Case Report

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Pyoderma Gangrenosum: A Nightmare for Breast Surgery-Two Case Reports

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ABSTRACT

Pyoderma gangrenosum (PG) is a rare, chronic, neutrophilic dermatosis characterized by painful ulcers that are often misdiagnosed as wound infections. We report two cases of postsurgical PG following breast surgery: A 46-year-old woman with a non-healing ulcer after a breast biopsy and a 37-year-old woman with wound dehiscence after bilateral reduction mammoplasty. Both cases were initially managed with repeated debridements, antibiotics, and wound care without improvement. The diagnosis of PG was made based on the increase in wound size and irregularity. Treatment with oral doxycycline and topical tacrolimus led to favorable healing within four months. Breast surgical tehniques, which aim to achieve aesthetic results using intraglandular flaps, have become an important part of clinical practice in breast surgery. Early diagnosis and appropriate management are crucial in postsurgical PG to avoid misdiagnosis and ineffective treatments that cause patient disfigurement.

Keywords: Pyoderma gangrenosum; breast surgery, reduction mammoplasty, doxycycline, tacrolimus

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Key Points

- Postsurgical pyoderma gangrenosum is a rare, chronic neutrophilic dermatosis often misdiagnosed as a wound infection.
- Early diagnosis and appropriate treatment management are crucial to prevent patient aesthetic deformity.
- The diagnosis of pyoderma gangrenosum was made based on the erythematous, irregular borders, and increase in wound size and irregularity.
- The wound bed should be kept moist, and maceration of the surrounding skin should be prevented and not traumatized in patients.
- The combination of oral doxycycline and topical tacrolimus is a good treatment option, especially in patients with limited disease.

Introduction

Breast cancer is the most commonly diagnosed cancer type in women worldwide and the second most common cause of cancer deaths (1). The increasing frequency of breast cancer has brought screening programs and biopsies to the forefront to catch the disease early. With the understanding of cancer biology and the development of treatment algorithms, surgical treatment has evolved from mastectomies to breast-conserving surgeries and currently to oncoplastic breast surgery techniques (2). Oncoplastic techniques for biopsy, which aim to achieve aesthetic results using intraglandular flaps while preserving oncological principles, have become an important part of clinical practice in breast surgery clinics.

Pyoderma gangrenosum (PG) is a rare, chronic, neutrophilic dermatosis characterized by painful ulcers. The disorder may be associated with various diseases, such as inflammatory bowel disease, hematological and rheumatological disorders, immune system dysfunction, and malignancies. Diagnosis is established by excluding other causes of ulceration. Although immunosuppressive agents are the primary treatment options, new therapeutic approaches are also under investigation (3).

Postoperative and peristomal PG is encountered in the clinic after surgery in general surgical practice (4). Postoperative PG is detected in the clinic with wound dehiscence or ulceration following the development of painful erythema in the surgical field and is often confused in the differential diagnosis with surgical site infection, necrotizing breast infection or dermatitis (5-7). Secondary infections are encountered when PG lesions are not managed well and are diagnosed in a delayed manner.

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In this study, we report two cases of PG in breast surgery patients and discuss the treatment outcomes of oral doxycycline and topical tacrolimus.

Case Presentations

The first case was a 46-year-old woman who presented with a non-healing ulcer on her left breast that had persisted for three months after a breast biopsy. The patient had a history of rheumatoid arthritis, and prior to referral to our center, her ulcerated lesion had worsened due to repeated debridements and surgical interventions (Figures 1A, 1B, appearance at presentation 1C). She had undergone previous surgical debridements, received topical antibiotics, and various wound care applications, none of which led to improvement. The tissue culture demonstrated *Escherichia coli* growth.

The second case involved a 37-year-old woman with a surgical wound persisting for two months after bilateral reduction mammoplasty. Post-surgery, wound dehiscence in the right breast and a preliminary diagnosis of a surgical site infection were considered. The necrotic area was managed with repeated debridements. The patient was followed up on an outpatient basis, according to chronic wound follow-up principles. Due to an increase in wound size and tissue defect enlargement, pyoderma gangrenosum (PG) was suspected, and a dermatology consultation was obtained (Figure 2). A minimal opening on the incision line in the left breast was managed with wet and dry dressings, and the area healed spontaneously without debridement. A well-defined ulcer, approximately 10x12 cm in size, was observed under the left breast. A skin sample from the lesion edge showed focal erosion, non-specific chronic inflammation in the upper-middle and deep dermis, and a marked increase in fibroblastic activity (Figure 3). The wound culture grew *Staphylococcus aureus*.

The physical examinations of both patients were normal except for the surgical incisions, with no lymphadenopathy or organomegaly detected. Neither the patients nor their family members had a history of inflammatory bowel disease or hematological diseases. Laboratory tests, including complete blood count with differentials, liver, kidney, and thyroid function tests, erythrocyte sedimentation rate, C-reactive protein levels, rheumatoid factor, and serum protein electrophoresis, were all within normal limits. No abnormalities were observed on chest X-rays. Tests for anti-nuclear, anti-cryoglobulin, and antiphospholipid antibodies were negative.

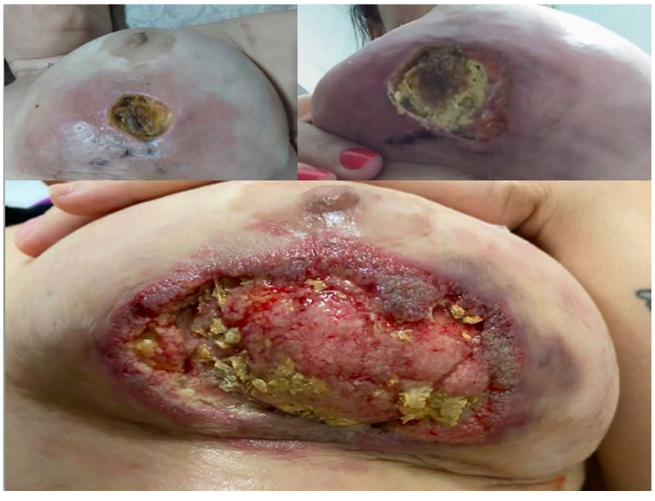

Figure 1. (Figure 1A, 1B, view at presentation-1C) The incision debrided before the patient presented to our center. (Figure 1C) shows the appearance at the time of presentation

Previous surgical pathologies were benign. Based on clinicopathological correlations, both cases were diagnosed as PG (Figure 4). The patients were administered 200 mg/day of doxycycline orally and topical 0.1% tacrolimus ointment twice daily. Epithelialization appeared in the lesions of both patients within the first two weeks.

Wound dressings were carefully changed after the diagnosis of PG without debriding and traumatizing the wound area. The wound bed was washed with saline or antiseptic solutions. Enzymatic debridement gels were used for necrotic areas and to moisturize the wound bed. When signs of infection regressed in the tissue defects of the patients, the frequency of dressing changes was initially reduced to every other day. When granulation was achieved in the wound bed and there was no suspicion of infection, bioactive wound dressings were used for rapid closure of the tissue defect and epithelialization. The frequency of dressing changes was then reduced to every 3-4 days to minimize the possibility of trauma. A collagen laminin-based dermal matrix (Dermalix®) containing resveratrol-loaded microparticles was used to fill the tissue defects and further promote granulation (8) (Figure 5).

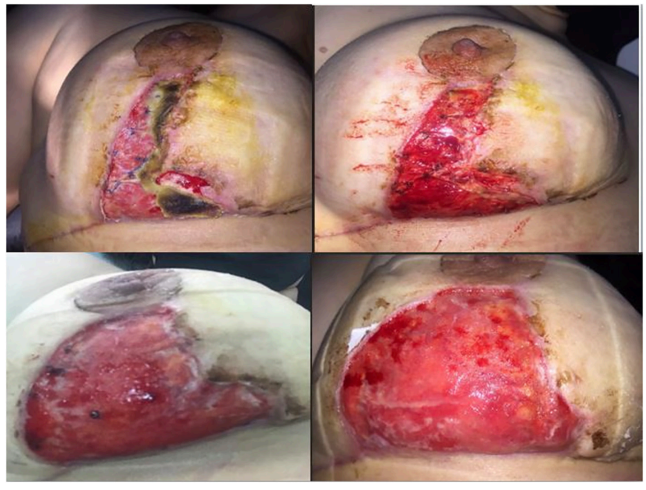

Figure 2. The appearance of the incision line after debridements until the diagnosis of pyoderma gangrenosum was made

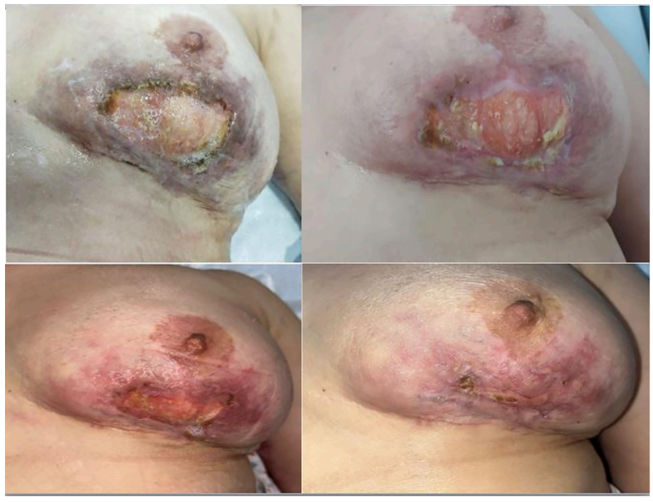

Figure 3. Treatment stages and healing process progressing to epithelisation

Complete recovery was achieved after six and two months of therapies, respectively (Figure 6), and the therapies were stopped. The patients did not experience any drug-related side effects. There were no recurrences or new lesions during the 12-month follow-up period. Written informed consent was obtained from both patients.

Discussion and Conclusion

Breast biopsy surgery and reduction mammoplasty using glandular flaps are performed to achieve cosmetically satisfactory results (9). Since the pouches in the resected area are closed after breast surgery, wound complications, such as seroma, infection, and wound dehiscence, occur at low rates (10). After reduction mammoplasty, incision gaps and suture line ischemia may occur, especially in cases where the inferior pedicle technique is used. The development of PG should be considered in patients who develop a suspected resistant wound infection after breast surgery, undergo debridement of the incision line and necrotic areas, and if the wound bed enlarges and atypical limited ulcers develop. PG development should be suspected in postoperative cases with inflamed and painful ulcers. The development of PG leads to catastrophic cosmetic results, especially in patients with implants and oncoplastic surgical techniques (7, 11, 12). Another important issue is the delay of adjuvant chemotherapy in cancer patients due to prolonged wound problems with late diagnosis of PG in oncological patients.

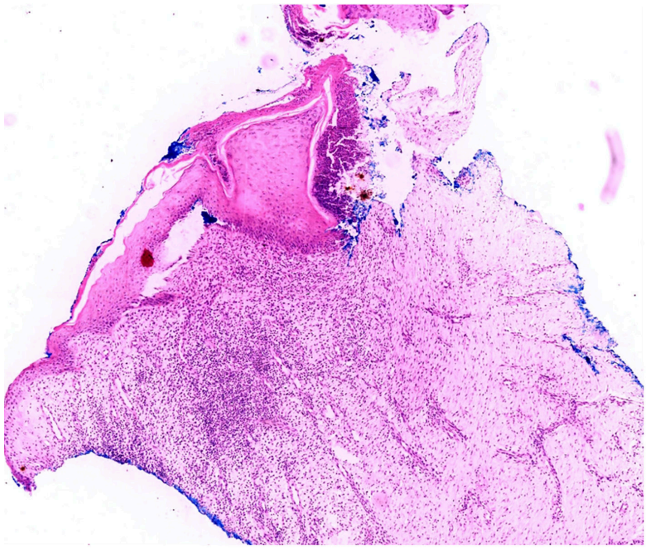

Figure 4. Histopathological examination of the ulcer edge of patient; focal erosion, non-specific chronic inflammation in the upper-middle and deep dermis, marked increase in fibroblastic activity (X10, H&E)

H&E: Hematoxylin and eosin

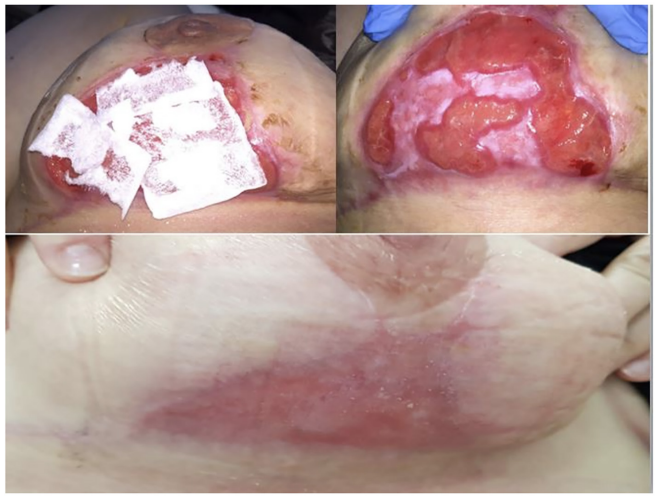

Figure 5. Stages of treatment, use of bioactive wound dressing and healing process progressing to epithelisation

The first rule of approach to all chronic wounds that develop after surgery, regardless of etiology, is to debride the wound bed to prevent the formation of a possible resistant infection and biofilm layer (13). This curettage and debridement, which removes necrotic, ischemic tissues, eliminates possible biofilm layers, and stimulates granulation tissue in the wound bed, is contraindicated in PG patients (13, 14). It leads to the triggering of a disease similar to the pathergy test used in the diagnosis of PG. Postoperative infection, dermatitis, and foreign body reactions due to sutures should be considered in the differential diagnosis of PG, although they occur less frequently.

The wound should not be traumatized in patients who develop PG after surgery. It is useful to wash the wound bed with antiseptic solutions and physiological saline (14). Enzymatic and autolytic debridement gels should be used for necrotic tissues in the wound bed and slough tissues that pose a risk for possible biofilm layer formation (14, 15). The wound bed should be kept moist, and maceration of the surrounding skin should be prevented. Wound dressings may be beneficial in wound healing. In the diagnosis of PG cases after surgery, it is important to measure and photograph the wound dimensions, which is one of the principles of chronic wound care treatment. Lack of reduction in size between two dressings or irregular limited increase in size should suggest the diagnosis of PG, not infection. Late diagnosis and lack of disease management skills may lead to catastrophic consequences for PG (16).

PG may manifest as a classical ulcerative form or atypical bullous, vegetative, or pustular variants (17). While systemic immunosuppressive agents are the preferred treatment for most cases of PG, local therapies, including topical and intralesional corticosteroids, topical sodium

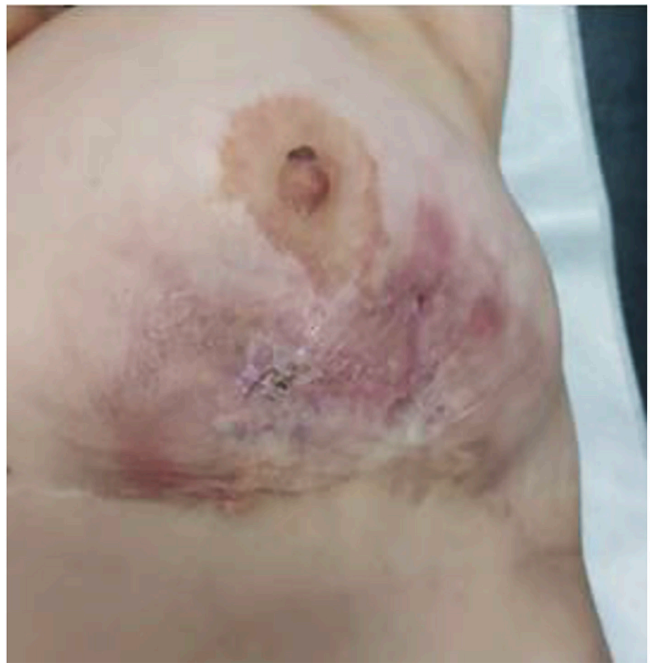

Figure 6. The stage where epithelisation is achieved and treatment is terminated

cromoglycate, benzoyl peroxide, hyperbaric oxygen therapy, skin grafts, and radiotherapy, are the most frequent options for a localized form (18). In severe cases, systemic immunosuppressive agents, such as systemic corticosteroids, dapsone, tumor necrosis factor-alpha (TNF-α) inhibitors, and cyclosporine are used (19). These treatment algorithms should be determined based on the severity of the disease and the level of treatment resistance.

Doxycycline is a tetracycline antibiotic that reduces proinflammatory cytokines such as interleukin (IL)-1β, IL-6, and TNF-α. Due to its anti-inflammatory properties and good safety profile, doxycycline is widely used in dermatology for various skin disorders, such as acne rosacea, bullous pemphigoid, and perforating dermatoses (20). Moreover, there are reports of successful outcomes in patients with PG treated with doxycycline. A retrospective study conducted in France compared the treatment results of 42 PG patients. Twenty-three patients were treated with 200 mg/day of doxycycline, either as monotherapy or in combination with topical steroids or topical tacrolimus, 15 patients were treated with systemic steroids, either as monotherapy or in combination, and four patients were treated with other treatment methods (colchicine, dapsone, or topical steroids only). The response rates to doxycycline and systemic corticosteroid treatment in PG were found to be comparable, with a lower recurrence rate in the doxycycline group (21).

Tacrolimus is an immunomodulator that inhibits T-lymphocyte activation by suppressing the expression of IL-2 genes (22). Tacrolimus also inhibits gene transcription for IL-3, IL-4, interferon-α, TNF-α, and granulocyte-macrophage colony-stimulating factor. A further action of tacrolimus is to block degranulation of mast cells, neutrophils, basophils, and cytotoxic T-cells. However, the specific mechanism by which tacrolimus improves PG remains unclear. Since central neutrophilic and peripheral lymphocytic infiltrates characterize PG, tacrolimus may act through inhibiting the accumulation and activation of lymphocytes and neutrophils in PG (23). The effect of topical tacrolimus was compared with topical corticosteroids in a study of 24 patients with peristomal PG (24). Eleven patients were treated with 0.3% topical tacrolimus monotherapy, and thirteen patients were treated with topical 0.05% clobetasol propionate. The treatment response and healing time were superior in the topical tacrolimus group compared to the topical steroid group. Seven patients in the tacrolimus group healed in an average of 5.1 weeks, while five patients in the clobetasol propionate group healed in an average of 6.5 weeks. Topical tacrolimus was more effective in patients with ulcer diameters greater than 2 cm. While topical tacrolimus does not cause skin atrophy, unlike topical steroids, it may lead to sensations of burning, itching, and may also predispose to the reactivation of the herpes simplex virus. The absence of these side effects in our patients increased the compliance with use.

PG development after breast surgery is very rare. When PG develops after breast surgeries, it can pose significant challenges for clinicians. Early diagnosis of PG can be achieved, particularly in cases with erythematous, irregular borders and an increase in size despite adhering to wound care principles.

The combination of oral doxycycline and topical tacrolimus is a good treatment option for PG, especially in patients with limited disease, due to their treatment efficacy and safety profile compared to immunosuppressive agents. However, prospective studies involving larger patient groups and longer follow-up periods are needed.

Ethics

Informed Consent: Written informed consent was obtained from both patients.

Footnotes

Authorship Contributions: Surgical and Medical Practices: G.A., K.B.Y.; Concept: M.D., K.B.Y.; Design: G.A., K.B.Y.; Data Collection and/or Processing: G.A., M.D.; Analysis or Interpretation: M.D., K.B.Y.; Literature Search: G.A., M.D., K.B.Y.; Writing: G.A., K.B.Y.

Conflict of Interest: No conflict of interest was declared by the authors.

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