Breast cancer and pyoderma gangrenosum: a complication after conservative surgery and radiotherapy

Flávia Kuroda1,2*, Cicero Urban1, Erica Mendes3, Anelise Rocha Raymundo4, Alessandra Amatuzzi Cordeiro Fornazari1, Teodora Roballo Durigan5

1Mastology Department, Hospital Nossa Senhora das Graças – Curitiba (PR), Brazil.  
2Post-graduation Program in Biotechnology, Universidade Positivo – Curitiba (PR), Brazil.  
3CLINIPAM – Curitiba (PR), Brazil.  
4Dermatology Department, Santa Casa de Misericórdia de Curitiba – Curitiba (PR), Brazil.  
5Universidade Positivo – Curitiba (PR), Brazil.  
*Corresponding author: flaviakuroda@hotmail.com

ABSTRACT

Pyoderma gangrenosum (PG) is a rare, ulcerative, and painful neutrophilic dermatosis of unknown cause associated with systemic diseases and/or pathergy phenomenon in 30% of cases. We report the case of a breast cancer patient submitted to oncoplastic conservative surgery followed by adjuvant radiotherapy, with long-term progression to PG. Its rare and challenging nature reinforces the need for early diagnosis to increase treatment effectiveness and reduce morbidity.


INTRODUCTION

Pyoderma gangrenosum (PG) is a dermatological inflammatory disease resulting from innate immune system dysfunction, with highly heterogeneous presentation and course1,2. It is a rare neutrophilic dermatosis characterized by papule, pustule, and vesicle formation rapidly progressing to painful skin ulcers, often located in the lower limbs, although they have been reported on the head, breast, oral cavity, trunk, perineum, and upper limbs1,3. These skin lesions present well-defined edges, peripheral erythema, moist base, subcutaneous tissue necrosis, painful high sensitivity, suppuration, and occasional bleeding4,5. The disease presents great morbidity, and its course may be chronic or recurrent.

Although they may occur spontaneously, more than 50% of lesions develop due to skin hyperactivity at trauma sites, with special emphasis on postoperative ones (PPG)6,7. Multiple case reports have described the progress of PG after cosmetic, oncologic, and reconstructive breast surgery, but few PG reports address breast cancer after conservative surgery associated with radiotherapy.

CASE REPORT

This case report describes a 50-year-old Caucasian, nulligravida patient with a history of hiatus hernia, dyslipidemia, and hypothyroidism, taking omeprazole, simvastatin, and levothyroxine. She also had a previous history of fibroids hysterectomy surgery, and a family history of breast cancer (her mother died at the age of 50 years).

The patient had a T2N0M0 left breast cancer – grade 2 invasive ductal subtype, triple-negative, and Ki-67 40%. She received neoadjuvant chemotherapy (CT) (doxorubicin and cyclophosphamide, followed by taxane – AC-T + carboplatin), which ended on February 6, 2018. On March 19, 2018, she underwent quadrantectomy + sentinel lymph node biopsy (SLNB) on the left side and bilateral oncoplastic surgery, using the lower pedicle technique (Figure 1). On the 15th postoperative day, the patient developed small dehiscence in the left breast T area, which was resutured. The wound healed completely, and the patient was referred to radiotherapy. She received left-breast external conformal radiotherapy at a total dose of 50 Gy (30 fractions) and a 60 Gy boost (30 fractions), ending on July 11, 2018. The patient progressed well with grade 1 radiodermatitis in the treated area.

In October 2019 (19th postoperative month and 15th post-radiotherapy month), she developed small periareolar ulceration on the left breast (Figure 2). At that time, infection was suspected, and the patient was treated with debridement, Hydrofiber dressing with silver and non-adherent membrane, and antibiotic therapy.
Figure 1. Preoperative surgical planning.

Figure 2. Pyoderma gangrenosum lesion progression. (A and B) October 2019 (19th postoperative month and 15th post-radiotherapy month). (C) November 2019: ulcer progression with necrosis foci. (D and E) December 2019: ulcer involving the entire breast, excluding the nipple and part of the areola.
Breast cancer and pyoderma gangrenosum: a complication after conservative surgery and radiotherapy

Mastology 2020;30:e20200032

(cefadroxil) for 21 days. The crusted ulcer gradually progressed, with necrotic foci and intense pain (Figure 2). In December 2019, the lesion had affected the entire breast, excluding the nipple and part of the areola (Figure 2). The patient was taking dipyrone, naproxen, and codeine/paracetamol, without pain control, and receiving wound dressing care.

On December 4, 2019, she was admitted for complementary tests, culture collection, and incisional biopsy. On that occasion, laboratory tests, upper endoscopy, colonoscopy, bone scintigraphy, and chest, abdominal, and pelvic computed tomography were performed, all of them without evidence of abnormalities. Based on the clinical history and progress, PG was the main diagnostic hypothesis, and an empirical treatment was started with oral prednisone at 80 mg once a day + local use of a porous regeneration membrane during hospitalization. On the 15th day of corticotherapy, the patient reported 70% to 80% pain improvement.

Histopathological results showed moderate epithelial hyperplasia, as well as chronic and severe acute neutrophilic inflammation. General bacterioscopy and mycobacteria and fungi culture were negative, but common germ culture was positive for *Burkholderia cepacia* and *Citrobacter freundii* complex.

During oral corticosteroid treatment, tiredness, weight gain, and lower limb pain were the patient’s main complaints. One month after treatment, she reported significant pain reduction and progressive improvement in wound appearance. In a period of two months using corticosteroid associated with Protopic® (tacrolimus), the wound had small residual ulcerated areas at the lesion edges (Figure 3). In three months, she was completely healed (Figure 3). Oral corticosteroid weaning was then initiated, firstly with 60 mg for 14 days, followed by 40 mg for another 14 days, and finally, 20 mg for 14 days. The patient completed corticosteroid weaning in May 2020, and her wound is now completely healed (Figure 3).

**DISCUSSION**

PG is considered a rare disease, with an estimated prevalence of 3 cases per 100,000 people, and 0.63 new cases diagnosed per year per 100,000 people[^1]. The disease presents a slight female predominance, and its incidence peak occurs between 20 and 50 years of age, with children and adolescents representing only 4% of cases[^3]. PG pathogenesis is not well known, but the condition is associated with underlying diseases, such as inflammatory bowel disease, rheumatoid arthritis, psoriatic arthritis, autoimmune hepatitis, hidradenitis suppurativa, acne, and hematologic disorders, in 50% to 70% of cases[^8,9]. In the present context, the patient had no previous history of these underlying diseases, and nothing significant was identified during the investigation.

PG diagnosis is mainly clinical and can be exclusionary, especially in case of a previous wound history, subjecting the patient to repeated antibiotic therapy and ineffective debridements[^10-12]. PG is currently classified into four clinical subtypes, based on its morphology: classic (ulcerative), bullous, pustular, and vegetative[^1]. These subtypes may coexist, but in general, the classical form is the most common, with pain being one of the main symptoms in this case[^7]. Although they may occur spontaneously, more than 50% of lesions develop due to skin hyperactivity at trauma sites, with special emphasis on PPG, i.e., in these cases (30%), the pathergy phenomenon is essential[^6-7]. In PPG, after a period of typical appearance (between four and six weeks), the

---

**Figure 3.** Pyoderma gangrenosum lesion progression after the start of corticotherapy. (A) 2 months of treatment: small ulcerated areas at the lesion edges. (B) 3 months of treatment: healed wound and start of corticosteroid weaning. (C) Complete corticosteroid post-weaning: fully healed wound.
surgical wound shows small dehiscence that usually coalesce into large ulceration areas in a process that goes beyond the surgical wound. Granulation tissue is practically non-existent, and pain is inconstant.

In general, breasts are an unusual site for PG manifestation, but we underline that approximately 80% of known breast PG cases are postoperative ones\(^1\). In a systematic review that included 87 PPG cases followed by cosmetic and reconstructive breast surgery, most of them (44%) occurred after resection surgery, and 16% after breast reconstruction by microsurgery\(^2\). A total of 32 cases (37%) were associated with breast cancer and 17% with autoimmune diseases\(^3\). In another review based on Latin American statistics from 1981 to 2018, 96 out of 232 PG cases were found in Brazil\(^1\). Only 11 of these cases were associated with breast procedures (eight breast resections, one breast implant, one phyllodes tumor, and one post-quadrantectomy case)\(^1\). The case described above presented a classical morphological progression (ulcerative), starting at the periareolar incision and extending throughout the breast, excluding the nipple. Contrary to the specialized literature, the lesion developed later, after the pathergy phenomenon – 19 months after cancer surgery.

PG has no gold standard treatment due to a lack of randomized controlled studies; however, the method most frequently reported is based exclusively on systemic steroid administration, followed by the combination of systemic steroids and corticosteroid-sparing agents\(^1\). Possible options include dexamethasone, cyclosporine, colchicine, thalidomide, sulfonamide, azathioprine, mycophenolate mofetil, tumor necrosis factor α (TNF-α) inhibitors, calcineurin inhibitors, immunoglobulin, and surgery\(^3\). In a systematic review on post-breast surgery PG, the most common treatments were steroids with 73 cases (84%) and/or cyclosporine A (22%)\(^2\). A few cases employed infliximab (n = 2), tacrolimus (n = 3), adalimumab (n = 1), and hyperbaric oxygen therapy (n = 4). Rapid response to immunosuppressive therapy was reported in most cases, with a mean treatment duration of 4.7 months. Skin grafting was performed in 19 patients, and local rotation or free flap in 11\(^1\). The case described showed a rapid response to steroid and complete lesion remission after three months of treatment, even though the breast had been previously irradiated.

CONCLUSION

PG is rare and challenging for the differential diagnosis of breast diseases. Knowledge related to clinical presentation, predisposing factors, and risk surgical conditions can contribute to early diagnosis and avoiding progress to extremely severe as well as treatment-resistant cases.

AUTHORS’ CONTRIBUTIONS

F.K.: study concept, data curation, formal analysis, methodology, project management, writing – review & editing.
C.U.: study concept, data curation, formal analysis, methodology, project management, writing – review & editing.
E.M.: data curation, methodology.
A.R.R: data curation, methodology.
A.A.C.F.: research, validation, formal analysis, writing – review & editing.
T.R.D.: research, writing – original draft.


