

Review Article

Pyoderma Gangrenosum : An enigma without a cure?

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Abstract:

Pyoderma Gangrenosum (PG) is a rare, chronic, recurrent distinctive cutaneous ulceration which is usually idiopathic, but may be associated with systemic diseases in at least 50% of patients who are affected. The diagnosis is made by excluding other causes of similar-appearing cutaneous ulcerations, including infection, malignancy, vasculitis, collagen vascular diseases, diabetes and trauma. The etiopathogenesis of PG is still not well understood. Clinically, it is classified into ulcerative, pustular, bullous and vegetative types. A few atypical and rare variants have also been described. The diagnosis mainly depends on the recognition of evolving clinical features as investigations only assist in the diagnosis. Therapy for pyoderma gangrenosum involves the use of anti-inflammatory agents, including antibiotics, corticosteroids, immunosuppressive and biologic agents.

Key word : *Pyoderma Gangrenosum, Cutaneous ulcer.*

Introduction:

Pyoderma gangrenosum (PG) is a rare inflammatory disease of unknown etiology that can cause pain, disfigurement, destruction of the tissue and even death. It is a noninfectious neutrophilic dermatosis¹.

PG was first described by Brocq in 1916 as “phagedenisme geometrique” and later named by Brunsting et al². The latter author considered PG to be the dissemination of a distant focus of infection (i.e. the bowel in ulcerative colitis or lungs in empyema)³. Presently, PG is considered a reactive inflammatory dermatosis and part of the spectrum of neutrophilic dermatosis. But the precise etiopathogenesis is not well understood. Different immunological factors and neutrophil dysfunction are considered to be involved in etiopathogenesis of PG. However, the immunological abnormalities associated with PG are not always consistently observed in all patients and it is unclear whether or not they are an epiphenomena.

Epidemiology:

The incidence of PG is uncertain, estimated to be 3-10 patients per million population per year.

In the United States, it occurs in about 1 in 100,000 persons each year^{4,5}. Although pyoderma gangrenosum affects both sexes, a slight female predominance may exist. All ages may be affected by the disease, but it predominantly occurs in the fourth and fifth decades of life. Children account for only 3-4% of the total number of cases.

Clinical Features:

The most common type of pyoderma gangrenosum is the classic (ulcerative) type (Fig 1); however, there are several

other less common variants like pustular, bullous and vegetative types as well. Classic pyoderma gangrenosum, as shown in Fig. 1 is characterized by necrotic, mucopurulent, painful deep ulcer with an edematous, violaceous, undermined border that overhangs the ulcer bed & it can expand serpigiously.

It usually appears on the lower limb and trunk but may occur at any site.



Fig. 1

Pyoderma gangrenosum may occur around stoma sites; this type, shown in the image below, is known as peristomal pyoderma gangrenosum (Fig 2). It is often mistaken for a wound infection or irritation from the appliance, but it is a pathergy phenomenon due to leakage of faeces or by the adhesive stomal appliance⁶.



Fig. 2

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Pyoderma gangrenosum may occur on the genitalia. This form, termed vulvar or penile pyoderma gangrenosum, must be differentiated from sexually transmitted diseases^{7,8}. An intraoral form of the disease, known as pyostomatitis vegetans, has been reported and occurs primarily in patients with inflammatory bowel disease.

Diagnostic Considerations:

Pyoderma gangrenosum is often misdiagnosed, and multiple attempts at grafting often occur prior to diagnosis. In fact, it is a diagnosis of exclusion because no specific criteria have been determined to confirm the diagnosis. All potential causes of similar lesions like vaso-occlusive diseases, systemic vasculitis, infections (deep mycosis, tuberculosis, syphilis, ecthyma gangrenosum), lymphoma, leukaemia, tissue injury, drug reaction must be excluded prior to making the diagnosis^{9,10}.

Routine blood works like complete blood count, comprehensive chemistry profile including liver function test, hepatitis profile and a urinalysis should be performed. Serum and/or urine protein electrophoresis, peripheral smear, and bone marrow aspiration or biopsy should be performed, if indicated, to evaluate hematologic malignancies. Other serum studies include a Venereal Disease Research Laboratory (VDRL) test, an antineutrophil cytoplasmic antibody test, activated partial thromboplastin time test, and an antiphospholipid antibody test, all of which can help to rule out granulomatosis with polyangiitis, vasculitis, and antiphospholipid antibody syndrome. Serum immunofixation electrophoresis is helpful to determine if a monoclonal gammopathy is present.

Tissue cultures of the ulcer for bacteria, fungi, atypical mycobacteria and viruses are needed.

Chest radiography may be performed. Angiography or doppler studies may be carried out in patients suspected of having arterial or venous insufficiency. Colonoscopy or other tests to exclude associated inflammatory bowel disease or ulcerative colitis may be useful in patients with symptoms. The histologic findings in pyoderma gangrenosum are not specific. However, a biopsy is suggested in all cases because it is useful in exclusion of other diseases, such as infections and malignancy. Microscopic features include massive neutrophilic infiltration, hemorrhage and necrosis of the overlying epidermis.

Management:

No specific therapy is uniformly effective for patients with pyoderma gangrenosum. In patients with an associated underlying disease, effective therapy for the associated condition may be linked to a control of the cutaneous process.

Topical therapies include gentle local wound care and dressings, super potent topical corticosteroids, cromolyn sodium 2% solution, nitrogen mustard, 5-aminosalicylic acid and immune modifier tacrolimus¹¹.

Systemic therapies include corticosteroids, cyclosporine, mycophenolate mofetil, azathioprine, dapsone, tacrolimus, cyclophosphamide, chlorambucil, thalidomide, tumor

necrosis factor-alpha (TNF-alpha) inhibitors (eg, thalidomide, etanercept, infliximab, adalimumab, clofazimine) and nicotine¹².

Intravenous (IV) therapies include pulsed methylprednisolone, pulsed cyclophosphamide, infliximab, IV immunoglobulin, and ustekinumab.

Other therapies include hyperbaric oxygen.

Care of the patient with pyoderma gangrenosum is often referred from the general dermatologist to tertiary centers where such patients are seen more frequently. Patients with pyoderma gangrenosum should receive follow-up care on a regular basis to monitor drug therapy and to measure the size of the lesions.

Discussion:

Pyoderma gangrenosum is a relatively uncommon skin condition of unknown etiology but suspected to be an autoimmune disorder. Around 50% of patients with PG have an antecedent or coincident (or subsequently develop) associated disease. The most common associations are inflammatory bowel disease. About 25% of pyoderma are related to inflammatory bowel disease, of which 1-2% are affected, and may predate the bowel symptoms for weeks to several years. In one study of 116 patients with ulcerative colitis, 2.4% had associated pyoderma gangrenosum¹³. Sometimes the lesions may be associated with flare up bowel symptoms but may also develop or worsen when bowel activity is quiescent. Other conditions like rheumatoid arthritis and many other diseases like chronic autoimmune hepatitis, myeloid blood dyscrasias, Takayasu's arteritis in Japan, Wegener's granulomatosis, collagenous colitis, endocrine disorders like hypergonadotropic hypogonadism are also associated with pyoderma gangrenosum^{14,15}.

Conclusion:

Thus, although PG is clinically characteristic, it remains an enigma with regard to its etiopathogenesis. There are various clinical and histological variants of the disease. The various therapeutic agents including biologics have been used in the management of the disease. It is suggested that skin ulcers with unusual features which fail to heal must be further investigated to exclude pyoderma gangrenosum¹⁰. Then confirmed cases should be further investigated for underlying systemic diseases.

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