Pyoderma Gangrenosum after Deep Inferior Epigastric Perforator Breast Reconstruction: Systematic Review and Case Report

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**Background:** Pyoderma gangrenosum (PG) is a rare skin disorder of the neutrophilic dermatoses spectrum that can mimic wound infections in surgical patients. PG after breast surgery has been reported but in limited amounts in autologous breast reconstruction patients. We present the first case of PG after a delayed bilateral deep inferior epigastric perforator flap breast reconstruction in the setting of systemic disease along with a systematic review.

**Methods:** PubMed, Ovid, and Web of Science were systematically searched to obtain cases of PG after autologous breast reconstruction. Sixty articles were identified but only 16 were relevant to this study.

**Results:** Systemic disease was present in 2 patients (13%). Wound onset occurred typically 5 days after surgery. Fever and/or leukocytosis was observed in 10 patients (63%). Wound cultures were positive in 2 patients (13%). Donor-site wounds were present in 9 patients (56%). Bilateral breast wounds were present in 67% of bilateral cases. Debridement was performed in 10 cases (63%). Skin graft or substitute was performed in 6 cases (38%). Resection of autologous flap was performed in 3 cases (19%). All patients were treated with systemic steroids (81%) and/or immunosuppressive medications (50%). Complete wound healing occurred by 4 months on average.

**Conclusion:** If early ulcerative wounds develop at multiple sites after autologous breast reconstruction with worsening after debridement and antibiotic therapy, then PG should be considered. It is imperative that an early diagnosis and subsequent treatment with steroids and/or immunosuppressive medications be initiated so further surgical procedures, flap loss, and scarring can be minimized. (Plast Reconstr Surg Glob Open 2017;5:e1239; doi: 10.1097/GOX.0000000000001239; Published online 21 April 2017.)

Pyoderma gangrenosum (PG), first described by Dr. Brunsting in 1930, is a rare skin disorder that is part of the inflammatory neutrophilic dermatoses spectrum characterized by ulcers, bullae, and/or pustules. It is often associated with systemic diseases such as rheumatoid arthritis, inflammatory bowel disease, and hematologic disease in up to 78% of cases. The most commonly affected area is the lower extremities; however, it can affect the breast as well as the entire body. The development of PG has been seen after surgery and is thought to be secondary to pathergy or the development of ulceration after minor trauma to the skin. Postoperative PG has been seen in multiple patients and is difficult to diagnose as it can present similarly to a wound infection or necrotizing fasciitis. PG is a clinical diagnosis of exclusion and is suspected when there is rapid progression of painful necrotic ulcers with irregular undermined violaceous borders. Other minor criteria for diagnosis include sterile dermal neutrophilia on pathology and rapid response to systemic steroids. The diagnosis of PG is often delayed in the surgical patient, and patients tend to be treated ineffectively with antibiotics and debridements, which can further exacerbate the PG.

The timely diagnosis and treatment of postsurgical PG in breast reconstruction patients is important to minimize poor aesthetic outcomes. A systematic review
of the literature has shown the development of PG after 6 deep inferior epigastric perforator (DIEP), 5-10 8 transverse rectus abdominis myocutaneous (TRAM), 11-18 and 2 latissimus dorsi (LD) 19,20 flaps used for autologous breast reconstruction. We present a case of a patient with history of psoriasis and hidradenitis who underwent delayed bilateral DIEP flap breast reconstruction complicated by PG affecting the breast and abdomen. She was treated successfully with high dose steroids and immunosuppressive medications. To date, this is the first case of PG after free autologous breast reconstruction in a patient with associated systemic diseases. A systematic review of the literature is also performed to further aid in the diagnosis and management of these complex patients.

METHODS

The databases from PubMed, Ovid, and Web of Science were searched for studies published through May of 2016 using the following terms: “pyoderma gangrenosum” AND “autologous breast reconstruction” OR “breast reconstruction” OR “breast surgery” OR “breast.” After duplicate articles were removed manually, there were 60 citations to review. Each abstract was reviewed by 2 independent reviewers to obtain the relevant cases to include in this study. Articles were included if they presented a report of PG after autologous breast reconstruction. If the abstract resulted in insufficient information to determine the specific breast surgery, then the article was further reviewed to determine inclusion criteria. Google translate was used to translate 3 of the articles from French, German, or Dutch to English. Articles were excluded if the article was not obtainable from our institutional database system or did not report a case of PG after autologous breast reconstruction. After reviewing the 60 citations and applying the inclusion and exclusion criteria, there were 16 articles that are included in our study. If there was any disagreement between the articles, then a discussion was held and a consensus formed. Data were extracted from each article if available and included patient age, type of autologous breast reconstruction, onset of wound, involvement of donor site and/or breast, presence of fever or leukocytosis, wound cultures, surgical/medical treatment, and healing outcomes (Table 1). A flow diagram of study selection is shown in Figure 1.

CASE REPORT

The patient is a 37-year-old woman with history of depression, anxiety, migraines, psoriasis, hidradenitis, total abdominal hysterectomy/bilateral salpingo-oophorectomy, left breast invasive ductal carcinoma, and BRCA-1 gene mutation status post bilateral mastectomies with immediate reconstruction using silicone implants at an outside...
institution in 2012 who now desires delayed autologous breast reconstruction. No radiation was given for her breast cancer but she underwent adjuvant chemotherapy and was placed on tamoxifen. On examination, she was obese (body mass index 31) with bilateral capsular contraction and small abdominal pannus without prohibitive scars or hernias, and had diffuse psoriatic plaques. Her vital signs and laboratory values were unremarkable. She stopped her apremilast and tamoxifen 2 months before undergoing a bilateral DIEP flap breast reconstruction in 2016. The patient had an uneventful course until postoperative day 4 when she was noted to have erythema along her abdominal incision and inferior bilateral native breast skin. Over the next 24 hours, she developed a fever (100.8 F) with increasing abdominal wound pain, erythema, induration, wound edge necrosis, bullae, drainage, crepitance, and minimal dehiscence (Fig. 2) so she was started on vancomycin. No leukocytosis was present. Blood, urine, and wound cultures obtained were negative. A computed tomographic scan on postoperative day 5 showed postoperative changes only. There was increased dehiscence of the abdominal wound spontaneously, so wet-to-dry dressings were performed followed by vacuum-assisted closure (VAC). Given her persistent tachycardia and pyrexia, the Infectious Disease team was consulted who recommended addition of ciprofloxacin and flagyl. On postoperative day 8, she developed a leukocytosis (WBC 12.3) with right breast flap erythema, ecchymosis, and draining pustules (Fig. 3). A right breast ultrasound showed no fluid collections. Dermatology was consulted the following day given her history of psoriasis, but this would not contribute to her postoperative wound development.

She was febrile and had a leukocytosis until postoperative days 10 and 14, respectively. Debridement of abdominal wall necrosis and VAC placement were performed on postoperative day 12. Intraoperative cultures were negative. Patient was reevaluated by Dermatology on postoperative day 14 who diagnosed the patient with PG given the characteristic painful necrotic ulcers. The patient was immediately started on methylprednisolone 1000mg followed by a 15-day prednisone taper, mycophenolate mofetil 500mg twice a day, and infliximab 5mg/kg. Gentle wound dressing changes were performed with Vaseline application to the wound bed to keep the wound moist and prevent trauma/pathergy when the dressings are removed. The wound was then covered with Army Battle Dressing (ABD) pads to allow for absorbance of exudate and provide physical protection of the wound. A biopsy was not recommended as PG is a clinical diagnosis and the biopsy can stimulate more inflammation resulting in ulcer expansion. Intravenous antibiotics were changed to prophylactic oral clindamycin. The Acute Pain Service was consulted during her hospital course to help manage
her painful abdominal ulcers. She was discharged home on postoperative day 19 in stable condition with an improving abdominal wound showing necrotic ulcers with a mucopurulent base, violaceous undermined border, and erythema along the periphery (Fig. 4). During her hospital stay, the bilateral DIEP flaps were healthy with strong arterial Doppler signals.

The patient was readmitted 6 weeks after her initial surgery with flu-like symptoms, fevers, tachycardia, hypotension, and leukopenia (WBC 4) consistent with SIRS. Her abdominal wound had granulation tissue present with no signs of infection and a viable umbilicus (Fig. 5). She was started on empiric broad spectrum antibiotics but after an infectious workup was negative, these were stopped as her symptoms were likely from a viral etiology. During her hospital stay, multiple other family members had similar flu-like symptoms that resolved spontaneously, supporting the diagnosis of a viral etiology. Her mycophenolate mofetil was continued during her stay until she became neutropenic. Before her readmission, she was started on cyclosporine as an outpatient, which was held during this hospital stay given the possible infectious etiology. She was discharged on hospital day 8. Since this time, the patient is doing daily dressing changes with Vaseline to the wound bed and covering with ABD pads. Her outpatient PG regimen consists of cyclosporine 100 mg daily, mycophenolate mofetil 2 g daily, and infliximab 5 mg/kg every 8 weeks. The patient also underwent photobiostimulation using red light (633 nm) for 20 minutes to her chronic abdominal wound to improve wound healing as recommended by Dermatology, and further treatments are planned. On follow-up at 3 months postoperatively, the right breast wound was completely healed and the abdominal wound was contracting with granulation tissue (Fig. 6). The abdominal wound completely healed by 5.5 months but had some cribriform scarring (Fig. 7).

**RESULTS**

There have been multiple reports of postoperative PG after breast surgery with only 16 cases occurring after autologous breast reconstruction. PG has occurred in 6 DIEP,5–10 8 TRAM,11–18 and 2 LD flaps used for breast reconstruction. The average patient age was 51 years.
The development of PG in the presence of known systemic disease (hypogammaglobulinemia, seronegative polyarthritis) occurred in 2 patients (13%), but free tissue transfer did not occur in these cases.15,20 PG associated with systemic disease is significantly higher (up to 78%) in other patient populations.3 There were no reported cases of having a family history of PG. The average time to PG wound onset after surgery was 10 days but had a median and mode of 5 days (range: 2 d to 2 mo). The presence of fever and leukocytosis occurred in 7 (44%) and 6 cases (38%), respectively, but the majority of the studies did not mention the presence or absence of these systemic findings. All wound cultures were negative except for 2 cases (13%), which grew out methicillin-resistant Staphylococcus aureus and Acinetobacter baumannii.5,7 There were 3 cases (19%) that had a history of previous breast infection before their autologous breast reconstruction, but none of these patients developed a subsequent breast infection.11,14,15

Most patients who underwent breast reconstruction using either TRAM or DIEP flaps developed abdominal donor-site wounds except for 2 cases (86%).5,18 The 2 cases of reconstruction using LD flaps did not report donor-site wounds on the back.19,20 There were 6 cases (38%) of bilateral breast reconstruction with 4 of these cases having developed bilateral breast wounds,5,9,11,18 1 case with unilateral involvement,6 and 1 case with unknown involvement.15 Debridement was performed in 10 cases (63%) with only one of these cases undergoing a single debridement as the only secondary procedure.5 The majority of patients who underwent debridement required multiple subsequent debridements, but most studies did not quantify the total number of debridements. Patients that underwent debridement without being on steroids or immunosuppressive therapy tended to have wound progression. The cases that did not undergo debridements were treated with steroids and/or cyclosporine. Skin grafts or skin graft substitutes were performed in 6 cases (38%), but this occurred after medical treatment was started.8,11-14,18 No issues with skin graft healing was reported. Resection of the autologous breast flap occurred in 3 cases (19%), which included 1 DIEP and 2 TRAM flaps. The loss of these flaps was secondary to arterial thrombosis,5 repeated radical debridements,12 and to remove a potential source of sepsis.16 The diagnosis of PG in these cases occurred after resection of the flaps. The simultaneous placement of breast implant or tissue expanders during the autologous reconstruction occurred in 2 cases (13%) with one of these cases requiring prosthesis removal secondary to worsening infection.11,19

All patients were treated with systemic steroids except for 3 cases (19%), which were treated with infliximab/hyperbaric oxygen (HBO),11 topical steroids/calcinieurin inhibitors,7 and cyclosporine.19 The second most commonly used medication in 6 cases (38%) was cyclosporine, a calcineurin inhibitor. Other immunosuppressive medications used were infliximab, intravenous immunoglobulins (IVIG), and tacrolimus but these were only in individual cases.11,12,16 HBO therapy was used in 2 cases (13%) with wound healing occurring between 2 and 3 months in these patients.11,13 The specific HBO treatments used in these cases were not well defined and were used in conjunction with other treatment modalities such as debridement, skin grafting, and immunosuppressive medications so it is unclear as to the effectiveness of HBO in these patients. Specific wound care was vague for the majority of the cases but seemed to favor the use of wet-to-dry dressings or the VAC. The range of complete wound healing was 15 days to 1 year with the majority occurring by 4 months. Cases that did not have complete wound healing tended to be in the process of wound healing.

**DISCUSSION**

PG is a rare, noninfectious inflammatory neutrophilic dermatosis occurring in 3 to 10 per million people each year and is associated with systemic diseases such as rheumatoid arthritis, inflammatory bowel disease, and hematologic disorders in up to 78% of cases.2 Postoperative PG is well established in the literature but can be hard to diagnose as it can present similar to a wound infection and is a diagnosis of exclusion. The initial presentation of PG is the development of erythema with pain out of proportion to examination followed by pustules or nodules that lead to necrotic ulcers that coalesce and are characterized by a mucopurulent base and violaceous undermined border.2 These patients are often initially treated with antibiotics and debridements, but this usually leads to progression of the disease.
Su et al. suggested a diagnostic criteria for PG, which includes the rapid progression (1–2 cm per day or 50% increase in 1 mo) of a necrotic ulcer with pain out of proportion to examination. Other causes such as vascular occlusion, vasculitis, malignancy, infection, drug reaction, inflammatory disorders, and exogenous tissue injury must be excluded, but this usually requires a skin biopsy and cultures. Other suggestive criteria of PG include development of ulceration at a site of minor trauma (pathergy), cribriform scarring, other associated systemic diseases, sterile dermal neutrophilia with inflammation, and rapid decrease in size (at least 50%) within 1 month of starting systemic steroids.

The treatment of choice for postoperative PG is high dose systemic steroids (methylprednisolone) followed by an oral prednisone taper over a period of 4 to 6 weeks. The steroid treatment will also aid in the diagnosis of PG as these lesions should regress rapidly. Topical steroids can be used for small localized PG lesions. Intralesional injection of steroids is controversial secondary to pathergy. A second-line agent that can be added is cyclosporine (2–5 mg/kg per day), which is a calcineurin inhibitor that targets T cells. Topical calcineurin inhibitors have also been used for PG. Tumor necrosis factor–alpha inhibitors such as adalimumab, etanercept, and infliximab are also used but usually in patients with associated systemic diseases. Other chemotherapeutic agents such as mycophenolate mofetil, azathioprine, mercaptopurine, and melphan have been utilized but are usually combined with systemic steroids. Antibacterial agents such as doxycycline, clofazimine, and dapsone can be used for wound prophylaxis but most wounds do not have positive cultures. Multiple topical agents besides steroids and calcineurin inhibitors have been used and include nicotine, benzoyl peroxide, hydrogen peroxide, and nitrogen mustard but there are limited data supporting their use. Other treatment modalities such as HBO, IVIG, and plasmapheresis have also been shown to be effective in the healing of PG wounds but are less common. HBO combined with other adjuncts for PG wounds has been shown to improve wound healing by arresting the ischemic process, enhancing angiogenesis, and reducing infection. Photobiostimulation has been shown to aid in healing of wounds in animals by increasing epithelialization and collagen synthesis, but there are no current studies of its use in patients with PG, so further research is needed.

Surgical treatment of PG is controversial because trauma to the areas of ulceration can lead to progression of the disease. These patients should be treated with medical therapy as soon as a diagnosis of PG is considered appropriate. Specific wound care management for PG in the literature is vague but includes application of Vaseline to the wound base, wet-to-dry dressings, and VAC. The use of VAC is debatable as it can traumatize the wound bed but has been shown to be safe and useful if performed under immunosuppressive therapy. The use of skin grafts or skin substitutes has shown to accelerate wound healing, but this should be performed in patients with large wounds in the setting of medical therapy.

Our patient has a history of systemic disease (psoriasis/hidradenitis) who underwent a delayed bilateral DIEP flap breast reconstruction. On postoperative day 4, she developed erythema to her donor site and bilateral native breast skin associated with a fever so antibiotics were started. Her abdominal wound progressed and she developed ulceration of the right breast flap along with a leukocytosis. Debridement of the abdomen was performed. She was diagnosed with PG by Dermatology and then treated immediately with steroids, mycophenolate mofetil, and infliximab. Since this time, her wounds have continued to heal with gentle local wound care and photobiostimulation but subsequently developed SIRS secondary to a viral etiology. Complete wound healing occurred by 24 weeks on follow-up.

CONCLUSIONS

This is the first article to show the development of PG after a free tissue transfer for autologous breast reconstruction in a patient with associated systemic diseases along with an updated systematic review of the literature. It is important to consider the diagnosis of PG in autologous breast reconstruction patients if early wounds develop at multiple sites in the presence of fever and/or leukocytosis, negative cultures, wounds worsen with antibiotics and/or debridement, and rapid wound improvement with steroids. If PG is contemplated, then a biopsy should be entertained to rule other potential causes and other teams consulted to aid in the diagnosis and management of the patient. Many surgeons are reluctant to start steroids early in the setting of a possible infection, but rapid use of steroids in the case of PG can potentially save a flap and decrease the amount of cribriform scarring.

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