Pyoderma Gangrenosum of the Breast: A Rare Complication of Rheumatoid Arthritis

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ABSTRACT

Pyoderma gangrenosum (PG) is a rare, neutrophilic dermatosis characterized by painful ulcerative skin lesions. PG is commonly associated with autoimmune disorders and hematologic malignancies. It typically presents on the lower extremities, but can occur anywhere on the body. PG is a rare cause of breast ulceration, with most reports in the literature occurring post-surgically.

Here we present a case of PG of the breast in a patient with no previous history of surgery involving the breast. Diagnosis of rheumatoid arthritis (RA) was made and treatment using 60 mg of oral prednisone was tapered over 4 weeks, which along with topical antibiotics, led to significant improvement of the lesion.

PG of the breast can be extremely distressing for affected patients. Though rare, PG of the breast is an important diagnosis to consider, especially when other causes of chronic ulceration have been excluded. Almost all cases of PG of the breast occur post-surgically. In those that arise de novo, however, there is an abnormally high prevalence of rheumatoid arthritis. This case highlights the importance of considering concurrent RA when managing a patient with PG of the breast. Early diagnosis can help guide treatment and reduce morbidity from this debilitating disease.

INTRODUCTION

Pyoderma gangrenosum (PG) is a rare and often chronic inflammatory, ulcerative skin disorder, affecting approximately 3-10 in 1 million people each year.¹ The etiology of PG is currently unknown, but it is thought to arise as a result of neutrophil and immune system dysfunction as well as genetic susceptibility.¹⁻³ The increased susceptibility for PG in patients with autoimmune disorders, inflammatory bowel disease (IBD), rheumatoid arthritis (RA), and hematologic disorders such as leukemias and lymphomas in approximately 50-70% of cases supports this theory of immune system and hematologic dysfunction (Table 1).³⁻⁵

Typically, the development of PG is characterized by an inflammatory papule, nodule, or pustule that eventually expands and undergoes necrosis to form a chronic ulcerative lesion.¹ PG lesions such as these are usually found on the lower extremities, but can occur anywhere on the body.⁶ PG is a rare cause of
breast ulceration, with most reports in the literature occurring post-surgically following breast reduction or augmentation.7–11 Herein we present a patient with PG of the bilateral breasts without history of surgery or previously diagnosed systemic disorder.

**CASE PRESENTATION**

A 68-year-old African-American woman with a past medical history of hypertension and diabetes mellitus presented for work-up of a large ulcerative lesion on her chest and bilateral breasts. The ulcerative lesion began as a small erythematous papule on the mid-chest and expanded gradually over the course of four weeks. Other causes of chronic ulceration of the breast were excluded including trauma, vascular disease, infection, cutaneous and breast malignancy, as well as drugs. A biopsy with findings consistent with pyoderma gangrenosum (PG) was made and the patient was subsequently worked-up for underlying systemic inflammatory disorders and malignancy. Past medical history was significant for hypertension, diabetes mellitus, and non-specified arthritis; patient denied personal history of RA, IBD, or symptoms suggestive of IBD. Patient also denied new medications or changes in medications. The patient reported no family history of IBD. However, there was a positive family history of RA in the patient’s mother.

Physical examination revealed a large 20x20 cm ulcerative lesion over bilateral breasts and chest characterized by an erythematous base with superficial necrotic eschar and yellow, purulent discharge (Figure 1). In addition to the ulcerative breast lesion, the physical exam was remarkable for swelling in the right wrist, right ankle, and left knee with decreased range of motion in affected joints and fingers. Basic labs were significant for microcytic anemia with hemoglobin of 7.3 g/dL and an MCV of 64.5 fL. Because other causes of ulcerative lesions such as trauma, infection, cutaneous or breast malignancy, and vascular disease were ruled out and biopsy findings were consistent with the diagnosis of PG, the patient was started on 60 mg of

### Table 1. Prevalence of diseases commonly associated with PG.

*Other diseases: pulmonary disease, hidradenitis suppurativa, acne conglobata, chronic hepatitis, diabetes mellitus, and sarcoidosis

<table>
<thead>
<tr>
<th>Associated Disorder</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>IBD</td>
<td>36%</td>
</tr>
<tr>
<td>Ulcerative Colitis</td>
<td>20%</td>
</tr>
<tr>
<td>Crohn Disease</td>
<td>16%</td>
</tr>
<tr>
<td>Arthritis</td>
<td>37%</td>
</tr>
<tr>
<td>Seronegative, with IBD</td>
<td>15%</td>
</tr>
<tr>
<td>Seronegative, no IBD</td>
<td>10%</td>
</tr>
<tr>
<td>Rheumatoid Arthritis</td>
<td>5%</td>
</tr>
<tr>
<td>Ankylosing Spondylosis</td>
<td>3%</td>
</tr>
<tr>
<td>Osteoarthritis</td>
<td>3%</td>
</tr>
<tr>
<td>Hematologic Disorder</td>
<td>12%</td>
</tr>
<tr>
<td>Monoclonal Gammopathy and Myeloma</td>
<td>10%</td>
</tr>
<tr>
<td>Polycythemia Rubra Vera</td>
<td>1%</td>
</tr>
<tr>
<td>Malignancy</td>
<td>1%</td>
</tr>
<tr>
<td>Thyroid Disease</td>
<td>6%</td>
</tr>
<tr>
<td>Malignancy – Other</td>
<td>5%</td>
</tr>
<tr>
<td>Other Diseases*</td>
<td>4%</td>
</tr>
</tbody>
</table>
prednisone daily and topical mupirocin ointment twice a day.

Given the strong correlation between PG and IBD, the presence of microcytic anemia, and the patient’s age, work-up for colorectal disease and malignancy was performed. Blood work was unremarkable, with the exception of the previously mentioned microcytic anemia. Fecal occult blood test was negative. Colonoscopy and esophagastroduodenoscopy (EGD) demonstrated melanosis coli but were otherwise unremarkable. Therefore, a colorectal source of systemic inflammation was unlikely.

The positive family history and physical exam findings of swollen joints and decreased range of motion consistent with RA made this diagnosis highly suspicious. Laboratory work-up returned an elevated ESR, CRP, and RF at 133 mm/hr, 7.3 mg/L, and 2770 IU/mL respectively. ANA and ANCA were both negative. Additionally, imaging of the right wrist, knees, and left foot demonstrated effusions and erosions of the heads of the metacarpals and metatarsals consistent with RA.

The patient was continued on systemic prednisone 60 mg daily along with silver sulfadiazine topical dressings, and began showing improvement and slow resolution of the PG lesion with decreased exudates and evidence of pink granulation tissue at the base. No other systemic disorders or malignancies were discovered, so PG was suspected to be secondary to the patient’s newly diagnosed RA. Patient was discharged with outpatient follow-up with rheumatology for treatment of RA and a prednisone taper, as well as follow-up with her primary physician for continued work-up of microcytic anemia.

**DISCUSSION**

Pyoderma gangrenosum (PG) is a rare, non-infectious, ulcerative skin disorder. It is typically characterized by a single inflammatory papule or pustule that expands into an ulcerative lesion with characteristic inflamed borders and an erythematous, necrotic base. The etiology and pathogenesis of PG is poorly understood. The cause is thought to be multifactorial, arising from a combination of genetic predisposition,

<table>
<thead>
<tr>
<th>Associated Disorder</th>
<th>History of Breast Surgery (# of patients)</th>
<th>No History of Breast Surgery (# of patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>17, 33, 35</td>
<td>31, 36, 37</td>
</tr>
<tr>
<td>IBD</td>
<td>0</td>
<td>31, 38, 39</td>
</tr>
<tr>
<td>RA</td>
<td>0</td>
<td>38, 39</td>
</tr>
<tr>
<td>Hematologic Disorder</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Breast Cancer/Tumor</td>
<td>8</td>
<td>0</td>
</tr>
</tbody>
</table>

Table 2. Common factors associated with PG of the breast.

n = 37, IBD: inflammatory bowel disease, RA: rheumatoid arthritis
neutrophil dysfunction, and immune system dysfunction.1-3 PG is considered a neutrophilic dermatosis, and several studies have demonstrated prominent neutrophil infiltrates in biopsy samples as well as evidence of abnormal neutrophil chemotaxis and trafficking.2 Similarly, elevations in IL-8 and IL-23 have been found in patients with PG, suggesting that aberrant immune system function leading to inflammation may contribute to the pathogenesis.12,13

It was once thought that PG was a pathognomonic cutaneous manifestation of IBD. IBD remains the most commonly associated disorder, with prevalence of PG ranging between 2-12% in IBD patients.14 However, it has since been found to be associated with several other systemic inflammatory disorders, hematologic conditions, and malignancy (Table 1).1,3 Like IBD, RA and other forms of arthritis have also been found in a number of patients presenting with PG.6,14 Similarly, hematologic disorders such as leukemia, lymphoma, and gammopathy along with other malignancies have been reported in the literature as well.1,14 PG is a diagnosis of exclusion. Therefore, a patient presenting with a chronic ulcerative lesion requires a considerable amount of work-up before a potential cause can be identified (Figure 2).15

PG is a rare cause of breast ulceration, with only 37 cases reported in the literature to date (Table 2). Of these 37, nearly all cases developed after breast surgery. This high incidence in post-sur
gical patients emphases the role of patery in the development of PG. Patery describes the phenomenon in which new lesions commonly develop in areas following trauma. Similar to the Koebner phenomenon that occurs in autoimmune diseases, patery in PG is thought to be suggestive of an aberrant and uncontrolled immune response.\textsuperscript{1,14} Interestingly, eight cases, including the patient presented here, did not have the typical history of surgery to the breast. Etiology was unknown in three of these cases, and the remaining was associated with IBD and RA in 2 and 3 patients, respectively. In a population-based study from the UK examining patients with PG, IBD was found to be by far the most commonly associated disease at 33\% of individuals while RA was only associated with PG in 11.8\% of cases.\textsuperscript{5} However, of the few patients with reported PG of the breast in the literature, RA appears to occur more frequently compared to previously reported statistics of PG that did not discriminate between body regions. This increased prevalence suggests that there may be a connection between RA and PG localized to the breast. The relationship between RA and PG is likely related to immune system dysregulation. However, it is unclear why localization to the breast is associated with a higher incidence of RA. More research is necessary before the true relationship and pathogenesis can be established.

With the increase in breast reconstructive surgery in recent decades, the prevalence of PG specifically localized to the breast appears to be increasing as well. Therefore, when working up a patient with an ulcerative lesion of the breast, it is important to consider PG as a potential diagnosis because of its implications on patient quality of life. PG can be very debilitating for a patient, as it can be a significant source of pain and functional or cosmetic deformity.\textsuperscript{1} A case study by Binus et al. even demonstrated that patients suffering from PG developed increased rates of depression.\textsuperscript{16} The work-up for PG can be extensive (Figure 1), but early identification of this painful, ulcerative disease can lead to improved treatment and decreased morbidity for affected patients.\textsuperscript{15} Additionally, in cases of PG in which no surgical or traumatic history can be identified, it is important to consider an underlying diagnosis of RA.

There are many treatment options available for PG. However, no “gold standard” treatment option exists to date. For mild disease, topical corticosteroids or calcineurin inhibitors like tacrolimus along with regular wound care are fairly effective.\textsuperscript{1} In patients with more extensive disease, systemic treatments are typically necessary and include systemic corticosteroids, systemic cyclosporine, and systemic glucocorticoid-sparing agents such as infliximab or azathioprine.\textsuperscript{1} Dapsone, although rarely used for this indication, has also been shown to be effective for treatment of PG. Although treatment options for PG have been effective, the lesions often take a significant amount of time to regress, and recurrences are common. Therefore, a careful review of systems and a physical exam is essential for the early recognition of PG and associated underlying disorders. Early recognition and treatment of these painful ulcers can potentially improve the course of the disease and minimize scarring in the future.

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**LEARNING POINTS**

1. Pyoderma gangrenosum (PG) is a rare, non-infectious, ulcerative skin disorder commonly associated with systemic inflammatory diseases.

2. PG of the breast is a rare manifestation usually associated with breast reduction or augmentation surgery. Of the few cases of
PG not preceded by surgery, a significant proportion is associated with underlying rheumatoid arthritis.

3. It is important to recognize PG and associated underlying conditions early, as early treatment can shorten the course of the disease and reduce morbidity for affected patients.

REFERENCES


