CASE REPORT

Superficial granulomatous pyoderma mimicking an infectious process

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ABSTRACT

Introduction: Superficial granulomatous pyoderma is a rare superficial variant of pyoderma gangrenosum. With clinical and histological features that mimic infectious processes, misdiagnosis is common. This report aims to present a rare, often overlooked disease, highlighting the need for timely histopathologic diagnosis to prevent unnecessary treatment and morbidity.

Case: Patient is a 42-year-old female with recurrent painful ulcers on her right leg. Initial histopathology was interpreted as granulomatous dermatitis secondary to cutaneous tuberculosis and was managed with anti-Koch's regimen for six months. However, the ulcers worsened, which led to right leg amputation. New similar ulcers eventually recurred over the other extremities where repeat biopsy have shown neutrophilic dermatosis with a three-layer granuloma that is distinctive for superficial granulomatous pyoderma. Patient was treated with oral corticosteroids which was effective in controlling the disease.

Conclusion: This report documents a rare case of superficial granulomatous pyoderma presenting as non-healing ulcer, previously misdiagnosed and treated with unwarranted surgery and anti-microbials. The awareness of the characteristic clinical and histopathological features is essential for diagnosis so as to provide rapid disease control and avoid potentially aggravating management.

Key words: Pyoderma gangrenosum, superficial granulomatous pyoderma, cutaneous tuberculosis

INTRODUCTION

Pyoderma gangrenosum is a rare, chronic, and recurring ulcerative neutrophilic dermatosis. Four clinical variants of pyoderma gangrenosum have been described including ulcerative, pustular, bullous, and vegetative type. The vegetative variant of pyoderma gangrenosum was recently termed as superficial granulomatous pyoderma (SGP).[1] It is a relatively rare disease entity that is characterized as a superficial ulcer, usually with a clean base, and a vegetating rather than undermined margins. Clinical diagnosis is often difficult since there is no specific pathognomonic clinical finding.[2] Histologically, it is distinctive due to findings of a characteristic suppuration and granuloma.[3] Many cases are often diagnosed at a late stage since it is initially disregarded and eventually mismanaged with unwarranted medical and surgical treatments. Several of these cases even led to amputations.[4]

There are only approximately 62 cases of SGP that have been described worldwide with no reported case in our local literature.[5,6] Most of these cases were initially misdiagnosed as a different disease.[6,7,8] The need for documentation and awareness of such disease entity as a major differential diagnosis in cases of a recurrent ulcer with granulomatous histology is therefore essential.

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CASE REPORT

A 42-year-old woman initially sought consultation due to acute severe pain over her right posterior leg, which was edematous, tender, and warm to touch.

Antibiotics were administered and cast immobilization was placed for seven days. Upon removal, multiple ulcers with purulent discharge were noted. Wound debridement and skin grafting were done with adequate healing. Six months later there was recurrence of painful ulcers over the same site. Skin biopsy was signed out as granulomatous dermatitis secondary to cutaneous tuberculosis. Patient was managed and completed the anti-Koch's regimen for six months which resulted in minimal improvement of lesions. A few months after treatment, there was still recurrence of ulcers on the right leg. Due to the worsening extent of lesion, above-the-knee amputation of the right leg was done with adequate healing of stump. However, the patient continued to experience the appearance of new similar ulcers, this time on her right forearm and medial and dorsal aspects of the left leg and foot. She eventually noted progression of the non-resolving ulcers on the left leg, which prompted consult at our institution.

Dermatologic examination on admission revealed irregularly shaped ulcer with cobblestone-like base topped with hemorrhagic necrotic tissues and slightly erythematous borders over the left leg (Figure 1a). There were also multiple ulcers seen on the dorsum & medial aspect of the left foot (Figure 1b) and her right forearm.

Skin biopsy specimen taken from the ulcer revealed subepidermal granuloma composed of superficial layers of neutrophils and hemorrhage, a middle layer of histiocytes and multinucleated giant cells, and a lower layer of mixed infiltrates of lymphocytes, plasma cells, neutrophils, and eosinophils (Figures 2 and 3). Based on the clinical and histologic picture, the case was diagnosed as superficial granulomatous pyoderma.

Laboratory work-up showed elevated ESR and leukocytosis with predominance of neutrophils. Venous duplex scan and X-ray of the leg yielded no abnormalities. Wound discharge was positive for Pseudomonas aeruginosa. Fungal and mycobacterial smears of wound discharge were negative.

The patient was treated initially with culture-guided antibiotics for Pseudomonas but had no improvement of the ulcers and symptoms. During that time, pyoderma gangrenosum was considered. On the third hospital day, she was started on oral prednisone (50 mg/day). Five days after initiation of treatment, the pain, edema, and induration surrounding the leg ulcer have resolved.

During the follow-up consultation, oral prednisone was maintained and eventually supplemented with dapsone (100 mg/day). The patient, however, developed acute hepatitis secondary to hemolytic anemia on her third month on dapsone, which then had to be discontinued. The wound healed well within five months, leaving atrophic scarring (Figure 4). Through the five-year follow up, the maximum period without lesions was 12 months. During that period, her disease had marked appearance of few new minute ulcers during flare-ups, which was managed by increasing the dose of steroids and gradual tapering down, with dose of oral prednisone ranging from 2.5 mg/day to 30 mg/day. On her third year of using systemic corticosteroids, azathioprine (100 mg/day) was added for a year, which further decreased her disease flare-ups. Currently, patient is on low dose of oral steroids with optimal control of the disease for more than 12 months.

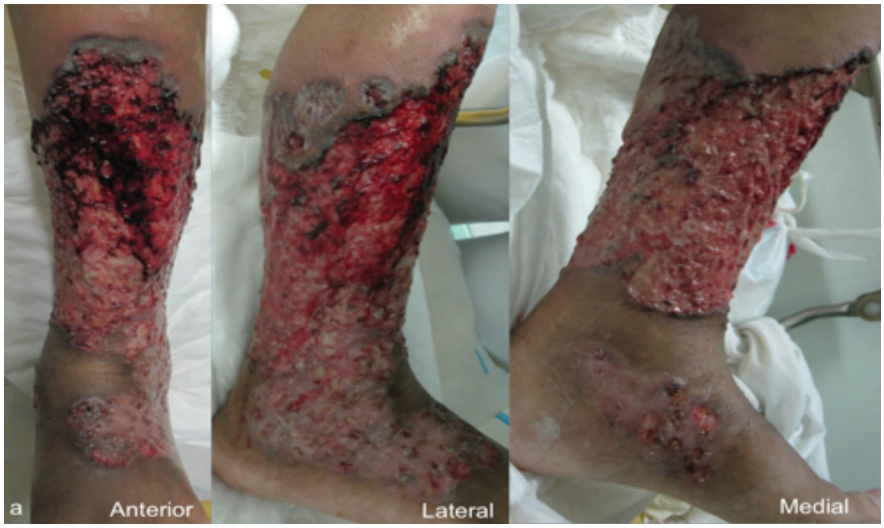

Figure 1A. Irregularly shaped ulcer with slightly erythematous borders and cobblestone-like base, topped with hemorrhagic-necrotic tissues, over the left leg (30 x 24 cm).

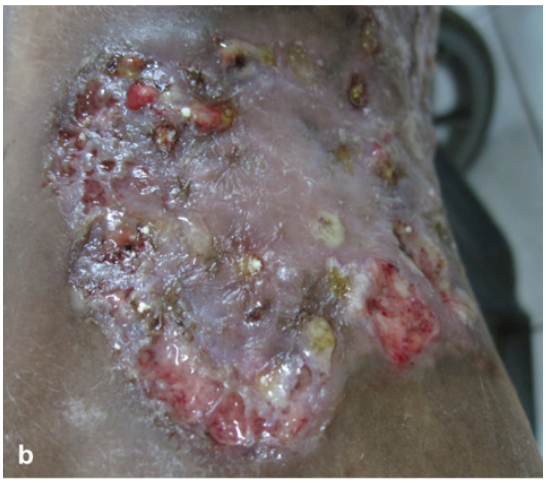

Figure 1B. Multiple punched-out ulcers with purulent crusting on the dorsal left foot (4.2 x 6 cm to 6.5 x 19 cm).

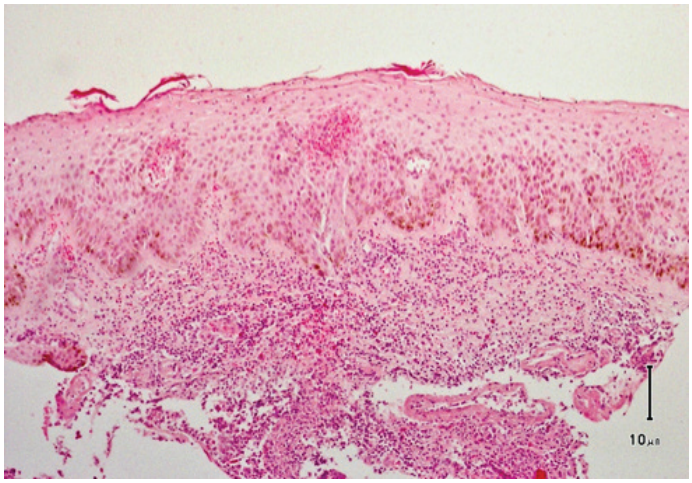

Figure 2. Low-power view showing pseudoepiteliomatous hyperplasia, subepithelial suppurative granuloma (H & E stain; x 100).

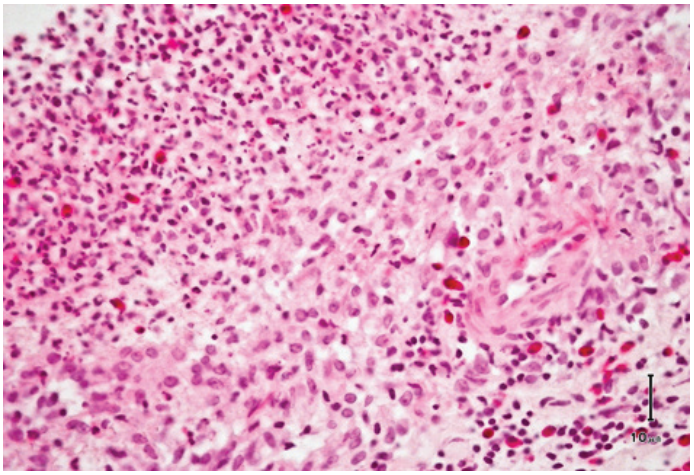

Figure 3. The three-layer granuloma composed of superficial layers of neutrophils and hemorrhage, a middle layer of histiocytes and multinucleated giant cells, and a layer of mixed infiltrates of lymphocytes, plasma cells, neutrophils & eosinophils (H & E x 400)

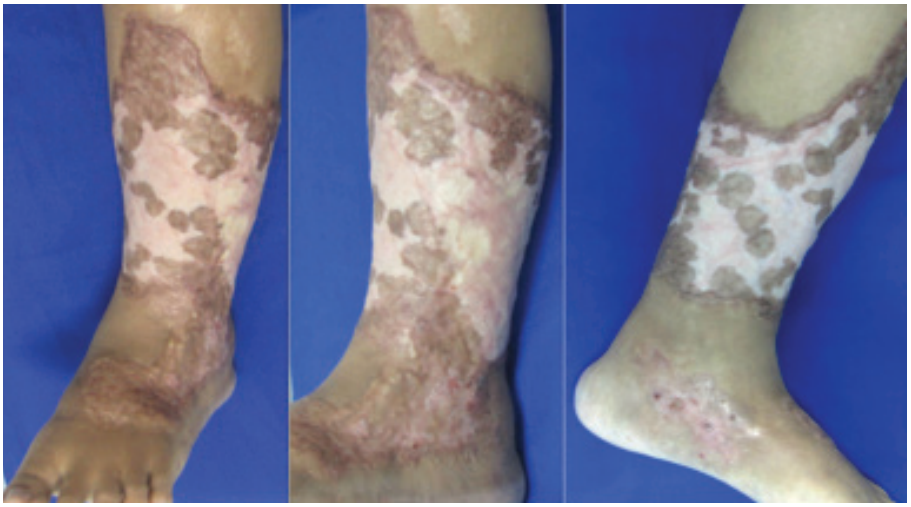

Figure 4. After 5 months of treatment leaving depigmented patches with hyperpigmented border and atrophic scarring.

DISCUSSION

SGP is one of the least common variant of pyoderma gangrenosum, with only a few reported cases worldwide.2,6 It is characterized as a superficial variant of vegetative pyoderma gangrenosum and was first described in a series of patients by Wilson-Winkelmann in 1988.[9]

In our case, the patient was otherwise well and had no comorbidities, until she presented with painful and recurrent ulcers on the extremities. Clinically, SGP lesions may appear as non-tender, well delineated superficial with exophytic or vegetating granulations, although there have been reports of multiple, painful lesions.[10,11,12] In contrast to the classical pyoderma, SGP has a predilection for the trunk and occasionally on the extremities, although involvement of face and the scrotum have likewise been reported in literature. It is rarely associated with other underlying systemic, autoimmune, or other diseases, unlike the majority of cases of pyoderma gangrenosum.

Features	Pyoderma Gangrenosum	Superficial Granulomatous Pyoderma
Location	Extremities	Trunk
Lesion	Deep ulcer, necrotic center	Superficial ulcer Granuloma
Border	Undermined	Vegetative
Base	Necrotic	Clean
Histology	Extensive abscess Hemorrhage/necrosis No sinus tract formation No foreign bodies	Three-layer granuloma No hemorrhage/necrosis; Sinus tract formation Foreign bodies may be found
Associated disease	Inflammatory bowel disease, rheumatoid arthritis, lymphoid tumors, etc.	Rare
Pathergy	Yes	Yes
Treatment	Topical and systemic corticosteroids, cyclosporine, dapsone, clofazimine, minocycline, oral tacrolimus, mycophenolate mofetil, TNF, intravenous immunoglobulin	Topical and systemic corticosteroids, dapsone, cyclosporine, infliximab, intravenous immunoglobulin
Course	Acute	Chronic
Prognosis	Frequent relapses	Frequent recurrence Good prognosis

Table 1. Characteristic variation of pyoderma gangrenosum and superficial granulomatous pyoderma

Some authors suggest that SGP may be due to unidentified organisms or antigens causing a localized delayed type hypersensitivity reaction.[3,9,13] However, the etiology remains undefined in most cases, as in our patient who had no apparent trigger for her condition.

Our patient's condition was initially diagnosed as mycobacterial infection and treated with anti-Koch's regimen. Initial improvement was seen, but recurrence of similar lesions caused further diagnostic dilemma. The clinical picture of the case may also lead a clinician to consider other infectious and noninfectious skin diseases such as atypical mycobacterial infection, deep fungal infection, blastomycosis, tuberculosis verrucosa cutis, Serratia granuloma or halogenoderma since they can similarly produce pyoderma-like lesions.[14] It was unfortunate that the patient had to undergo right leg amputation due to the worsening of her lesions that recurred after completion of the anti-tuberculosis medications.

There are no diagnostic modalities that can specifically point directly to SGP. Histopathology may be helpful, but the final diagnosis is usually established by exclusion of other differential diagnoses.

Frequent misdiagnosis and mismanagement of this disease at its onset may also be due to the histopathological picture of superficial granulomatous pyoderma showing neutrophilic dermatosis, which might be misinterpreted as an infectious disease.5 More common infections like mycobacterium or fungi may also produce suppurative granuloma, which are commonly considered as the main histological differentials of SGP.[8]

It is also not uncommon for SGP to be mistaken for pyoderma gangrenosum due to their similarities; but distinctive features in location, histologic picture, prognosis, and management set SGP apart (Table 1). Consistent with our patient's histopathology, superficial granulomatous pyoderma ulcer has a characteristic three-layer granuloma: a superficial layer of neutrophils, middle layer of granulomatous inflammation with histiocytes and multinucleated giant cells, and a layer composed of mixed inflammatory infiltrate with lymphocytes, numerous plasma cells, neutrophils, and eosinophils.[7] Sinus tract formation and foreign bodies are also characteristic features that are not regularly seen in classical pyoderma gangrenosum.[14]

While classical pyoderma gangrenosum treatment is usually with systemic steroids with addition of azathioprine or cyclosporine, SGP is usually more indolent and more easily controlled with conservative approach utilizing local anti-inflammatory agents, except in some cases reported that required more aggressive treatment.[13] Topical tacrolimus has also been successfully used for SGP.[15,16] Interestingly, reported cases of aggressive SGP that were recalcitrant to conservative management were those that had involvement of the face[6], and necessitated treatment with cyclosporine[13], immunoglobulin[7], and infliximab.[17]

The combination of steroids and dapsone is commonly used as treatment for neutrophilic dermatoses. The use of sulfonamides and sulfones has also been shown to control pyoderma gangrenosum in some cases, due to their anti-inflammatory action against neutrophil adherence.[18] Hematologic toxicity of dapsone may limit its use, as was observed in our patient. Azathioprine, on the other hand, is a cytotoxic drug that is usually given for its steroid-sparing effects, but has variable response.[18]

Dapsone, azathioprine, cyclosporine, cyclophosphamide, and chlorambucil are used due to their immunosuppressive effects. More importantly, they are used to help reduce the exposure to systemic steroids.[19]

Treatment response in SGP is variable and unpredictable.[8] SGP appears to exist as a clinical continuum, with classic pyoderma gangrenosum being on the more aggressive end, and superficial pyoderma representing the slowly progressive and milder end.[10] This may help explain why some cases of SGP, including what the patient presented, do not respond well to initial conservative management or require longer treatment duration before ample clinical improvement. There seems to be a subset of SGP patients that possess certain features closer to classic pyoderma gangrenosum. In such cases, more aggressive treatment modalities may be needed.[6]

In most reports, healing varies from three months to several years.9 The patient eventually responded well to systemic steroids, a treatment regimen that has been used in most cases of mild pyoderma and superficial pyoderma.[20] Once proper treatment was started, the patient required at least five months before her disease was completely controlled. Superficial granulomatous pyoderma tends to heal spontaneously, but recurrences are common.[6]

CONCLUSION

This report highlights the case of a 42-year-old woman with superficial granulomatous pyoderma, a rare disease entity that although generally slowly progressive and has a benign prognosis, has an initial presentation that mimics a myriad of other conditions. This may lead to serious debility if overlooked or mismanaged, with patients receiving unwarranted medical treatment and surgical management further leading to unnecessary economic burden, emotional distress, physical disfigurement, and even exacerbation of the disease of the patient. A correlation of the clinical picture with prompt histologic diagnosis is warranted to start proper treatment and attain disease control, which may require several months to achieve. Awareness of such disease entity as a major differential is therefore important.

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