Superficial Granulomatous Pyoderma Gangrenosum Involving the Face: A Case Series of Five Patients and a Review of the Literature

Eran Shavit, Michael Cecchini, James J. Limacher, Scott Walsh, Ashely Wentworth, Mark Denis P. Davis, and Afsaneh Alavi

Abstract

Background: Pyoderma gangrenosum (PG) is a rare neutrophilic dermatosis characterized by painful and ulcerating lesions on the skin. It rarely involves the face and is often difficult to diagnose. There are few cases reported in the literature of PG involving the face.

Aim: To share our experience with 5 patients in whom the final diagnosis was PG involving the face, and to review the literature.

Methods: We report a series of 5 patients with a final diagnosis of PG involving the face and reviewed relevant literature. We searched through PubMed and EMBASE using keywords such as “face” and “pyoderma gangrenosum,” “blastomycosis-like pyoderma gangrenosum, vegetative pyoderma gangrenosum and granulomatous pyoderma gangrenosum.”

Results: We report 5 patients (4 females) with pyoderma gangrenosum involving the face. All 5 had a final diagnosis of superficial granulomatous PG. All cases presented with nonhealing facial ulcer most commonly on cheeks and a common histopathology of mixed inflammatory infiltrates, multinucleated giant cells, and plasma cells with some granulomatous inflammation.

Conclusions: PG can involve the face, and all 5 of our patients had the superficial granulomatous as the most common form.

Keywords

pyoderma gangrenosum (PG), granulomatous pyoderma gangrenosum (GPG), blastomycosis-like PG, pyoderma, facial ulcer, neutrophilic dermatoses

Introduction

Pyoderma gangrenosum (PG) is a rare neutrophilic dermatosis that presents as an inflammatory ulcerative disorder. It most often affects the lower extremities but can involve other areas of the skin. However, involvement of the face has rarely been reported. We present 5 cases of unusual ulcerating and vegetating facial plaques mimicking halogenoderma and blastomycosis-like pyoderma with granulomatous histology. In all patients, the final diagnosis was superficial granulomatous PG.

Many consider PG a diagnosis of exclusion. There are four major types of PG: bullous, ulcerative, pustular, and superficial granulomatous. Superficial granulomatous PG presents as a localized vegetative or ulcerative lesion located usually on the trunk. The lesions in the localized vegetative subtype, and in contrast to the other subtypes, are more likely to be confined to the skin commonly with no systemic association. This subtype is expected to be more responsive to a
Table 1. Case Series of 5 Patients With Granulomatous Pyoderma Gangrenosum (GPG) of the Face.

| Case | Age and gender | PMH | Medications | Laboratory | Dermatological manifestations | Histopathological findings | Identified underlying disease | Management |
|------|----------------|-----|-------------|------------|-------------------------------|---------------------------|-----------------------------|------------|
| 1    | 51-year-old Caucasian female with 3 years history of nonhealing facial ulcer | Acne, smoker, family Hx of IBD in sibling | None | Blood cultures showed no growth. PCR for HSV and a DFA assay for VZV were negative. ESR and CRP were mildly elevated. The remainder of the blood chemistry panel, infectious serology, imaging, and endoscopy were normal. | 6 × 7-cm well demarcated vegetative crusted plaques on bilateral cheeks with several discrete, round, 1- to 2 cm crusted plaques on the temple the vegetating plaques had serous discharge, and prominent coral reef-like, violaceous borders | A dense superficial, perivascular and perifollicular infiltrate consisting of neutrophils, lymphocytes, histiocytes, multinucleated giant cells, and plasma cells with areas of pseudocarcinomatous hyperplasia of the infundibulum epithelium. Special stains for organisms were negative. | None | Prednisone 1 mg/kg OD and Dapsone 100 mg OD Azathioprine 150 mg OD Acitretin 25 mg OD Leflunomide 10 OD mg and IVlg (2 grams/kg q 4 weeks) |
| 2    | 87-year-old female with 8 months history of facial ulcer | Multinodular goiter, dyslipidemia, deep vein thrombosis, and osteoporosis | Simvastatin, Alendronate | Laboratory examinations were unremarkable and multiple tissue cultures were negative. | Painful ulcerated erythematous plaque (1.5 × 1.0 cm) with violaceous border and yellowish discharge, located on the right cheek. | A mixed dermal infiltrate composed of neutrophils, lymphocytes, with aggregates of histiocytes and multinucleated giant cells, and scattered plasma cells without secondary vasculitis. PAS, GMS, and ZN were all negative. | None | Oral prednisone 60 mg OD AZA 150 mg OD |
| 3    | 15-year-old male facial ulcer for 2 weeks | Ulcerative colitis, acne | Prednisone, Mesalamine, Minocycline | Progressive crusted ulcerations involving the face and upper trunk. (2 weeks after cessation of prednisone) | Suppurative granulomatous inflammation with comedones. DIF negative | UC (known) | Prednisone 40 mg OD |
| 4    | 42-year-old Caucasian female | Otherwise healthy | None | Cultures of biopsy specimens for fungi were negative. ANA, C3,C4,RF negative. PEP demonstrates a monoclonal gammopathy in the gamma region. On immunofixation, monoclonal IgA lambda in the gamma fraction. (MGUS). | Red, painful and then ulcerated, spread to encroach on her anterior face and right ear. A large cribiform patch is present on the right cheek, with finger-like projections. | Granulomatous and neutrophilic dermal inflammation and deep dermal scar. Within the central dermis, there is a prominent palisading granuloma with epithelioid histocytes and multinucleated giant cells. Within the center of the granuloma, there is a zone of necrosis with neutrophils. In the adjacent dermis, there are mixed inflammatory cells associated with dermal fibrosis. | MGUS | Prednisone 40 mg OD Cyclosporine 100 mg BID |
| 5    | 17-year-old female | Otherwise healthy | None | Extensive survey included laboratory tests was negative or normal. | Well-demarcated, violaceous, overhanging borders and cribiform ulceration with surrounding violaceous discoloration of the borders. | Granulomatous inflammation | None | Prednisone 60 mg OD MMF 500 mg BID |

Abbreviations: ACE = angiotensin converting enzyme; ANA = antinuclear antibody; ANCA = antineutrophil cytoplasmic antibody; AZA = Azathioprine; BID = twice daily; CRP = C reactive Protein; CT = computed tomography; DFA = direct fluorescent antibody; DIF = direct immunofluorescence; DVT = deep venous thrombosis; Eos = eosinophils; ESR = Erythrocyte sedimentation rate; ESRD = End stage renal disease; GMS = Gomori’s methenamine silver stain; HSV = herpes simplex virus; IBD = inflammatory bowel disease; ILS = Intralesional steroids; F = female; Meds = Medications; MGUS = Monoclonal gammopathy of determined significance; MMF = Mycophenolate mofetil; OD = daily; PAS = Periodic acid Schiff; PCR = polymerase chain reaction; PEP = protein electrophoresis; plas = plasma cells; PMH = past medical history; Prn’s = polymorphonuclear neutrophils; RF = rheumatoid factor; UA = Urinalysis; US = ultrasonography; VZV = varicella-zoster virus; ZN = Ziehl-Neelsen.
less aggressive antiinflammatory therapy, but this is not always the case. Controversy exists as to whether it is a variant of PG or a separate disorder. Clinically, the lesions exhibit a raised, sometimes verrucous, well-defined plaque studded with small pustules. We present 5 cases of the superficial granulomatous or vegetative type presenting as facial ulcers in a distinct distribution.

**Case Series**

We report the characteristics (demographics, clinical description, histopathology, associated diseases, response to treatment) of 5 patients with a final diagnosis of PG involving the face from 2 academic medical centers in North America (United States and Canada). Consent was obtained from all patients.

**Literature Review**

We conducted a database search of PubMed and EMBASE for PG involving the face. Our search included keywords “face” AND “pyoderma gangrenosum” OR “blastomycosis-like pyoderma gangrenosum” OR “vegetative pyoderma gangrenosum” OR “granulomatous pyoderma gangrenosum.” We searched from the year 1980 to June 2018 and included published papers in the English language.

The 5 patients who received a diagnosis of pyoderma gangrenosum involving the face are summarized below in Table 1. Photographs of each of the patients’ facial PG and histopathology is presented in Figure 1. A summary of the literature describing patients presenting with pyoderma gangrenosum involving the face is provided in Table 2.

**Discussion**

We summarize 5 patients who presented with ulcerating and vegetating facial plaques and received a final diagnosis of PG. Intriguingly, the findings were consistent with the superficial granulomatous form of PG in all cases. On clinicopathologic correlation, the presentation mimicked halogenoderma with heavy neutrophilic and granulomatous histology. An associated systemic disorder was found in a minority of patients, as case number 3 was associated with IBD and case 5 with monoclonal gammopathy of undetermined significance (MGUS). These share similarities to those described by Matthews et al. Some histopathological findings in our cases can be seen in the granulomatous variant of PG, including the presence of neutrophils and plasma cells. Multinucleated giant cells are more typically found in patients with a background of IBD.

Superficial granulomatous PG is an uncommon variant of PG presenting as painful distinct ulcers and only rarely reported on the face. This clinical presentation on the face is unique, as only few reports were found. The clinical and histopathological findings may differ somewhat from that of the classic PG. Only few dozen cases of superficial granulomatous PG have been published in the literature, of which only six cases with facial involvement; however, only four
| Case | PMH | Age/gender | Laboratory | Dermatological manifestations | Histopathological findings | Management |
|------|------|------------|------------|------------------------------|---------------------------|------------|
| Matthews et al, JAMA Derm 2018 | Diverticulosis, colonic polyps | 55 ys old F | Blood cultures showed no growth, Findings of PCR analysis for HSV and a DFA assay for VZV were negative. | Intradermal neutrophilic inflammation with ulceration and intracorneal neutrophils. Special stains were negative for microorganisms. | High-dose corticosteroid therapy |
| Persing et al, 2012 | Otherwise healthy | 37 ys old F | Methicillin-sensitive Staphylococcus aureus per cultures | 6 × 7-cm well demarcated vegetative crusted plaques on bilateral cheeks with several discrete, round, 1- to 2 cm crusted plaques on the temple | Fluconazole Oral prednisone 50 mg OD and topical mupirocin 2% ointment |
| Akhras et al, CED 2009 | S/P Rt. Eye enucleation Due to retinal detachment. | 71 ys old F | Normal ANCA and ACE levels. Chest and sinus X-rays were all normal, and a head CT scan of showed only soft-tissue abnormalities with no bony involvement. | Erythema and cribriform scarring in the right periorbital area. A flesh-colored nodule appeared, which enlarged over 9 months and persisted | Prednisone 40 mg ILS Minocycline Dapsone Cyclosporine MMF Infliximab |
| Lachapelle et al, 2001 | Unknown | 44 ys old F | Pus was sterile. Mycobacterial or mycotic infections, and leishmaniasis were negative, either by direct examination or by culture. A blood control chemistry, UA, ESR, CRP immunoglobulin profile was unaltered. HIV-1 and -2, CMV, HSV, HBV, HCV, brucella, yersinia, or syphilis were negative. | A dense accumulation of Pmn's, features of the ulcerated area; edema, granulation tissue and clumps of Pmn's intermingled with many epithelioid and giant cells. | Prednisone 40 mg Dapsone Systemic Cyclosporine (5 mg/kg/day) |
| Peretz et al, 1999 | Type 2 DM myomatous uterus with menometrorrhagia, resulting in an iron deficiency anemia | 44 ys old F | Routine blood tests and UA were normal, except for high ESR (120h) and Anemia (hemoglobin level of 10 g/dL) RF, ANA, C3, C4, serum immunoglobulins; serum PEP, stool for parasites and occult blood; X-ray (of the chest, left shin, hands, and facial bones); isotopic bone scanning; abdominal US, chest and abdominal CT were all found to be within normal limits. Repasted smears and tissue cultures for bacteria, mycobacteria, and fungi were negative. Smears, cultures and PCR for Leishmania were negative. | Red confluent plaques were present on the forehead extending to the left palpebral and temporal areas (13 × 7 cm in diameter). Red purplish, discretely vegetant margins, partly covered by thick yellow adherent crusts. Also a few pustules were present. | Minocycline Co-trimoxazole Prednisonem |
| Quinby et al, 1989 | Otherwise healthy | 33 ys old M | Unknown | Unknown | Oxophenarsine hydrochlortide local corticosteroids, minocycline, tetracycline, or sulfa drugsb |
| Wilson-Jones et al, 1988 | Otherwise healthy | 33 ys old M | Unknown | Unknown | 40 biopsy specimens showed focal neutrophilic abscesses of the papillary dermis, often with peripheral palisading histiocytes and foreign-body giant cells. Pseudoeplitheliomatous, vegetative hyperplasia and sinus tract formation were observed frequently. |
reports were in the English language. With additional recent case report from this year, a total of 7 reports are summarized in Table 1.

Although PG has a wide range of presentation, the mean age in some reports has been reported to be between 50 and 63 years. However, it seems that the cases of superficial PG may be represented at an earlier age, as seen in our case series and in previous reports (Tables 1–2). Moreover, in our sample study, 40% (2/5) of the cases were pediatric cases (cases 3 and 5). The gender preponderance was in accordance with the reported literature of PG, more commonly represented in the female population than in the male population, both in our cases and in the previously reported cases.

To emphasize the rarity of the facial presentation, in a literature review reported by Langan et al, of 46 cases of granulomatous PG, 52% of lesions were located on the trunk, 31% on the extremities, only 9% presented on the face, 5% in the groin, and 2% on the scalp. In this case series, only 18% of the cases had underlying systemic disease. In accordance with their findings, most of our cases in the series had no underlying disease. It is possible that blastomycosis-like PG is related to the vegetative PG subtype, and that subtype is not associated with any systemic disease. Nevertheless, we were able to demonstrate one case as having an underlying hematological malignancy that was only diagnosed after our initial investigation.

Blastomycosis-like pyoderma has some clinicopathological resemblance to the presentation of superficial PG but mandates the growth of at least one pathogenic organism from the culture of a tissue-biopsy specimen. While our cases all clinically similar to infection but in all cases the culture and special tissue staining were negative. Moreover, empirical therapies with either antibiotics or antifungal medications were futile. In contrast to this, Persing et al (Table 2) reported a case with 2 revealed sources of infection, and this raises a question whether this is indeed a case of PG or truly pyoderma as some resemblances do appear. Our cases are unique, since they may resemble the blastomycosis-like pyoderma, but are not truly infectious. Therefore, they are not pyoderma per se, rather pyoderma-like.

Consistent with other previous reports of superficial PG, this was difficult to treat. As indicated by our cases, and in the previously reported cases, combined regimen may be required. We believe that our series represent a poorly characterized, unique, and neglected group of facial dermatoses of the face, namely superficial granulomatous PG.

Our article suffers from some limitations, small sample size, and recall bias. Further prospective evaluations are required to better assess these unusual presentations. However, it is possible that more cases will be revealed as soon as the awareness rises for this uncommon entity. In conclusion, superficial PG of the face is an uncommon clinicopathological diagnosis. The aim of our report was to draw the attention to this rare clinicopathologic variant.

### Table 2. Continued

| Case | PMH | Age/gender | Laboratory | Dermatological manifestations | Histopathological findings | Management |
|------|-----|------------|------------|-----------------------------|---------------------------|------------|
| Abbreviations: ACE = angiotensin converting enzyme; ANA = antinuclear antibody; ANCA = antineutrophil cytoplasmic antibody; AZA = Azathioprine; CRP = C reactive Protein; CT = computed tomography; DFA = direct fluorescent antibody; DM = Diabetes Mellitus; ESR = Erythrocyte sedimentation rate; ESRD = End stage renal disease; F = female; GF = granulomatous features; GM = granulomas; GFU = granulomas and follicular units; IBD = inflammatory bowel disease; ILS = Intralesional steroids; MMF = Mycophenolate mofetil; OD = daily; PCR = polymerase chain reaction; plasc = plasma cells; PMH = past medical history; Pmn’s = polymorphonuclear neutrophils; PEP = protein electrophoresis; RF = rheumatoid factor; UA = Urinalysis; US = ultrasonography; varicella- zoster virus; ys = years. |
| 1. | a25 cases published in this report from Mayo clinic with only one case presenting lesions on the forehead (but not limited to the face, the case also presented with lesions in left leg and back). | bIt is unknown which therapy was provided to each individual case (including case number 2 with facial presentation). | | | | |
Declaration of Conflicting Interests
The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding
The author(s) received no financial support for the research, authorship, and/or publication of this article.

ORCID iDs
Eran Shavit https://orcid.org/0000-0003-2397-6316
Afsaneh Alavi https://orcid.org/0000-0003-1171-4917

References
1. Shavit E, Alavi A, Sibbald RG. Pyoderma gangrenosum: a critical appraisal. Adv Skin Wound Care. 2017;30(12):534-542. doi:10.1097/01.ASW.0000526605.34372.9e
2. Alavi A, French LE, Davis MD, Brassard A, Kirsner RS. Pyoderma gangrenosum: an update on pathophysiology, diagnosis and treatment. Am J Clin Dermatol. 2017;18(3):355-372. doi:10.1007/s40257-017-0251-7
3. Afifi L, Sanchez IM, Wallace MM, Braswell SF, Ortega-Loayza AG, Shinkai K. Diagnosis and management of peristomal pyoderma gangrenosum: a systematic review. J Am Acad Dermatol. 2017;78(6):1195-1204. doi:10.1016/j.jaad.2017.12.049
4. Quimby SR, Gibson LE, Winkelmann RK. Superficial granulomatous pyoderma: clinicopathologic spectrum. Mayo Clin Proc. 1989;64(1):37-43. doi:10.1016/S0025-6196(12)65301-4
5. Goto M, Okamoto O, Fujiwara S, et al. Vegetative pyoderma gangrenosum in chronic renal failure. Br J Dermatol. 2002;146(1):141-143. doi:10.1046/j.1365-2133.2001.04510.x
6. Matthews NH, Wong V, Robinson-Bostom L, Lajevardi N. Facial neutrophilic dermatosis mimicking iododerma and associated with inflammatory bowel disease. JAMA Dermatol. 2018;154(5):619-621. doi:10.1001/jamadermatol.2017.6060
7. Lachapelle J-M, Marot L, Jablonska S. Superficial granulomatous pyoderma gangrenosum of the face, successfully treated by ciclosporine: a long-term follow-up. Dermatology. 2001;202(2):155-157. doi:10.1159/000051624
8. Kim JW, Park JH, Lee D, Hwang SW, Park SW. Vegetative pyoderma gangrenosum in Behcet's disease. Acta Derm Venereol. 2007;87(4):365-367. doi:10.2340/00015555-0221
9. Akhras V, Sarkany R, Walsh S, Hyde N, Marsden RA. Superficial granulomatous pyoderma treated preoperatively with infliximab. Clin Exp Dermatol. 2009;34(5):e183-e185. doi:10.1111/j.1365-2230.2008.03018.x
10. Persing SM, Laub D. Superficial granulomatous pyoderma of the face: a case report and review of the literature. Eplasty. 2012;12:e56.
11. Peretz E, Cagnano E, Grunwald MH, Hallel-Halevy D, Halevy S. Vegetative pyoderma gangrenosum: an unusual presentation. Int J Dermatol. 1999;38(9):703-706. doi:10.1046/j.1365-4362.1999.00752.x
12. Wilson-Jones E, Winkelmann RK. Superficial granulomatous pyoderma: a localized vegetative form of pyoderma gangrenosum. J Am Acad Dermatol. 1988;18(3):511-521. doi:10.1016/S0190-9622(88)70074-2
13. Langan SM, Powell FC. Vegetative pyoderma gangrenosum: a report of two new cases and a review of the literature. Int J Dermatol. 2005;44(8):623-629. doi:10.1111/j.1365-4632.2005.02591.x
14. Binus AM, Qureshi AA, Li VW, Winterfield LS. Pyoderma gangrenosum: a retrospective review of patient characteristics, comorbidities and therapy in 103 patients. Br J Dermatol. 2011;165(6):1244-1250. doi:10.1111/j.1365-2133.2011.10565.x