Case Report of Treatment Resistant Pyoderma Gangrenosum

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Abstract

This is a case of a 38-year-old married female diagnosed with Pyoderma Gangrenosum (PG) for 4 years. This patient was very anxious and frustrated. The patient was using all the standard treatments for PG, oral steroids 40mg/day, colchicine 2mg/day, topically tacrolimus 0.1%, topically metronidazole, oral 3rd generation of cephalosporin antibiotics 1gm/day, and oral dapsone 100mg/day but lesion was getting worse. The patient family and her husband were very supportive and all the negative options of physical and mental abuse, and not taking proper medicine have been completely ruled out by taking a detailed history from the patient alone. The patient is willing to get the cure and take and apply for all the medicines properly. All the other diseases have been ruled out that can be associated with PG such as inflammatory bowel diseases, trauma, vasculitis, arthritis, *etc*. The patient has been to many physicians but has not been able to get better and the lesion is getting worse day by day and because of this patient started the symptoms of depression and start losing weight. PG is a very worrisome disease and usually, PG cure rate is unpredictable. Patients having PG have emotional problems too because of lesions. The patient usually isolates herself from society and lost all her confidence.

Keywords: *Depression, pathergy, Pyoderma Gangrenosum, treatment resistance, inflammatory bowel diseases.*

INTRODUCTION

A 38-year-old female patient came to us with diagnosed case of PG. The patient had an ulcerative lesion on her left lateral side of the leg with oozing of blood, necrotic base with purulent exudates visible on this lesion. The patient was not mentally well and lost all her hopes [1]. The patient was receiving all the standard treatments but not getting better [2]. The patient has had this lesion for more than 4 years. The lesion was started as a painless papule and getting expanded day by day [3]. She did not have any disease that can be co-associated with PG [4]. To confirm the diagnosis, we planned to do the skin biopsy and culture of the lesion [5]. Pyoderma gangrenosum (PG) is a chronic, neutrophilic dermatosis involving the skin and can be associated with many diseases. PG usually not getting better completely and some patients of PG like this patient are completely resistant to all the standard treatments options such as antibiotics, dapsone, oral steroid, tacrolimus, *etc* [6].

CASE DISCUSSION

The 38-year-old married female diagnosed case of PG came to us with the complaint of not getting better irrespective of receiving all the standard treatments for severe PG for 4 years. The patient had an ulcerative lesion on the mid-left lateral side of the leg. The patient told us that this lesion started as a small papule 4 years back with severe itching and over time the papule converted into a pustule and then painful ulceration developed **Fig. (1A)**. The patient has developed an ulcer size around 4x3 cm and oozing of blood, pustular exudate, necrotic base with dilated vessels and visible sub-cutaneous tissue can be noticed on the base of the ulcer visible in **Fig. (1B**) [7]. Our team picked that case and we wanted to reconfirm the diagnosis and rule out necrobiosis lipodica, any chronic fungal or nocardial infection. The patient did not have any blood sugar impairment with normal HbA1c and no high blood pressure noted. Our team ruled out the other disease, cancers, malignancies, and syndromes that can be associated with this kind of lesion. We planned to do the skin biopsy, run special stains and cultures to rule out fungal infection. Lesion biopsy pictures in **Fig. (2A-2C)** show that there wasn't necrobiosis lipodica, acute and chronic inflammation getting deep from the dermis to subcutaneous tissues. Granulation tissue can be visible with dilated vessels and no fungal infection is visible on special stains [8]. The patient was on medications for the

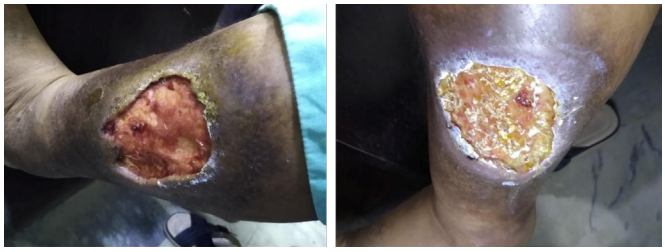

Fig. 1: (A) Shows the annular lesion of the PG 2 years back. **(B)** Shows current condition of lesion after taking all the standard medicine of PG and not getting better.

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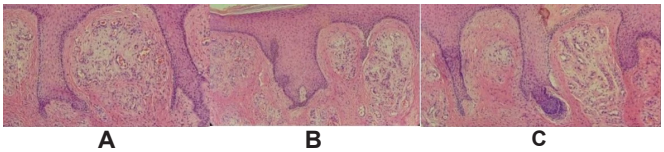

Fig. (2): (A-C) In biopsy sectioned, it reveals stratified squamous lined tissue with surface ulceration and granulation tissue. Dermis show acute and chronic inflammation extending deep into the subcutaneous tissue. There are congested dilated vessels. No evidence of vasculitis seen. No fungal organism seen on special stain. No evidence of granuloma or malignancy seen.

treatment of the PG, including oral steroids 40mg/day, colchicine 2mg/day, topically tacrolimus 0.1%, topically metronidazole, oral 3rd generation of cephalosporin antibiotics 1gm/day, and oral dapsone 100mg/day but nothing is working against this lesion.

DISCUSSION

Pyoderma gangrenosum (PG) is a rare, chronic, noninfectious neutrophilic dermatosis involving the skin and is strongly correlated with underlying diseases of gastrointestinal, arthritides, hematological, hepatic, vasculitides, autoimmune, drugs, and solid organ tumors [9]. Diseases mostly associated with PG include inflammatory bowel disease, arthritides like rheumatoid arthritis and seronegative arthritis, hematologic malignancies especially hairy cell leukemias and myelogenous leukemias, and monoclonal gammopathies in particular immunoglobulin A gammopathy. The pathogenesis of PG is still yet to be fully elucidated; however, an immune-mediated response has been implicated with defects reported in both the cell-mediated and humoral arms. Neutrophils play a definitive role in the disease process and upregulation of certain proinflammatory and neutrophil chemotactic factors like IL-1-Beta, IL-8, IL-6, IL-17, and TNF alpha has been reported within the lesions.

Other mechanisms reported are Arthus reaction which causes circulating immune complexes to deposit in the vessels and stimulate the classic and alternative complement cascade, however, the direct immune-fluorescence staining is performed on postcapillary venules revealed inconsistent results with no complement factors, immunoglobulins, and fibrin seen in the vessels [10].

Different types of PG have been discussed in the literature. Ahmadi and Powell distributed the lesions in two main categories [11]. a) The main classification in which ulcerative, pustular, bullous, and vegetative types are included and b) Atypical presentation in which pathergic, peristomal, dorsal hand, head, and neck, multisystem and paraneoplastic types are included. There are 2 types of major classifications for PG *i.e.* main and atypical classification and its further subclassifications.

Main Classification: a) Ulcerative PG lesions: represents the most common type amongst all and presents as small, tender, red-blue plaques, papules, and pustules with violaceous undermined borders evolving into painful ulcers. Underlying granulation tissue, necrotic tissue, or purulent exudate may be present at the ulcer base. An atrophic cribriform scar appears in the healing stage. In 70% of the cases, lesions are mostly located on the legs but may be present on any other part of the body and are usually associated with fever, malaise, myalgias, and arthralgias, b) Pustular PG usually appears during acute exacerbations of IBD and presents as discrete painful pustules with surrounding erythema mostly on the extensor surfaces of the limbs. They often resolve with treatment of IBD but some may erupt as ulcerative classic PG lesions, c) Bullous PG presents as rapidly evolving hemorrhagic bullae located on the arms. The clinical features and histopathological findings are somewhat similar to sweet's syndrome, but the bullous lesions typically ulcerate and heal with scarring. Bullous PG is strongly affiliated with myeloproliferative disorders and can also present in patients with a remarkable disease flare of IBD, d) Vegetative PG is also called superficial granulomatous pyoderma. It appears as a slowly progressive, discrete, non-painful, superficial ulcer on the trunk with a non-purulent base lacking the violaceus undermined border of classic PG requiring a less aggressive course of treatment. It is not usually associated with any systemic disease.

Atypical Presentations: a) Atypical PG is a superficial variant of classic PG and can occur at any site but mostly involves arms or face. It can appear as bullous and may be difficult to distinguish from sweet syndrome. It is usually linked to hematologic malignancies and IgA gammopathies, b) Peristomal PG contributes to about 15% of the cases and at times coexist with pustular vasculitis or PG at other sites. It is most commonly associated with IBD, however other associations include diverticular disease, bowel carcinoma, perforated bowel, neurogenic bladder, systemic sclerosis, and collagenous colitis. Biopsy shows giant cells and at times bacteria mainly due to the colonization of the affected skin. This makes the treatment difficult as the lesions are commonly interpreted as infectious or broken-down surgical wounds.

Major and minor criteria are mostly used to diagnose the PG. Major criteria include, a) Pain out of proportion to the size of the lesion and rapidly progressive necrolytic lesion growing >1cm/day in size with an irregular, undermined, and violaceous border preceded by a papule, pustule, or bulla, b) Other causes of ulcers have been excluded.

Minor criteria include, a) History of pathergy and history of cribriform scarring of the lesion, b) Presence of PG-associated systemic diseases such as IBD, polyarthritis, hematologic malignancies such as myelodysplasia or leukemia, and monoclonal gammopathy, c) Histopathological findings indicating the PG lesions, d) Quick response to the oral corticosteroid treatment with a 50% reduction in lesion size.

As mentioned earlier, PG is a diagnosis of exclusion and requires a thorough analysis of the lesions. History,

physical examination, and skin biopsy for histopathology and cultures to rule out any fungal infection is routinely performed but are non-specific as findings can be variable. Appropriate lab tests to rule out any other infections should be performed as needed. Differentials for PG include Sweet's syndrome, Bechet's disease, Wegener granulomatosis, SLE, bacterial, viral, and fungal infections, and various others. Of note, the sweet's syndrome is easily confused with the PG lesions and can be differentiated by findings such as sudden onset non-ulcerating lesions that heal without scarring. Following are the Treatment usually use for PG:

a) Mild or early disease can be treated with topical therapy. Wet compresses, hydrophilic occlusive dressings, antimicrobial agents, topical steroids, and topical tacrolimus use have been beneficial in the treatment of mild or early PG lesions.

b) For more severe diseases or in the case of topical treatment-resistant cases, oral corticosteroids have been effective. The role of immunosuppressants has been implicated in cases where corticosteroids do not alleviate the situation.

However, immunosuppressants solely have never been used due to their significant side effect profile especially bone marrow suppression. A limited number of patients have benefitted from cyclosporin, cyclophosphamide, mycophenolate, and tacrolimus in sudden onset PG cases. It is recommended to treat the underlying systemic illness along with PG treatment if present. Surgical debridement of the lesions is contraindicated as it may result in a pathergy reaction.

CONCLUSION

PG is a very worrisome disease. Proper treatment of PG is not available and complete recovery from PG is skeptical. In our patient, the physician initially tried oral steroids 10mg/ day, oral dapsone 50mg/day with wet wrapping. After 2 years of usage, the patient was not getting better then physician updated the regime with oral steroids 40mg/day, colchicine 2mg/day, topically tacrolimus 0.1%, topically metronidazole, oral 3rd generation of cephalosporin antibiotics 1gm/day, and oral dapsone 100mg/day. After using all these above-mentioned updated treatments patient is still in the same position. All associated syndromes such as inflammatory bowel disease, arthritis, hematological malignancies, and solid tumors in the body have been ruled out. The patient's lesion is showing resistance to treatment. PG is the disease of exclusion. Proper evaluation, detailed history, skin biopsy, emotional support, and tailored treatment are required for handling the PG.

CONSENT FOR PUBLICATION

Written informed consent was taken from the patient.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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