





CASE REPORT

Pyoderma gangrenosum confined to the irradiated chest wall of the reconstructed breast

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Abstract

Pyoderma gangrenosum (PG) is a diagnosis of exclusion worsened by surgical debridement. This report presents two atypical manifestations of PG in the reconstructed breast, whereby the disease is only confined to the irradiated chest wall tissue bed, sparing the abdominal donor sites and the contralateral reconstructed breast.

KEYWORDS

autologous breast reconstruction, DIEP flap reconstruction, pyoderma gangrenosum, pyoderma gangrenosum in irradiated tissue

1 | INTRODUCTION

First described in 1930, pyoderma gangrenosum (PG) is a rare skin condition of enigmatic etiology.¹ Characterized by necrotic and purulent tissue ulceration, it is considered a diagnosis of exclusion once infectious etiologies have been ruled out. Patients diagnosed with PG often have a history of inflammatory bowel disease, rheumatoid arthritis, myeloproliferative disorders, autoimmunity, or diabetes. However, PG can also present idiopathically.² Exhibiting the attribute known as pathergy, PG may also be exacerbated by minimal tissue trauma.² This is why experts often oppose surgical intervention. Although rare, PG has been described in the setting of previous breast surgery, including autologous flap reconstruction.^{3,4} Despite these reported findings, insufficient literature exists highlighting the development of PG after reconstruction of a previously irradiated breast.^{5,6} In this report, we describe two cases of PG developing exclusively in the irradiated chest wall tissue bed after mastectomy with delayed autologous tissue reconstruction, sparing nonirradiated tissues. Ethical approval was obtained through the Institutional Review Board, and written consent was obtained from both patients.

2 | CASE 1

A 36-year-old previously healthy woman with a prior history of stage III invasive ductal carcinoma of the right breast with known axillary disease underwent modified radical mastectomy. She completed a full course of neoadjuvant chemotherapy and adjuvant postmastectomy radiation therapy (PMRT). She had no prior history of inflammatory bowel disease, rheumatoid arthritis, or other conditions associated with PG. Four months after PMRT, she underwent unilateral delayed autologous tissue breast reconstruction with a deep inferior epigastric perforator (DIEP) flap (Figure 1A). The procedure was uneventful, and the patient was discharged home in stable condition on postoperative day (POD) 5. The following day (POD 6), she presented to the emergency department (ED) with fever to 40.5°C, and significant erythema and induration of the right reconstructed breast (Figure 1B). Output from her surgical drain was serosanguinous. Serum laboratories showed a prominent leukocytosis ($13.9 \times 10^9/L$). The lateral aspect of her incision was incised and explored in the ED, but no pus was identified. She was admitted for broad-spectrum antibiotics for presumed surgical site infection.

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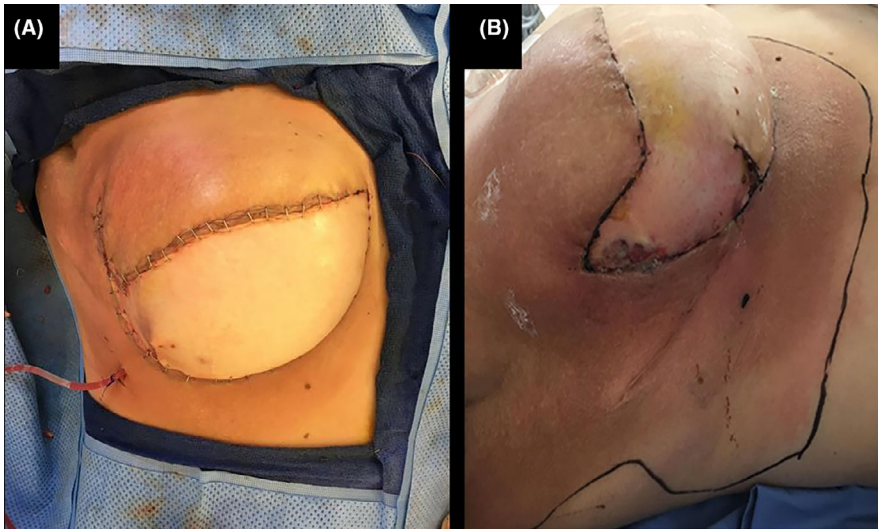


FIGURE 1 Patient with delayed unilateral DIEP flap reconstruction after PMRT presents with breast erythema and fevers on POD 6. A, POD 0 completed right DIEP flap. Her surrounding skin is hyperpigmented at baseline due to prior history of adjuvant radiation therapy for breast cancer. B, Presentation to the ER with fever and redness of the right breast 6 d after delayed DIEP flap reconstruction

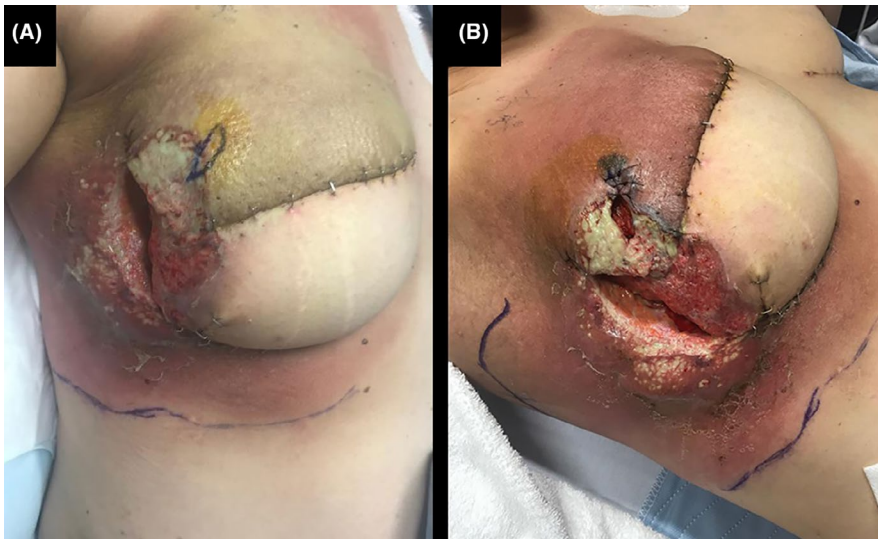


FIGURE 2 Progression of pyoderma gangrenosum in the irradiated mastectomy tissues of patient 1. A, Ongoing erythema and necrotic ulceration of the right breast. The violet surgical marking at the superior aspect of the wound delineates the boundaries for wedge biopsy. B, Progression of ulceration and wound breakdown at the wedge biopsy site is consistent with pathergy, a common attribute of PG

Despite intravenous antibiotic therapy, her fevers and leukocytosis persisted, and her examination failed to improve. She was taken to the operating room on POD 11 for exploration and washout. Intraoperatively, the flap appeared viable with healthy granulation tissue and bleeding edges. Prominent induration and fibropurulent material were noted on the deep surface of the wound bed on the irradiated native chest skin. Overall, the patient's DIEP flap appeared completely viable, and the necrotic ulcerations were confined only to the irradiated chest wall. Involved tissues were biopsied and sent for culture, and the wound was irrigated and packed with wet-to-dry gauze. Despite this operative intervention, she had ongoing erythema, fevers, and pain, prompting infectious disease and dermatology consultation (Figure 2A). With all cultures exhibiting no growth after 5 days of incubation, a wedge biopsy of both healthy and unaffected tissue was obtained. Dermatopathologic analysis demonstrated diffuse neutrophilic dermal inflammation, and in light of these findings and the absence of a clear infectious source, PG was determined to

be the likely diagnosis. The patient also developed pathergy at the wedge biopsy site consistent with PG (Figure 2B). With PG the most likely diagnosis, the patient was then treated with oral prednisone. Her pain significantly decreased, and her examination improved. She was discharged on hospital day 23 on this regimen and local wound care consisting of silver-impregnated dressings (AQUACEL® Ag). As an outpatient, therapy with topical tacrolimus 0.1% ointment was initiated during dressing changes and her oral steroids were weaned. Seven months later, the wound had significantly improved and remained stable off oral and topical medications (Figure 3). The wound had fully healed at one-year follow-up.

3 | CASE 2

A 49-year-old woman with a history of stage III left breast cancer status post-bilateral mastectomy with direct-to-implant reconstruction and adjuvant PMRT, presented with



FIGURE 3 Patient 1 at 7-mo follow-up

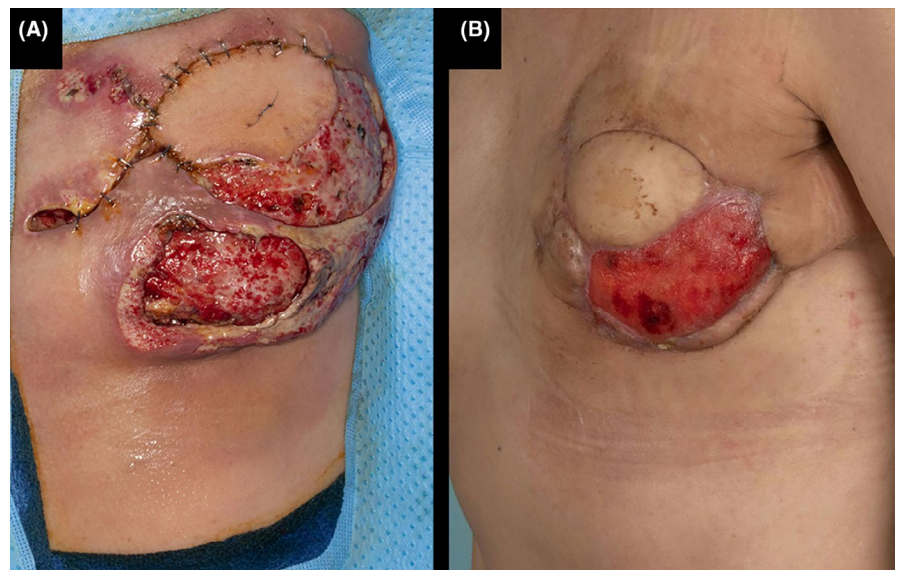
Baker grade IV capsular contracture of the left breast. She had no prior history of inflammatory bowel disease, rheumatoid arthritis, or other concerning conditions associated with PG. PMRT was completed 9 months prior to her presentation. She elected to pursue removal of bilateral implants, capsulectomy, and bilateral autologous reconstruction with abdominal tissue. She underwent left DIEP free flap and right muscle-sparing transverse rectus abdominis myocutaneous free-flap reconstruction. On POD 1, she returned to the operating room for venous congestion of the left DIEP flap due to kinking of the pedicle. The flap was salvaged without complication. Her hospital course was otherwise uneventful, and she was discharged on POD 4. The following day (POD 5), the patient was febrile to 38.5°C and presented to clinic for evaluation. On examination, the left breast exhibited erythema of the previously irradiated mastectomy skin. There

was no fluctuance and only serosanguinous output from the surgical drain. Serum laboratories showed leukocytosis ($13.2 \times 10^9/L$). She was admitted and started on broad-spectrum antibiotics. On POD 6, because her examination failed to improve she underwent flap re-exploration. Consistent with the patient presented in Case 1, intraoperative findings showed a completely viable DIEP flap, with necrotic ulcerations along the inferior mastectomy flap skin. Tissue biopsies were sent for culture and pathological analysis. Postoperatively, the wound further demarcated (Figure 4A). Intraoperative cultures remained negative, and histologic analysis showed acute inflammation of the chest wall skin and no organisms. Infectious disease and dermatology were consulted, given the constellation of findings suggested that a wedge biopsy be obtained, including affected and unaffected tissue, for dermatopathologic review. Pathology again revealed dermal necrosis with neutrophilic inflammation; no microorganisms were present. Therefore, a presumptive diagnosis of PG was made, antibiotic therapy was discontinued, and treatment with oral cyclosporine was initiated. The wound stabilized and the patient's pain and erythema improved. The patient continued to improve with an extended course of systemic oral cyclosporine and topical wound care. At 12 weeks postoperatively, the patient's wound was clean, granulated, and healing (Figure 4B).

4 | DISCUSSION

Pyoderma gangrenosum after breast reconstruction is a rare complication sparking systematic reviews to illuminate risk factors.⁷⁻⁹ In this report, both patients received adjuvant PMRT, had no prior history of any PG associated conditions, and developed PG involving only the irradiated mastectomy chest wall tissue bed; the donor sites and autologous flaps

FIGURE 4 Presentation of pyoderma gangrenosum in patient 2. A, Progression of mastectomy flap necrosis and ulceration consistent with PG. DIEP flap tissues remain spared. B, Patient 2 at 12-wk follow-up. Wound is clean with healthy granulation tissue and peripheral epithelialization



were spared. Furthermore, Case 2 had bilateral reconstruction and developed PG only on the previously irradiated side; the contralateral reconstructed breast was unaffected. To date, such presentations of PG have not been described. A thorough review of current literature outlining patient factors associated with PG, as well as PG diagnosis and management, could help elucidate the potential etiology of these two atypical patient presentations.

4.1 | Risk factors

The most common comorbidities associated with the development of PG include inflammatory bowel disease (Crohn's disease, ulcerative colitis), hematologic conditions (leukemias, monoclonal gammopathies), and arthritic diseases (rheumatoid arthritis, ankylosing spondylitis); presence of neoplasia is also a potential risk factor. Skin trauma, either in the setting of accidental trauma or surgery, is also a well-described risk factor. Reported cases of postoperative PG have developed in the setting of cardiac surgery, hernia repair, and breast surgery.² In regard to both patients in the current report, neither had any significant comorbidities associated with PG, and their PG manifested in the setting of breast reconstruction, after oncologic resection of their breast cancer and adjuvant PMRT; this decreases the likelihood that their PG is directly related to their breast cancer or an underlying, undiagnosed comorbidity. For both patients in the current report, skin trauma in the setting of breast reconstruction is the most likely risk factor inciting the development of PG.

4.2 | Diagnosis and management

The diagnosis of PG is primarily dependent upon disease presentation and the clinical course of the patient; there are currently no specific laboratory or histopathological tests that can confirm the presence of PG.² Obtaining a biopsy is typically recommended when evaluating ulcerated skin lesions, as it can diagnose other common etiologies (ie, infection, vasculopathy, cancer). Histologically ruling out these other diseases can aid clinicians in narrowing the differential diagnoses, especially if PG is suspected. For both patients in the current report, a wedge biopsy of both healthy and unaffected tissue revealed neutrophilic dermal inflammation, a frequent finding in PG. As was true in Case 1, postbiopsy pathergy can further affirm the diagnosis of PG in the postoperative setting.

Once PG is suspected, the goals of treatment are to reduce pain and facilitate wound healing by suppressing tissue inflammation. Moreover, due to pathergy, tissue debridement should be avoided as it may exacerbate skin ulceration and lead to disease progression. Topical treatments

options include corticosteroids, cyclosporine, tacrolimus, or 5-aminosalicylic acid.² For instances when PG is extensive, systemic use of corticosteroids (ie, methylprednisolone) or cyclosporine may be utilized and are associated with a more predictable therapeutic response.² In the current report, Case 1 was effectively treated with oral steroids and topical tacrolimus and Case 2 experienced a great therapeutic response with systemic oral cyclosporine.

4.3 | Etiology

Approaching nearly a century since the work of Brunsting et al, complete knowledge of PG etiology continues to elude researchers and clinicians. Evidence pointing to abnormal immunoregulation, specifically neutrophil reactivity, chemotaxis, or aberrations in immunoglobulin function, has only recently shed light on the multifactorial pathogenesis of PG.² Overexpression of interleukins at the site of skin ulceration, specifically IL-8 and IL-16, is another potential cause.^{10,11} Pathergy, whereby skin ulcerations are worsened with minimal tissue trauma, suggests that PG etiology is likely a result of aberrant pro-inflammatory responses. Despite current preliminary findings, complete knowledge of PG etiology remains enigmatic and requires further investigation.

Regarding both cases, tissue trauma in the setting of surgery was the most likely risk factor triggering development of PG in these patients. Nonetheless, PG confinement to only the previously irradiated chest wall tissues, sparing both the autologous flap, contralateral side, and abdominal donor site, is a novel presentation that remains undescribed within current literature. Regarding the role of PMRT in the pathogenesis of PG, current reports and systematic reviews have failed to link the two.^{5,6} While many patient factors have been associated with PG, prior radiation therapy is not currently described as a risk factor.^{2,7-9,12} This is despite evidence that radiation exposure fundamentally alters interleukin homeostasis in human tissues, including IL-8.^{8,13-15} Since PG is a diagnosis based exclusively on a patient's history and clinical course, these two cases are presented in hope that future patients with PMRT who develop PG after breast reconstruction can avoid unnecessary debridement and decrease time to diagnosis. The potential impact of prior radiation therapy and the development of PG warrant further investigation within a larger patient cohort.

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The authors have no financial or commercial conflicts of interest to disclose. Data are available upon reasonable request. Ethical approval was obtained through the Institutional Review Board, and written consent was obtained from both patients.

CONFLICT OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

JBH MD, LRP MD, EAK MD, WJC III MD, SSN MD, SCL MD, AMR MD, SLS PA-C, and CMT MD: contributed to manuscript conception and design, acquisition of data, analysis and interpretation of the data, and drafting of the manuscript and revising it critically, and provided final approval of the version to be published.

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