

Case Report:

Pyoderma gangrenosum breast with leukaemoid reaction: a rare clinical entity

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ABSTRACT

Breast ulceration is an alarming sign for clinicians and it places a significant physical and psychological burden on the patient. We report the rare presentation of Pyoderma gangrenosum (PG) of the breast with secondary leukaemoid reaction. A 26-year-old lady was referred to us from medicine department for evaluation of recurrent ulcers involving both breasts for the last three months. Physical examination revealed symmetrical bilateral ulcers on both breasts; nipples were spared. The total leucocyte count was high (40,800/mm³). Patient was thoroughly investigated to rule out any associated systemic disorder. Based on the clinical presentation and haematological picture a diagnosis of PG with leukaemoid reaction was made. Patient was treated with systemic steroids, clofazimine and topical immunomodulators. After 6 weeks of treatment, the ulcers resolved significantly and her leucocyte count became normal. The patient is on regular follow-up and is doing well.

Key words: *Pyoderma gangrenosum, Breast, Leukaemoid reaction*

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INTRODUCTION

Pyoderma gangrenosum (PG) is an uncommon, ulcerative cutaneous condition of uncertain aetiology.¹ It is associated with systemic diseases in at least 50% of patients who are affected.² The diagnosis is made by excluding other causes of similar-appearing cutaneous ulcerations, including infection, malignancy, vasculitis, collagen vascular diseases, diabetes and trauma. In a process termed pathergy, new ulcerations may occur after trauma or injury to the skin in 30% of patients who already have pyoderma gangrenosum.²

The classic ulcerative form of PG usually observed on the legs, and a superficial variant (atypical PG) tends to occur on the hands. Patients with PG may have involvement of other organ systems that manifests as sterile

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neutrophilic infiltrates. Culture-negative pulmonary infiltrates are the most common extracutaneous manifestation.² Other organs systems that may be involved include the heart, the central nervous system, the gastrointestinal (GI) tract, the eyes, the liver, the spleen, the bones, the lymph nodes and the breast. Although breast cancer would be the most likely differential clinical diagnosis in any patient with breast ulceration, other rare causes should be considered. We report the case of a young lady who presented with bilateral breast ulcerations due to PG.

CASE REPORT

A 26-year-old lady presented with painful ulcers on both breasts of 3 months duration. The first manifestation of ulcers first became apparent following consumption of oral

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medication prescribed by a local practitioner for fever. The ulcer started as a small boil with yellow discharge and then increased in size at a rapid pace. Right breast was affected first followed by left. The ulcer healed after a fortnight to some extent. Subsequently, the ulcers recurred on both breasts for which she was treated with topical as well as systemic medications by a local practitioner. The present episode was the third recurrence. She had no history of recent gastrointestinal upset, arthritis or other systemic symptoms. The patient had not previously undergone any surgical intervention nor a biopsy from the ulcer site. However, she had received 4 units blood transfusion for severe anaemia before reporting to us.

Clinical examination revealed two ulcers, located in the upper medial quadrant of both breasts, measuring approximately 7×10 cm (right breast) and 3×5 cm (left breast) in size. The necrotic ulcers had violaceous undermined borders which were rapidly advancing. The ulcers were very tender. Nipples were not involved (Figure 1). Oral examination showed erosion in both retromolar pillars. Abdominal examination was unremarkable. Laboratory evaluation revealed haemoglobin 9.7 g/dL with a normal mean corpuscular volume (90.4 fL); elevated total leucocyte count ($40,800 / \text{mm}^3$); the platelet count was 2.25 lakh/ mm^3 . In the peripheral blood smear erythrocytes were normocytic and normochromic, neutrophils were markedly increased and platelets were adequate in number. No abnormal cells or haemoparasites were seen. The erythrocyte sedimentation rate (ESR) was elevated (26 mm at the end of the first hour). Screening for auto antibodies was negative. The culture and sensitivity testing of the ulcer swab showed the growth of *Enterococcus faecalis*. Urine culture showed the growth of *Klebsiella oxytoca*. Serum biochemistry was normal.

Ultrasonography and mammography of both breasts were normal.

Punch biopsy taken early in the disease and from the advancing, erythematous border showed an infiltrate of chronic inflammatory cells confined to the dermis (Figure 2). Features suggestive of vasculitis were evident at the edge of the ulcer, with a perivascular lymphocytic infiltrate and fibrinoid necrosis of the dermal vessel wall. Occasionally, extravasation of red blood cells and areas of thrombosis was also seen. Ulceration of the epidermis secondary to dermal inflammation was present (Figure 2).

The patient was treated with oral prednisolone 50 mg daily and clofazimine 400 mg daily along with topical corticosteroids (0.1% betamethasone cream) and topical tacrolimus 0.03% for the first 4 weeks; systemic steroids were tapered off and stopped. Symptomatic treatment was administered for fever and anaemia. With this treatment, the patient's condition significantly improved (Figures 3 and 4). After 6 weeks of treatment, the ESR was 18mm at the end of the first hour and the TLC became normal ($9000/\text{mm}^3$). Peripheral blood smear showed decrease in neutrophil counts while other findings remained as before, after 6 weeks of treatment. She has been counselled to come for regular follow-up visits and is still continuing oral clofazimine along with topical immunomodulators.



Figure 1: Clinical photograph showing necrotic ulcers with violaceous undermined borders which were rapidly advancing in the upper medial quadrant both breasts

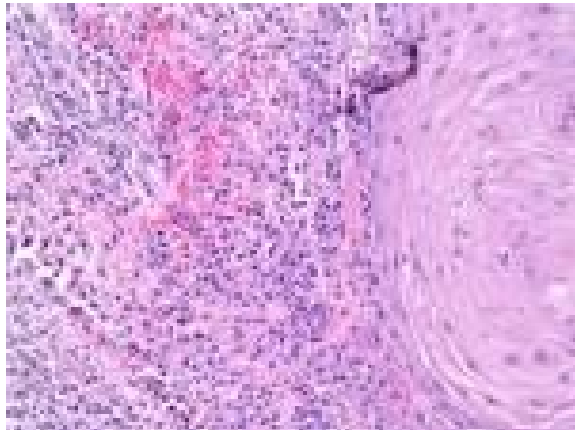


Figure 2: Photomicrograph showing lymphocytic infiltrate within the dermis suggestive of vasculitis at the edge of the ulcer, with a perivascular lymphocytic infiltrate and fibrinoid necrosis of the dermal vessel wall (Haematoxylin and eosin, × 1000)

DISCUSSION

The incidence of PG is uncertain, but it is estimated to be 3-10 patients per million population per year.¹ PF can occur at any age but is seen most commonly between 20 and 50 years of age;¹

The aetiology of PG is unknown and the pathogenesis is poorly understood. Although the disease is idiopathic in 25%-50% of patients, an underlying immunologic abnormality may exist as suggested by its frequent association with systemic diseases like infla-

mmatory bowel disease (IBD), pulmonary, cardiac, autoimmune disorders; and neoplasia.¹⁻³

Occurrence of the phenomenon of pathergy, (i.e., the development of new lesions or aggravation of existing ones following trivial trauma) frequently observed in PG would suggest altered, exaggerated, and uncontrolled inflammatory responses to non-specific stimuli.¹

The term leukaemoid reaction describes an elevated white blood cell count, or leucocytosis, that is a physiological response to stress or infection. Leukaemoid reactions are generally benign and constitute a response to a significant disease state. Haemorrhage, drugs, infections, asplenia and diabetic ketoacidosis are the common causes of leukemoid reaction.

Immune status dysregulation particularly neutrophil dysfunction (i.e., defects in chemotaxis or hyperreactivity) in individuals with PG has been suggested. Evidence of abnormal neutrophil trafficking and metabolic oscillations have also been described in PG. These two factors would have resulted in the development of leukaemoid reaction.



Figure 3: Clinical photograph of right breast obtained after 6 weeks of treatment with oral prednisolone, topical tacrolimus and clofazimine



Figure 4: Clinical photograph obtained after 6 weeks showing healed lesions in the left breast

Diseases commonly associated with PG include inflammatory bowel disease, ulcerative colitis, Crohn's disease. Haematologic disorders commonly associated with PG include leukaemia or preleukaemic states (predominantly myelocytic) and monoclonal gammopathies, primarily of immunoglobulin A variety.⁴⁻⁶

Reported therapies for PG have often focussed on treatment of the underlying condition. Therefore, most information available relates to systemic therapies, probably because many PG lesions mimic the activity of the underlying disease.⁷

First-line therapy includes immuno-suppressants, such as corticosteroids (prednisolone/methylprednisolone) and cyclosporin.⁸ Other therapeutic options include immuno-modulators, biologicals and antileprosy drugs. When an underlying disease is absent, as in our patient PG can respond variably to standard therapy. Further, PG can even recur after definitive surgery for the underlying disease, (e.g., colectomy).⁹

A case of PG of the sinus mammarium has been documented in a patient with ulcerative colitis.⁹ In this case the cutaneous ulcer was resistant to conventional systemic medical therapy although the treatment resulted in improvement in the systemic disease. Basing on the histopathologic finding of vasculitis at the edge of the lesions antithrombotic topical injections were used as an adjunct to standard treatment.⁹ This case report suggested that perilesional injections of calcic heparin were successful in inducing remission.⁹

A retrospective analysis (n=20) showed that topical steroids have little role in healing.³ Conversely, other authors have demonstrated improvement of the lesions with intralesional steroids.¹⁴

Surgery has to be used with caution since it can trigger PG. Any surgical procedure has to

be done as an adjunct to immunosuppression only in patients with stable disease or partial remission. Autologous split-skin grafts have been used with variable outcome.¹⁰ A significant disadvantage of split-skin grafts is the necessity to create a new wound at the donor site. Therefore, surgical intervention is not recommended in standard practice.

In comparison with the previous cases of PG with pathergy complicating coronary artery bypass grafting (CABG),¹¹⁻¹² our patient's case seemed to be unusually severe, as evidenced by the leukaemoid reaction. Two cases of postoperative PG that presented with leukaemoid reaction, have been reported.¹³

Till date 43 cases of PG of the breast have been reported.¹ In 30 of the cases PG lesions were secondary to trauma to the breast tissue, such as surgical intervention, reconstruction of the breast, biopsy, and intramuscular injection.¹ It is likely that, the pathergy phenomenon may be the reason for PG lesions occurring after breast trauma.

Our patient had a rare presentation of PG of the breast with leukaemoid reaction, in which presently, there are no signs of underlying malignancy. This case highlights the importance of considering PG as one of the differential diagnoses of breast ulcers. Careful specialist clinical assessment could establish an early diagnosis and formulate an effective management plan. Our knowledge about pathogenesis and individual risk factors for the development of PG is still rather limited. This hampers the efforts for prevention. However, the appearance of new ulcers can be prevented in patients known to have the disorder by avoiding excessive trauma to the skin.

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