

Pyoderma gangrenosum in a patient with antiphospholipid antibody negative systemic lupus erythematosus: A case report

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In any description of leg ulcers in systemic lupus erythematosus (SLE), pyoderma gangrenosum (PG) earns a mention at least for its being quite rare in such patients. The causative role of aPL (antiphospholipid antibody) in dermatological manifestations of SLE is undermined by the occurrence of PG in aPL negative SLE patients. To the best of our knowledge, there are only two reports of PG in aPL negative SLE patients; in one, PG preceded the diagnosis of SLE by several years while the other was associated with the reactivation of the disease in an already diagnosed SLE patient. In view of the rarity of this association, we hereby present another similar case to substantiate the documentation of the association of the entities.

Keywords: pyoderma gangrenosum, systemic lupus erythematosus, anti-phospholipid antibody

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INTRODUCTION

PG is a sterile inflammatory neutrophilic dermatosis. Clinically, it sets in as a sterile pustule which breaks down into painful ulcers of variable dimensions with undermined edges and violaceous borders. Diagnosis of PG is secured by its typical clinical presentation in a patient who is predisposed to it. Diagnosis becomes easier by excluding diseases which share a similar clinical picture. In the typical clinical setting, a nonspecific histopathological feature of the ulcer favors the diagnosis of PG. Diagnostic laboratory parameters are lacking in PG. Etiology of the condition has not been established as yet. While pyoderma gangrenosum has been commonly described in an aPL antibody positive SLE, its association with aPL negative SLE is very rare. To the best of our knowledge, there are only two reports of pyoderma gangrenosum (PG) in antiphospholipid antibody (aPL) negative SLE patients; in one, PG preceded the diagnosis of SLE by several years while the other was associated with the reactivation of the disease in an already diagnosed SLE patient^{1,2}.

CASE REPORT

A thirty-year-old female patient, a known case of SLE, presented to us with a three-month history of a painful ulcer over her right leg. The ulcer resulted from disruption of a bullous lesion at the site. There was no history of antecedent trauma at the site, abdominal pain, bloody diarrhea, jaundice, pain or swelling in joints, bleeding tendency, cough, chest pain, polyuria, polydipsia, polyphagia, or significant drug intake. General physical examination revealed edema of the right leg and foot. Cutaneous examination revealed a discoid rash over malar areas, lupus hair, livido reticularis of trunk and a well defined ulcer on the right leg, 9×5cm in size with purplish undermined borders and a necrotic base studded with small abscesses (Figure 1). Cutaneous tenderness was present. All peripheral pulses were normally palpable and sensations over both feet and legs were normal. Mucosae, palms and soles were free from any lesions. Investigations revealed a hemoglobin level of 8 mg/dl with a positive direct coomb's test. Antinuclear antibody (ANA) and anti double stranded DNA (antids-DNA) were



Figure 1. Lesion of pyoderma gangrenosum with undermined edges and violaceous border.

positive, while as anti-cardiolipin antibody, lupus anticoagulant and antineutrophilic cytoplasmic antibody (c ANCA) were negative with a normal radiograph of the right leg and foot. Venous and arterial duplex sonography of the right leg showed no evidence of reduced perfusion or arteriosclerosis. A clinical diagnosis of pyoderma gangrenosum was made on the following clinical features: rapid onset of the lesion, resistance to topical treatment and underlying SLE along with the clinical picture of the lesion. The diagnosis was supported by skin biopsy, which revealed intense edema and neutrophilic infiltrates with patches of necrosis of both dermis and epidermis. The ongoing dose of steroids was increased and along with the antiseptic washes for secondary infection and limb elevation, healing of the lesion with atrophic scarring occurred over a span of few months.

DISCUSSION

Pyoderma gangrenosum begins as an inflamed erythematous papule, pustule or a nodule. Initially, the lesion resembles a furuncle or an arthropod bite. On ulceration, the lesion is characterized by a swollen necrotic base and a raised dusky violaceous undermined border. Ulcers of PG do not have any unique or diagnostic histopathological signatures; however, features of epidermal and dermal necrosis with central intense neutrophilic infiltrate and a peripheral mixed inflammatory infiltrate in a clinically classical ulcer support the diagnosis. Systemic symptoms such as fever, malaise, and arthralgia are common. The ulcers coalesce to form larger ulcers which often heal with cribriform or sieve-like scarring².

Epidemiological features of PG include a worldwide distribution affecting mostly the age group of 20-50 with women being more often affected than men³. Infants and adolescents are uncommonly affected and the elderly are the least affected⁴. The general incidence has been estimated to be between 3 and 10 per million per year⁵. A thorough look at the available literature leads us to the conclusion that no body area is spared; however, the pretibial area of the legs is the most common involved site. Extracutaneous manifestations include involvement of the upper airway mucosa, eye, genital mucosa, sterile pulmonary neutrophilic infiltrates or splenic infiltrates, and neutrophilic myositis. PG has been reported to occur after breast surgeries as well⁶. A well-known feature is pathergy, wherein new lesions develop at sites of trauma. This parallels to the Koebner phenomenon in psoriasis. Four clinical variants of pyoderma gangrenosum. Classic or ulcerative type, pustular type, bullous type and the vegetative type are known. About 50% of pyoderma gangrenosum patients have an associated underlying disease (Table 1)^{7,8}.

Ulcerative colitis has been found to be associated with pyoderma gangrenosum in up to 15% of the cases⁹. The sterile nature of the pustules has derailed the infectious theory for causation of PG. Suggestions of aberrant immunological response, as an etiological mechanism, to yet unidentified factors is to be proved¹⁰. However, the features of sterile pustules, the phenomenon of pathergy, association with many autoimmune diseases,

Table 1. Diseases associated with pyoderma gangrenosum

Ulcerative colitis	Acne conglobata and fulminans
Chron's regional enteritis	Familial recurrent arthritis (PAPA syndrome)
Hepatitis C	Vasculitis
Seronegative rheumatic arthritis	Wegener's granulomatosis
Spondylitis	Takayasu's disease
Lymphoproliferative disorders	SLE
a. Monoclonal gammopathy	Antiphospholipid antibody disease
b. Leukemia	Necrotising vasculitis
c. Lymphoma	Behcets disease
d. Myelodysplastic syndrome	Paroxysmal hemoglobiuria
Drugs	Diabetes mellitus
e. Propylthiouracil	
f. Pegfilgrastim: A granulocyte stimulating factor	
g. Gefinib: An epidermal growth factor receptor inhibitor	

response to steroids and immunosuppressants correlate better with the immunological theory for the etiology of the disease. In patients with a rapidly progressive or severe disease, initial use of supra-pharmacological doses of steroids (prednisolone) are administered to carry away the flame of inflammation. Simultaneous or subsequent addition of an immunosuppressant (cyclosporine A) to the treatment regimen is performed for steroid sparing. Use of cytotoxic drugs (Cyclophosphamide) should be considered in resistant cases, particularly in those with an associated Chron's disease. Sulphones, most commonly dapsone, are useful in cases with a mild disease. Limited surgery such as grafting has a role in stable disease/patches; however, in an acute and progressing disease, surgical debridement of the ulcer/s is contraindicated¹¹ to avoid the phenomenon of pathergy from plaguing the diseased patches. Relapses are known to occur in 66-70% of the cases¹².

Many aspects of the disease including risk factors, pathogenesis, prognostic factors and treatment have not yet been adequately studied. However, the association of PG with aPL negative SLE seems to be very rare and it would better keep it in mind as a possible etiology of pyoderma gangrenosum.

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