. There was no history of fever, vomiting, joint pain or cough.

She had visited many medical centers in the past and received numerous courses of both topical and oral antibiotics without improvement.

The patient was on Insulin for her diabetes but was taking no medications for blood pressure. Past and family history were unremarkable.

CLINICAL EXAMINATION

Her vital signs were normal, except for the blood pressure, which was 145/85. General examination revealed only mild abdominal tenderness but no organomegaly, there were no palpable lymph nodes.

Skin examination: There were multiple ulcer-

Correspondence: *Dr. Ali S. Alghamdi, Dermatology consultant, Aseer Central Hospital, Kingdom of Saudi Arabia, Abha*
Email : asgh60@yahoo.com

ations in the groin, axillae, buttocks and abdomen. The ulcers in both axillae were very deep and tender. Whereas, the ulcers in the groin and buttocks were not deep but painful and wet. The rest of the ulcers on her body were shallow, not oozing and not very painful (Fig. 1). Some lesions exhibited clear koebner (pathergy) phenomenon after minor trauma and scratching. (Fig. 2)

Nails: There were erythematous scaly patches over some nailfolds associated with edema. Mucous membranes and hairs were not involved.

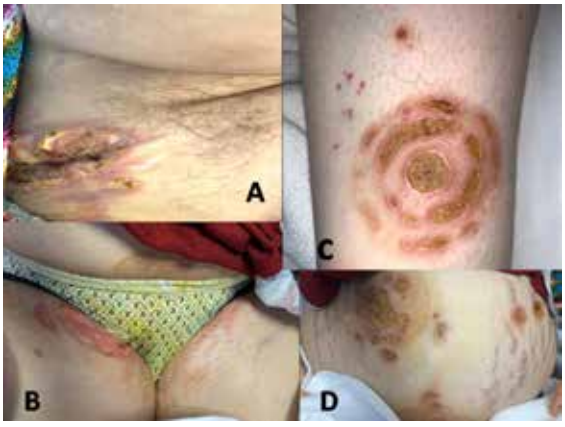

Fig. 1 Multiple ulcerations some are very deep (A) and some are superficial (B-D)

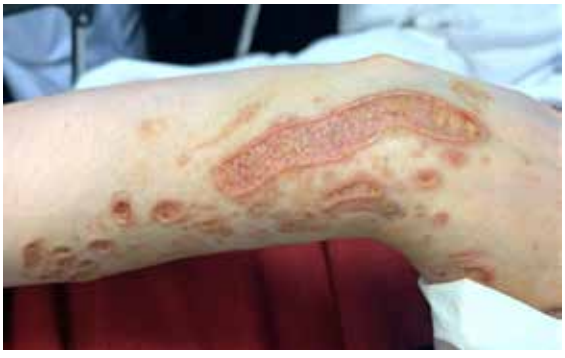

Fig. 2 Koebner phenomenon over the extremities

COURSE IN THE HOSPITAL

The patient was admitted to our hospital under care of gastroenterology team as query inflammatory bowel disease (IBD) case for evaluation. Two skin biopsies were taken from the abdominal skin and buttocks, both revealed ulcerative epidermis with heavy neutrophilic infiltrate in the dermis & deep dermis follicular abcesses. No vasculitic changes were seen, and also special stains for fungi were negative.

Hemogram revealed raised leucocyte count, predominantly neutrophils, low hemoglobin, significantly raised ESR(90 mm/hr), and adequate platelet count. Other significant laboratory abnormalities included low serum albumin and high blood sugar levels. Coloscopy was essentially normal.

Other investigations including c-ANCA, P-ANCA were negative. Hepatitis B, C and HIV serology all were negative. Bacterial wound culture showed no growth.

So the provisional diagnosis of pyoderma gangrenosum was made. She was started on methyl prednisolone 50 mg once daily given intravenously, which lead to dramatic increase in her blood sugar (500 mg/dl). Also, cyclosporine 100 mg orally twice a day was started, and she improved reasonably within a week. She was then discharged on tab prednisolone 30 mg daily and cyclosporine 100 mg twice a day. The patient came to our clinic after 1 month with good improvement in her skin lesions. But, because of her high blood sugar and blood pressure, it was decided to taper both steroids and cyclosporine. The patient was then started on adalimumab 80 mg subcutaneously, followed by 40 mg subcutaneously after a week, and then 40 mg every other week. Cyclosporine was stopped after 2 weeks of starting adalimumab. The patient then came to our clinic with dramatic improvement after 6 weeks, and remained under control without any new lesions. All of her old lesions healed completely with remaining scars and postinflammatory hyperpigmentation only. (Fig. 3 & 4)

DISCUSSION

Pyoderma gangrenosum (PG) is a rare, chronic, recurrent neutrophilic inflammatory condition characterized by the presence of painful and necrotic ulcerations with a neutrophil-rich infiltrate. It has four major clinical forms: Ulcerative, bullous, pustular, and superficial granulomatous.[1]

It can occur at any age but most commonly affects women between 20 and 50 years of age. Almost half of patients have an underlying systemic disease, most commonly inflammatory bowel disease, arthritis or a hematologic disorder (e.g. IgA monoclonal gammopathy, acute myelogenous leukemia, myelodysplasia). The lesions of PG usually begin as a tender papulopustule with surrounding erythematous or violaceous induration, these lesions then undergo necrosis leading to a central shallow or deep ulcer; loss of tissue can expose underlying tendons or muscles. Cutaneous lesions are painful and most frequently occur on the lower extremities in patients with classical PG, especially the pretibial area but they can be anywhere and can be rarely generalized. It may involve mucous membranes and peristomal sites.

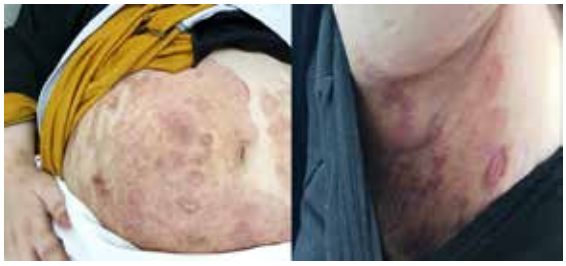

Fig. 3 Healed lesions with scar and postinflammatory hyperpigmentation

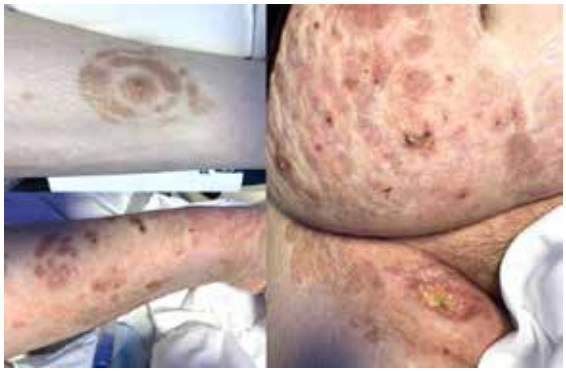

Fig. 4 Healed lesions with scar and postinflammatory hyperpigmentation at 6 months after starting the therapy

The lesion of pyoderma gangrenosum may occur secondary to minor trauma such as scratching (Koebner phenomenon or Pathergy). It has been described in roughly 20% to 30% of patients.[2] (Fig. 2)

The pathogenesis of pyoderma gangrenosum (PG) is multifactorial and involves neutrophilic dysfunction, inflammatory mediators, and genetic predisposition.[3] PG lesions show an overexpression of IL-8; IL-17; tumor necrosis factor-alfa; chemokines 1, 2, 3, and 16; and matrix metalloproteinase (MMP) 2 and 9.[4] Histopathology of pyoderma gangrenosum is not specific. Microscopic features include massive neutrophilic infiltration, hemorrhage, and necrosis of the overlying epidermis.

The management of PG is complicated and must include different approaches of pain control, wound care and treatment of the inflammatory process, there is no definitive treatment guidelines for PG. The management approach generally depends on the number, size and depth of the lesions, the rate of expansion and appearance of new lesions, the associated disorder, the medical status of the patient.

The goal of treatment is to decrease the inflammation and to promote healing, also to treat the patient's underlying condition (IBD and leukemia).

The localized ulcers can be treated by class I topical corticosteroids such as clobetasol propio-

nate 0.05%, topical calcineurin inhibitors such as tacrolimus 0.1% or intralesional corticosteroids. First-line therapy for more severe or extensive PG is systemic glucocorticoids,[5] typically begin treatment at 1 to 2 mg/kg of oral prednisone daily. The response usually is good. But, because long-term therapy is associated with significant adverse effects, slow glucocorticoid taper should begin once progression of PG has stopped. Systemic steroid sparing therapies include, cyclosporine,[6,7] mycophenolate mofetil,[8,9] azathioprine, dapsone, tacrolimus, cyclophosphamide, thalidomide.[10]

Because of the rarity of the disease there are only few reports of using biologic medications for pyoderma gangrenosum. For patients with recalcitrant, severe disease many biological treatment have been used to treat including tumor necrosis factor-alpha (TNF-alpha) inhibitors etanercept, infliximab,[11-13] adalimumab and anti IL-12 and IL-23 blocker ustekinumab.[14-16] Adalimumab is a fully-human monoclonal antibody against TNF-α, many of case reports,[17-20] and in a small placebo-controlled trial[21,22] approved the efficacy of adalimumab in treating pyoderma gangrenosum, particularly in patients with PG and concomitant Inflammatory bowel disease (IBD), Since the TNF-α play a major role in the pathogenesis of the disease progression.

Fonder et al report a case of IBD with pyoderma gangrenosum, treated successfully with adalimumab,[23] the same results have also was been reported in other case reports.[24,25]

Another case of pyoderma gangrenosum, acne, and hidradenitis suppurativa in end-stage renal disease was successfully treated with adalimumab.[26]

In a semi-systematic review done by Abdallah et al, 356 patients, 275 were treated with infliximab, 43 were treated with adalimumab, 36 were treated with etanercept, and 2 were treated with certolizumab. An 87% overall response rate and a 67% complete response, the best response was with adalimumab. Although, there were no statistically significant differences in response or complete response rates.[27]

In our patient, we started her on adalimumab after reasonable response to oral prednisolone and cyclosporine combination. But, due to very high blood sugar and high blood pressure we had to start her on adalimumab at dose of 80 mg then 40 mg every 2 weeks, and she improved after 2 months of starting adalimumab and continue to be controlled for almost 2 years of her first dose.

CONCLUSION

Adlimumab is good option to treat sever pyoderma gangrenosum, it is effective and safe medication.

REFERENCES

1. Powell FC, Su WP, Perry HO. Pyoderma gangrenosum: classification and management. J Am Acad Dermatol. 1996; 34:395-409.
2. Callen JP, Jackson JM. Pyoderma gangrenosum: an update. Rheum Dis Clin North Am. 2007; 33:787-902.
3. Braswell et al, Pathophysiology of pyoderma gangrenosum (PG): an updated reviewJ Am Acad Dermatol. 2015; 73(4):691-98.
4. Marzano AV, Fanoni D, Antiga E, et al. Expression of cytokines, chemokines and other effector molecules in two prototypic autoinflammatory skin diseases, pyoderma gangrenosum and Sweet's syndrome. Clin Exp Immunol. 2014; 178:48-56.
5. Prystowsky JH, et al. Present status of pyoderma gangrenosum. Review of 21 cases. Arch Dermatol. 1989; 125:57-64.
6. M C Fedi et al, Recalcitrant pyoderma gangrenosum responsive to cyclosporine, Int J Dermatol. 1993; 32(2):119.

7. W L Matis et al, Treatment of pyoderma gangrenosum with cyclosporine, Arch Dermatol. 1992; 128(8):1060-64.
8. Daniels et al. Mycophenolate mofetil is an effective treatment for peristomal pyoderma gangrenosum, Arch Dermatol. 2004; 140(12):1427-29.
9. Eaton PA, et al. Mycophenolate mofetil as therapy for pyoderma gangrenosum, Arch Dermatol. 2009; 145(7):781-85.
10. Malkan et al. Treatment of pyoderma gangrenosum with thalidomide in a myelodysplastic syndrome case, Int Med Case Rep J. 2016; 16;9:61-4.
11. Regueiro M, Valentine J, Plevy S, Fleisher MR, Lichtenstein GR. Infliximab for treatment of pyoderma gangrenosum associated with inflammatory bowel disease. Am J Gastroenterol 2003; 98:1821-26.
12. Brooklyn TN, Dunnill MG, Shetty A, et al. Infliximab for the treatment of pyoderma gangrenosum: a randomised, double blind, placebo controlled trial. Gut 2006 ;55:505-509.
13. Agarwal A, Andrews JM. Systematic review: IBD-associated pyoderma gangrenosum in the biologic era, the response to therapy. Aliment Pharmacol Ther 2013; 38:563-72.
14. Vallerand, Ustekinumab for the treatment of recalcitrant pyoderma gangrenosum: A case report, SAGE Open Medical Case Reports, DOI: 10.1177/2050313X19845206.
15. J. S. Westerdahl, et al. Ustekinumab as adjuvant treatment for all pyoderma gangrenosum subtypes. J Dermatolog Treat. 2022; 33(4):2386-90.
16. Zhi Mei Low et al. Treatment of severe recalcitrant pyoderma gangrenosum with ustekinumab, Australas J Dermatol. 2018; 59(2):131-34.
17. A. Campanati et al. Finally, recurrent pyoderma gangrenosum treated with Adalimumab: case report and review of the literature. J Eur Acad Dermatol Venereol. 2015; 29: 1235-47.
18. Louisa Hinterberger et al. Adalimumab: a Treatment Option for Pyoderma Gangrenosum After Failure of Systemic Standard Therapies. Dermatol Ther. 2012;2:6.
19. Kleinfelder et al. Multiple Facial Lesions of Recalcitrant Pyoderma Gangrenosum Successfully Treated with Adalimumab. J Clin Aesthet Dermatol. 2019; 12(5):28-32.
20. K Arivarasan et al. Biologics for the treatment of pyoderma gangrenosum in ulcerative colitis. Intest Res. 2016; 14(4):365-68.
21. Brooklyn TN, Dunnill MG, Shetty A, Bowden JJ, Williams JD, Griffiths CE, et al. Infliximab for the treatment of pyoderma gangrenosum: a randomised, double blind, placebo controlled trial. Gut. 2006; 55:505-509.
22. Yamasaki et al. Adalimumab in Japanese patients with active ulcers of pyoderma gangrenosum: Final analysis of a 52-week phase 3 open-label study. J Dermatol. 2022; 49:479-87.
23. Fonder et al. Adalimumab Therapy for Recalcitrant Pyoderma gangrenosum, J Burns Wounds. 2006; 20; 5:e8.
24. Jin-Hyup Lee et al. Treatment of Recalcitrant Pyoderma Gangrenosum with Ulcerative Colitis by Adalimumab Injection, Ann Dermatol. 2017; 29(2):260-62.
25. A Campanati et al. Finally, recurrent pyoderma gangrenosum treated with Adalimumab: case report and review of the literature, J Eur Acad Dermatol Venereol. 2015; 29(6):1245-47.
26. J de Wet et al. Pyoderma gangrenosum, acne, and suppurative hidradenitis syndrome in end-stage renal disease successfully treated with adalimumab, Dermatol Online J. 2017; 23(12):13030.
27. Abdallah et al. Pyoderma gangrenosum and tumour necrosis factor alpha inhibitors: A semi-systematic review, Int Wound J. 2019; 16:511-21.