

Pyoderma Gangrenosum after Breast Mastectomy and Primary Rectus Abdominis Flap Reconstruction

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(Received May 26, 2017; Accepted July 5, 2017)

Pyoderma gangrenosum is an intractable disease of unknown cause involving recurrent ulcerative lesions on the skin, and may accompany ulcerative colitis, rheumatoid arthritis, leukemia, systemic lupus erythematosus, and other conditions. Here, we report a rare case of pyoderma gangrenosum in the thoracic abdomen following post-mastectomy reconstructive surgery. A 39-year-old presented at the hospital with a complaint of left papilla erosion. Skin biopsy at the site revealed invasive skin cancer, with Paget-like progression in the cancerous nipple and suspected malignancy of skin appendages. After partial mastectomy including the areola, invasive ductal breast carcinoma was diagnosed. The patient underwent a subsequent full mastectomy with simultaneous sentinel lymph node biopsy and primary breast reconstructive surgery using a rectus abdominis myocutaneous flap. Two weeks post-surgery, healing of the abdominal surgical wound was found to be delayed, and suture abscess was suspected. Despite localized treatment, an ulcerative lesion developed in the thoracic region, and pyoderma gangrenosum was diagnosed following skin biopsy. After the introduction of steroid pulse therapy, no progression of the lesion was observed. This report describes the disease characteristics, diagnosis, and treatment of post-surgical pyoderma gangrenosum and discusses the case in the context of previous literature.

Key words: Breast cancer, pyoderma gangrenosum, breast reconstruction

INTRODUCTION

Pyoderma gangrenosum is a refractory disease of unknown origin characterized by reoccurring ulcerative lesions on the skin, with rapid disease progression that leads to necrotic ulcer. The condition may accompany ulcerative colitis, Crohn's disease, rheumatoid arthritis, leukemia, or systemic lupus erythematosus. Fifty percent of cases develop after trauma to the skin such as surgical wounds, arteriovenous puncture, and laparoscopy, through a process called pathergy [1].

Because post-surgical pyoderma gangrenosum (PSPG) presents in surgical wounds at an early post-operative stage, it is commonly diagnosed as a wound infection and treated ineffectively with antibacterial agents and debridement. However, due to the lack of therapeutic effect of these standard treatments and rapid progression of the disease, early diagnosis is important.

Here we report a case of thoracoabdominal PSPG following total mastectomy for breast cancer and reconstructive surgery that was treated successfully with pulse steroid therapy.

CASE REPORT

A 39-year-old female, with no history of pregnancy or birth, received consultation for a chief complaint of nipple erosion, present for the past half year. A blackish discoloration of the left nipple extending to part of

the areola and nipple erosion were confirmed (Fig. 1). The patient had no notable family or previous medical history. No abnormal findings were observed on either ultrasound of the breast or mammography.

Macroscopically, mammary Paget's disease was suspected. Dermal invasion of cancer cells and cancer cell clusters in the basal layer of the epidermis were confirmed following punch biopsy of the areola (Fig. 2).

Results of immunohistological investigation were as follows: CK (AE1/3) positive, CK7 positive, CK20 negative, p63 negative, melan-A negative, E-cadherin positive, GCDFP-15 weak positive, chromogranin A negative, synaptophysin negative, CD56 negative, CD99 negative, ER 50 %, PgR 10 %, HER2 3+, Ki67 90 %, p53 40 %.

Immunohistological staining pattern results were negative for squamous cell carcinoma, malignant melanoma, and Merkel cell carcinoma. While the findings were not inconsistent with mammary Paget's disease, the marked infiltration of cancer cells into the dermis negated a typical diagnosis of Paget's disease. A definitive diagnosis of malignant skin adnexal neoplasm was proposed. To ensure a reliable diagnosis, partial resection of the breast, including the nipple and areola complex, was performed.

Histopathologically, invasive proliferation of cancer cells was observed mainly in the dermis (Fig. 3a). Immunohistological investigation yielded the following



Fig. 1 Erosion in left nipple and areola.

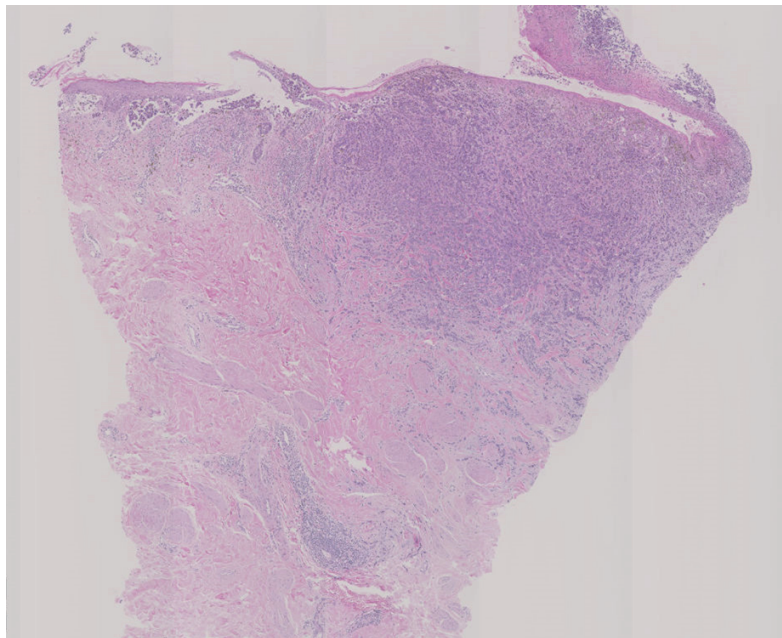


Fig.2 Histopathological examination (H&E), Carcinoma cell invasion from epidermis to dermis.

results: CK (CAM 5.2) positive, S-100 negative, HMB-45 negative, melan-A negative, EMA positive, CEA positive, E-cadherin positive, ER 60 %, PgR 30 %, HER2 3+, Ki67 70 %, p53 20 %. The presence of cancer cells within the mammary duct of the nipple was confirmed (Fig. 3b), with epidermal involvement of the nipple consistent with, and the high degree of infiltration inconsistent with mammary Paget's disease.

Residual cancer cells were observed in the deep margin, and a follow-up full mastectomy, sentinel lymph node biopsy, and primary breast reconstructive surgery using the rectus abdominis myocutaneous flap were performed simultaneously. Cancer metastasis was observed in the operative sentinel lymph node, and additional sampling of the axillary lymph node was also performed. A final diagnosis of pT1bpN1M0, luminal HER2 stage IIA invasive ductal carcinoma of the left

breast was made.

Postoperative conditions were good. All stitches in the chest were removed on postoperative day 7, and all stitches in the abdomen on postoperative day 10. However, wound dehiscence of approximately 2cm was observed in the chest suture on postoperative day 12, and on day 13, scar formation was observed in the midline of the abdominal wound and managed conservatively.

Two months after surgery, an abdominal ulcer was identified, which was suspected to be a suture abscess. The absorptive suture within the area of the abscess was removed; however, healing prognosis was poor (Fig. 4). At the same time, postoperative adjuvant chemotherapy was started in the form of 4 cycles of epirubicin/cyclophosphamide chemotherapy (90 mg/m², 600 mg/m²), followed by 4 cycles of docetaxel (75 mg/

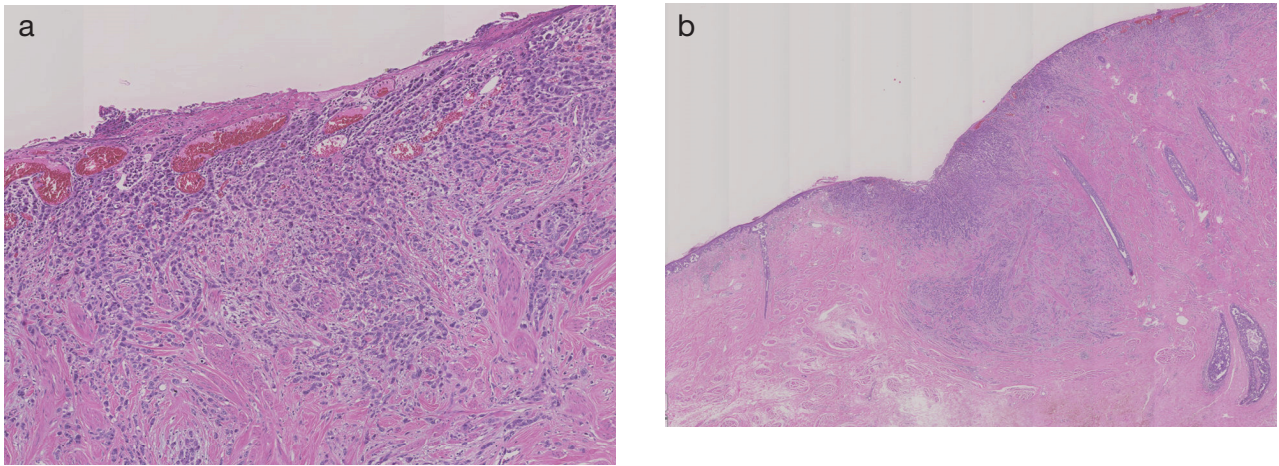


Fig. 3 a: Histopathological examination (H&E), Carcinoma cell invasion from epidermis to dermis at the nipple and areola. b: Histopathological examination (H&E), Invasive carcinoma with intraductal component of carcinoma was observed in the nipple. This finding was atypical of Paget's disease.



Fig. 4 Abdominal surgical wound dehiscence, small ulcer, and blackish brown discoloration 2 months postoperatively.

m²) and trastuzumab (initial dose at 8 mg/kg, loading dose at 6 mg/kg every 3 weeks for a 1-year period).

At the fourth month when docetaxel was started, an abscess appeared in the upper abdomen, followed by the appearance of an abscess in the chest, with frequent occurrences of abdominal abscesses until the completion of docetaxel therapy.

Wound and exudate culture were negative, oral administration of minocycline hydrochloride and clarithromycin were introduced, and topical therapy was carried out using a variety of ointments including gentamicin, mixed killed-bacterial formulations, and povidone-iodine.

No prophylactic administration of granulocyte-colony stimulating factor was performed, as there was no presentation of febrile neutropenia during chemotherapy and non-hematologic toxicity was minimal. There

was no noticeable deterioration of the lesion during the period of chemotherapy-induced neutropenia.

Eight months after surgery (Fig. 5a, 5b), a skin biopsy revealed marked neutrophil infiltration around capillaries and skin appendages in the superficial and deep layers of the dermis (Fig. 6).

There was no observation of abscess formation, fungal infection, or vasculitis, and a diagnosis of pyoderma gangrenosum was made. Therapeutic management was initiated, with oral administration of prednisolone 0.5 mg/kg/day for 1 month. The current dosage is continued at 0.5 mg/kg/day, and there have been no observations of new ulcer formation (Fig. 7).

DISCUSSION

In 1930, Brunsting *et al.* reported pyoderma gangrenosum as an intractable skin disorder characterized

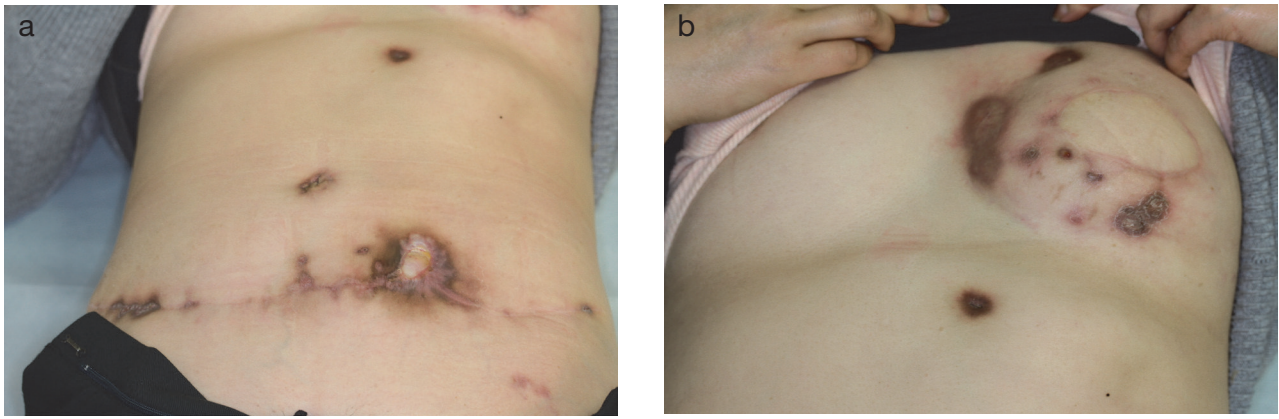


Fig. 5 a: Delayed wound healing at the lower abdominal surgical wound and upper abdominal blackish brown discoloration 8 months postoperatively.
b: Multiple ulcers and discoloration of the left chest and upper abdomen 8 months postoperatively.

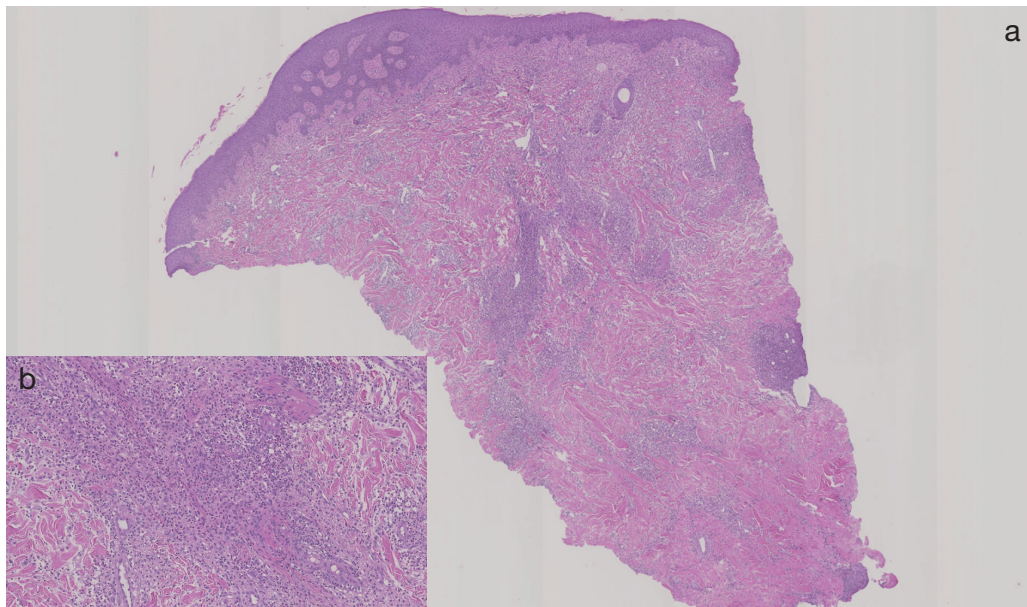


Fig. 6 a: Histopathological examination (H&E), Massive neutrophil and inflammatory cell infiltration was observed in the dermis, with no apparent vasculitis or mycosis in low magnification.
b: Histopathological examination (H&E), Massive neutrophil and inflammatory cell infiltration was observed in the dermis, with no apparent vasculitis or mycosis in high magnification.

by pustules and ulcers [2], and since Perry reported its association with ulcerative colitis in 1957 [3], it has been reported as a complication of diseases such as Crohn's disease, aortitis syndrome, rheumatoid arthritis, leukemia, malignant lymphoma, myelofibrosis, and other blood diseases [4-6]. In addition, there have been reports of periostal presentation after ostomy surgery as well as reports of idiopathic presentation [6].

Although the incidence of pyoderma gangrenosum is unclear, it is estimated to affect 3-10 per 1 million people per year, occurring in any age group, with peak incidence from 20 to 50 years old and slightly more frequent in women. Generally approximately 50% of cases present with the above-mentioned underlying conditions [7].

Various classifications of diagnostic criteria have been proposed, including major items such as rapid disease progression, painful necrotizing skin ulcers, irregularity in presentation, and irregular purple margin, with many cases of unknown etiology, and minor items that may include the presence or absence of underlying disease, dermal sterility, neutrophil infiltration, and responsiveness to systemic steroid administration [8].

About 50 % of cases are precipitated by dermal injury, a process termed pathergy [1], which may include venipuncture, laparoscopy, and surgical wounds. In many cases, PSPG that develops in the early postoperative period is diagnosed as wound infection, and standard therapies such as antibacterial treatment



Fig. 7 After treatment with corticosteroid, no new lesions were apparent 10 months postoperatively.

Table 1 Results of systematic review of post-surgical pyoderma gangrenosum

| Type of surgery | Number of cases | Average age | M | F | Post-op days before PG onset |
|-----------------|-----------------|-------------|----|-----|------------------------------|
| Breast | 56 | 45.0 | 0 | 56 | 7.2 |
| Cardiothoracic | 30 | 63.4 | 23 | 7 | 6.7 |
| Abdominal | 30 | 56.4 | 16 | 14 | 7.5 |
| OBGYN | 28 | 35.3 | 0 | 28 | 5.2 |
| Orthopedic | 27 | 56.0 | 11 | 16 | 8.8 |
| Head and neck | 8 | 59.6 | 3 | 5 | 5.0 |
| Puncture-other | 41 [#] | 54.0 | 24 | 16 | 8.4 |
| Total | 220 | 52.8 | 77 | 142 | 7.0 |

[#]Sex was not disclosed for one patient

PG, pyoderma gangrenosum; OBGYN: obstetrics and gynecology

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and surgical debridement are performed. However, disease progression is rapid. The presence of fever and leukocytosis occurred in 7 (44 %) and 6 cases (38 %), respectively [9]. On the present case, there was no history of febrile neutropenia during chemotherapy and non-hematologic toxicity was minimal. No fever and leukocytosis were seen during the onset of pyoderma gangrenosum. A review of 220 cases of PSPG identified 37 cases (16.8 %) with a history of pyoderma gangrenosum, and 56 cases (25 %) had presentation in the region of breast surgery, including reduction mammoplasty (25 cases, 45 %), breast reconstructive surgery (14 cases, 25 %), breast tumor resection and total mastectomy with no reconstruction (6 cases, 11 %), augmentation mammoplasty (4 cases, 7 %), and other surgical procedures (including excision biopsy and mastopexy; 7 cases, 12.5 %) [10].

The median age of onset was 45 years old (19–75 years) and postoperative presentation occurred at a median of 7.2 days.

Incidents of pyoderma gangrenosum precipitated by other surgical procedures include those with cardiovascular involvement (30 cases, 14 %), abdominal

involvement (30 cases, 14 %), obstetrics (28 cases, 13 %), orthopedic surgery (27 cases, 12 %), and head and neck involvement (8 cases, 3 %) (Table 1) [10].

Treatment may be systemic or localized topical treatment, and localized topical administration of triamcinolone diacetate applied to the edge of the area twice per week is effective, but the general approach involves the topical application of steroids and secondary application of topical antibacterial agents [11]. Systemic antibacterial therapy is ineffective, localized wound debridement leads to rapid progression of ulcers via pathergy, and skin transplants graft temporarily followed by rejection [10]. For systemic therapy, steroids are generally the most effective treatment. However, as the optimal dosage is undetermined, a treatment regimen involving a starting prednisone dose of 100–200 mg/day is recommended, with gradual dose reduction while observing the symptoms. In grave cases, methylprednisolone is administered over a 5 day period at 1 g/day followed by prednisone, immunosuppressive therapy with a sulfa drug [11], combined administration of oral prednisone (1 mg/kg/day) and intravenous injection of methyl prednisolone (0.5–1 mg/kg/

day), cyclosporin A (5 mg/kg/day), or in combination with tacrolimus, dependent on the symptoms [10].

Other approaches, while not covered by insurance, include the chimeric anti-TNF- α monoclonal antibody infliximab, which has been reported as effective [12]. In a case of severe ulcerative colitis and pyoderma gangrenosum, granulocyte and monocyte adsorption apheresis was effective [13].

The present case initially presented in a manner consistent with a surgical wound in the abdomen, was suspected to be a suture abscess, and was treated conservatively. While the patient's diagnosis was delayed, symptoms were not severe. However, it is expected that good therapeutic effects can be obtained if an early diagnosis of PSPG is possible.

CONCLUSIONS

We experienced a case of post-surgical pyoderma gangrenosum following primary breast reconstructive surgery after breast cancer surgery. While a rare disease, it is important that pyoderma gangrenosum be kept in mind in the presentation of skin diseases characterized by refractory ulcers and pustules.

ACKNOWLEDGEMENT

We would like to thank Editage (www.editage.jp) for English language editing.

CONFLICTS OF INTEREST

The authors declare no conflict of interest related to this article.

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