CASE REPORT

Pyoderma Gangrenosum Arising De Novo Over an Unusual Site: A Case Report

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Summary

Pyoderma gangrenosum (PG) of the breast is a rare rapidly progressive neutrophilic dermatosis, which usually co-exists with severe underlying systemic conditions. A woman presented with a non-healing ulcer over her right breast with characteristic sparing of nipple-areola complex (Bork-Baykal phenomenon). It was diagnosed as pyoderma gangrenosum on the basis of clinico-pathological correlation and managed successfully with systemic corticosteroids and anti-inflammatory drugs along with wound care. The diagnosis and treatment of PG is challenging particularly at unusual sites given the paucity of robust clinical evidence and lack of consensus opinion regarding specific management guidelines. It is imperative that PG is considered as a clinical diagnosis in any patient with enlarging, sterile, necrotic lesions unresponsive to appropriate antibiotics. Early recognition of PG at rare locations can prevent devastating sequelae such as over-zealous surgical debridement and deep tissue infections associated with a chronic open wound leading to severe cosmetic morbidity.

Key words: *Pyoderma gangrenosum, Neutrophilic dermatosis, Bork-Baykal phenomenon*

Introduction

Pyoderma gangrenosum (PG), a rare inflammatory skin condition of unknown etiology.[1] Annually, three to ten in a million are reported as newly diagnosed cases with 50–70% suffering from underlying systemic diseases like autoimmune (inflammatory bowel disease and rheumatoid arthritis) or hematologic disorders (leukemia and lymphoma).[2] PG generally presents as an initial papule, pustule or nodule after minor trauma, progressing to painful deep necrotic ulcers that wax and wane over time and may mimic an infection. Common sites are lower extremities (pretibial area) followed by trunk, head, neck, hands, peristomal skin and extracutaneous tissues (lungs, liver, bones) infrequently.[3]

Breast PG is seldom encountered, with only 43 cases reported worldwide, 70% of which emerged after breast surgical intervention.[4] PG is often erroneously diagnosed as a necrotizing

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infection where surgical intervention initiates pathergic phenomenon and accelerates necrotic process. Herein, we report mammary PG in the absence of systemic association or antecedent surgical manipulation.

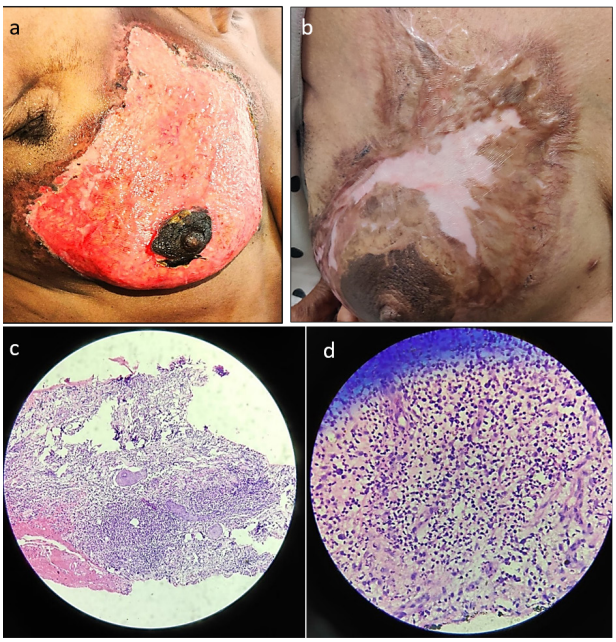
Case report

A 52-year-old female presented with a progressively enlarging painful raw area over the right breast since one month. It had started few months ago as a small pus-filled reddish lesion which increased in size and ulcerated. She denied trauma, surgical procedures, fever, weight loss, abdominal or joint pain, diarrhea or similar lesions elsewhere in the past. She had received multiple antibiotic courses without improvement. General and systemic examination were within normal limits except pallor. Local examination showed a single, tender, well-defined eight by seven cm ulcer over the right breast with violaceous margins, undermined edges and healthy pink granulation tissue with sparing of areola and nipple (Figure 1a).

Differential diagnoses kept were pyoderma gangrenosum, Paget's disease, pemphigus vegetans and atypical mycobacterial ulcer. Laboratory investigations (complete hemogram, liver and renal function tests, C reactive protein, erythrocyte sedimentation rate), chest X ray, ultrasonography of abdomen and pelvis, electrocardiography, 2D Echocardiography and gastroenterology evaluation were normal except anemia of chronic disease and iron deficiency (Hemoglobin-7.8mg/dL, peripheral blood smear showed microcytosis and anisocytosis). Pus culture and Ziehl Neelsen stain were negative. Histopathology (hematoxylin and eosin stain) showed unremarkable epidermis, perivascular mononuclear and dermal neutrophilic infiltration with micro-abscess in subcutaneous (Figure 1c&d). Special stains for acid fast bacilli and fungi were negative.

A final diagnosis of pyoderma gangrenosum was made. Patient was started on tablet prednisolone one mg/kg (tapered off gradually over four months) along with antibiotics (ciprofloxacin, metronidazole, piperacillin-tazobactam and meropenem). Two monthly pulses of injection methylprednisolone (1000 mg for three consecutive days per month) were administered with tablet colchicine 0.5mg twice daily and capsule doxycycline 100mg once daily with wound care. After the first pulse, the ulcer showed marked improvement with shrinking margins. Complete resolution with post-inflammatory pigmentary changes and cribriform scarring was seen after ten months (Figure 1b).

Figure 1 (a) A single, well defined 8cm x 7cm ulcer over the right breast with violaceous margins, undermined edges and healthy pink granulation tissue with sparing of areola and nipple; (b) The ulcer showed complete resolution with post inflammatory dyspigmentation and scarring after ten months; (c) Histopathology (hematoxylin and eosin stain) showing unremarkable epidermis, perivascular mononuclear and dermal neutrophilic infiltration with micro-abscess in subcutaneous tissue in scanner view; (d) Histopathology (hematoxylin and eosin stain) showing neutrophilic infiltration in subcutaneous tissue in 40x.



Discussion

French dermatologist Brocq termed pyoderma gangrenosum as "geometric phagedenism", considering it a bacterial infectious disease.[5] Today, it is classified as a neutrophilic

dermatosis, as histological examination exhibits predominantly neutrophilic infiltrates, without evidence of infection.[6] Although the underlying pathogenesis remains unclear, autoimmune mechanisms of dysregulated inflammation, neutrophilic dysfunction, and genetic factors have been implicated.[7]

Previously, no criteria consistently or reliably distinguished PG from necrotizing soft tissue infections, particularly in the absence of systemic diseases. Recently, a validated set of criteria have been published [1 major criterion: biopsy of ulcer edge demonstrating neutrophilic infiltrate- and 8 minor criteria: (1) exclusion of infection; (2) pathergy; (3) history of inflammatory bowel disease or inflammatory arthritis; (4) history of papule, pustule, or vesicle ulcerating within 4 days of appearing; (5) peripheral erythema, undermining border, and tenderness at ulceration site; (6) multiple ulcerations, at least 1 on an anterior lower leg; (7) cribriform or "wrinkled paper" scar(s) at healed ulcer sites; and (8) decreased ulcer size within 1 month of initiating immunosuppressive medication(s)],[8] wherein one major criterion (skin biopsy demonstrating neutrophilic infiltration) and four out of eight minor criteria (exclusion of infection, history of papule ulcerating within four days, undermined borders and tenderness and decreased size of ulcer within one month of initiating immunosuppressive medication) are mandatory for diagnosis and were fulfilled in our case.

Another subtle clinical clue that helped us confirm the diagnosis of PG was the typical sparing of nipple-areola complex (Bork-Baykal phenomenon).[9] This quaint appearance has been also been reported with capillary malformations and large melanocytic nevi.[10] It is probably attributable to the immunologic privilege imparted by increased quantum of melanocytes in this area. Pathergy (development of skin lesions that resist healing after tissue injury) is an important feature.

Previous cases of PG have been documented after breast surgery and silicon augmentation mastopexy. However, the development of de novo ulcers in the absence of any systemic associations is extremely rare. The clinical course of PG is unpredictable. Skin biopsies for histology and microbiology are critical to narrow the differential diagnosis. Infections that can mimic PG include atypical mycobacterial ulcers, cutaneous tuberculosis, cutaneous leishmaniasis, sporotrichosis, and other deep fungal infections. The non-infectious differential comprises vasculitis, thrombophilia, cutaneous malignancies and drug-induced conditions.[6] Initial wound cultures yielding skin flora such as *S. aureus* are often erroneously considered the culprit. In true PG, targeted antimicrobial therapy eventually fails, and lesions can progressively enlarge with debridement.

Treatment of PG remains challenging as no single effective therapeutic regimen or consensus guideline exists. Initial investigation for associated underlying systemic disease is crucial as treating this can hasten resolution. For mild disease such as single or superficial lesions, conventional evidence-based first-line treatments involve topical medications such as high-potency corticosteroids or calcineurin inhibitors.[7] There is a paucity of data to inform clinical decision-making when considering second-line systemic therapies (methotrexate, azathioprine, mycophenolate mofetil, cyclophosphamide, dapsone, thalidomide, and intravenous immunoglobulins) which are mainly used as steroid-sparing agents for maintenance or in combination with first-line agents for refractory disease. Our case responded remarkably to two pulses of methylprednisolone with daily colchicine and doxycycline (used as anti-inflammatory agents) for ten months.

Conclusion

Pyoderma gangrenosum of the breast is a rare entity, to be considered when rapidly progressing ulcerative lesions are observed. Though often correlated to previous surgical treatment or systemic inflammatory and hematologic disorders, our patient developed it de novo. A vigilant clinical examination (particularly for characteristic clues like the

Bork-Baykal phenomenon), histopathological evaluation and systemic assessment is paramount, while treatment with topical or systemic glucocorticosteroids along with adjuvant drugs and wound care is the optimum first-line therapeutic approach.

Conflict of Interest Declaration

All authors have no financial/conflict of interest to disclosed.

Acknowledgement

Nil

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