A rare case of pyoderma gangrenosum associated with septal perforation, bilateral pinnaerosion, auto amputation of digits and multiple keloids.

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ABSTRACT

Pyoderma gangrenosum (PG) was first explained by Dr. Brunsting, Goeckerman, and O’Leary, in 1930, as enlarging necrotic ulcers with erythematous to bluish undermined borders surrounded by spreading erythema. Six major variants of this skin condition, include (1) ulcerative or classic, (2) pustular, (3) bullous or atypical, (4) vegetative, (5) peristomal, and (6) drug-induced PG. PG of the head and neck is very rare, with an estimated incidence of 5% among all PG cases. Very few cases of nasal septal involvement have been reported in the literature, one of which was associated with IBD. The association with bilateral pinna erosion, multiple keloids, multiple digital amputation, sub-mucous cleft palate, and loss of digits. A review of literature was also undertaken. Results: Patient underwent multiple sessions of treatment for pyoderma gangrenosum, septal perforation and pinna erosion was managed conservatively and is on follow-up with various specialists. Conclusion: Based on observations and review of literature, regular follow up, personal care, proper and regular multimodality management are required for these kind of cases.

Key words: Pyoderma gangrenosum, septal perforation, pinna erosion, digital amputation management are required for these kind of cases.

INTRODUCTION

Pyoderma gangrenosum (PG) is a rare inflammatory disease of unknown etiology characterized by neutrophilic infiltration of the dermis and destruction of the tissue. PG was described by Brocq in 1916 as "phagedenisme geometrique" and later named by Brunsting et al. 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). Presently PG is considered a reactive inflammatory dermatosis and part of the spectrum of neutrophilic dermatosis. It is estimated to be 3-10 patients per million population per year. It may be associated with various other conditions and may not be presenting as an isolated condition. The precise etio-pathogenesis of PG is not well understood. However immunological factors and neutrophil dysfunction can be considered to be involved in etiopathogenesis of PG.

The following immunological factors are considered for its etiopathogenesis.
1. Frequent association of PG with autoimmune diseases.
2. Pathergy phenomenon indicating an abnormal response to an inciting stimuli such as trauma.
3. Deposition of immunoglobulins in the dermal blood vessels.

Monoclonal or polyclonal hyper globulinemia may also be associated with PG.

Defective cell-mediated immune response in PG

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. PG is considered part of the spectrum of the neutrophilic disease. Impaired phagocytosis by neutrophils has been suggested in the pathogenesis of PG.

Neutrophil analysis in PG showed evidence of abnormal neutrophil trafficking and aberrant integrin oscillations.

Interleukin-8 (IL-8), a potent leucocyte chemotactic agent, is shown to be overexpressed in PG ulcers. In the recently described “PAPA syndrome” (pyogenic sterile arthritis, PG and acne) there is an overexpression of the IL-16 gene and the IL-16 protein is chemotactic to neutrophils. It can be concluded that the factors triggering/maintaining the various immunological/neutrophil abnormalities are multiple and include genetic predisposition, para inflammatory, paraneoplastic or para immune phenomena. The predisposed patient experiences an inciting event such as minor trauma, and instead of normal response that recognizes and removes the damaged tissue, the patient’s abnormal response results in lesions of PG. PG can also arise as a consequence of drug therapy like propylthiouracil, pegfilgastrim (granulocyte stimulating factor), gefinib (epidermal growth factor receptor inhibitor), and isotretinoin.

The description of PG by Brunsting et al., in their original article, is still very relevant for the classic ulcerative form of the disease. The borders of ulcers are well defined because of their striking blue color which clearly outlined the lesions as it extended peripherally in rough, serpiginous configuration. The blue zone consisted of an edematous boggy strip from 5-8 mms wide in which there had been exclusive undermining and necrosis of the subcutaneous tissue, the epidermis remaining as a thin, gray translucent film extending over the crater of the lesion in a ragged, irregular fashion. On the advance of the underlying process, often at the rate of 1-2 cms in 24 hrs, a zone of erythema extends as an areola into the area of normal skin. The lesion occurred as crops of small, discrete pustules surrounded by an inflammatory areola. Within a few days, the centre of the pustule softened and the covering became blue and broken down. The lesion either underwent involution or extended peripherally to coalesce with others.

The following table gives a brief description of various forms of PG.

<table>
<thead>
<tr>
<th>Form of PG</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>Ulcerative</td>
<td>Extends peripherally, with well-defined borders</td>
</tr>
<tr>
<td>Pustular</td>
<td>Pustules surrounding the lesion</td>
</tr>
<tr>
<td>Bullous</td>
<td>Large, blister-like lesions</td>
</tr>
<tr>
<td>Vegetative</td>
<td>Lesion extends as crops of small, discrete pustules surrounded by an inflammatory areola</td>
</tr>
</tbody>
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Rare variants:

**Peristomal PG** is a rare subset seen around enterostomy/colostomy in patients with IBD. It is considered a pathergy phenomenon due to irritation to the peristomal skin caused by leakage of faeces or by the adhesive stomal appliance.

**Genital involvement in PG** may be seen in association with ulcers elsewhere in the body. Vulvar, penile, and scrotal involvement has also been described as a solitary manifestation of PG. When genital lesions are present Behcet's disease has to be ruled out in addition to other causes of genital ulcers. Genital and buttock PG present more in the infantile age group than in others. PG in association with HIV infection may show involvement of perineum complicated by secondary bacterial infection.

**PG in infants and children** is rare (4% only). In children, the lesions are generalized and with involvement of genital areas. However, clinical appearance, location, and response to treatment resemble those of the classic lesions in adults. The difference between adults and children are depicted in Table 2.

Table 2: Differences between child and adult pyoderma gangrenosum.

<table>
<thead>
<tr>
<th>Feature</th>
<th>Children</th>
<th>Adults</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Morphology of initial lesion</strong></td>
<td>Pustules</td>
<td>Macules/papules</td>
</tr>
<tr>
<td>Site</td>
<td>Absent</td>
<td>Present</td>
</tr>
<tr>
<td><strong>Associated diseases</strong></td>
<td>Absent</td>
<td>Present</td>
</tr>
<tr>
<td><strong>Pathergy test</strong></td>
<td>Absent</td>
<td>Present</td>
</tr>
<tr>
<td><strong>Prognosis</strong></td>
<td>Good</td>
<td>Variable</td>
</tr>
</tbody>
</table>

**Extractcutaneous neutrophilic disease** refers to sterile neutrophilic infiltrates occurring in various internal organs. Pulmonary neutrophilic infiltrates are the most commonly reported extracutaneous sign. *Pyostomatitis vegetans* is considered as oral pustular PG characterized by a pustular, vegetative process of mucous membrane. The oral lesions usually coincide with the active exacerbations in IBD. Approximately 50% of patients with PG have an associated systemic disease. These diseases may precede, follow or occur simultaneously. Depending upon the associated conditions PG was also be classified as follows:

- Parainflammatory (parainnune) (associated with IBD, collagen vascular diseases, arthritis, etc.)
- Paraneoplastic (associated with malignancy)
- Hemotologic (leukemias, polycythemia)
- Drug induced
- Idiopathic

**CASE REPORT**

A 9 year old female came to the dermatology department with complaint of recurrent itching all over the body since 6 years. She also developed perforation of the nasal septum which was noticed by whistling sound from the nose since 4 years. There is also loss of terminal phalanges along with multiple keloid development all over the body. Black necrotic lesions started all over the body when she was one and half years of age with history of fever and later had peeling of skin in many areas followed by keloid formation. On examination multiple keloids with hyperpigmented patches, smooth surface plaques, along with few areas of thickened hard plaques all over the buttocks, back of the thigh, lateral parts of the thigh, legs and atrophied toes and fingers along with bilateral partial erosion of the pinna seen. Routine blood investigation were normal with viral markers negative, syphilis non reactive, HIV negative, mild raise in the ESR, liver and kidney function tests were normal, serum calcium normal, abdominal ultrasound was normal. These lesions were like lesions of pyoderma gangrenosum and responded well to oral prednisolone. She complained of mild nasal discharge, and nasal endoscopy revealed nasal septal perforation. Nasal endoscopic biopsy of the lesions showed an active inflammatory infiltrate, mainly of neutrophils. Systemic investigations failed to show any pulmonary or renal lesions of Wegener's granulomatosis. Cyttoplasmic immunofluorescent pattern anti-neutrophil cytoplasmic antibody was negative. In this case, intense neutrophilic infiltration was observed not only in skin lesions but also in nasal lesions histo-pathology, which may indicate that the nasal lesions had a pathogenesis in common with the skin lesions.

**DISCUSSION**

Pyoderma gangrenosum (PG) can be differentiated into classic and atypical forms. The classic form is characterized by ulcers and the atypical form by deep erosions with bullous blue-gray margins. Development of cutaneous lesions at sites of trauma, is a common feature of both forms of PG, (Fig 3). Approximately 50% of patients who have PG have underlying systemic diseases, most commonly inflammatory bowel disease, myeloproliferative disorders, and various forms of inflammatory arthritis. The diagnosis of PG is one of exclusion. The management of this disorder begins with treatment of any underlying disease and local or systemic glucocorticoids or immunomodulating therapies. The following is the management protocol followed for the management of pyoderma gangrenosum.

Fig 5: Suggested treatment algorithm for pyoderma gangrenosum.
CONCLUSION
PG is a rare disease and the incidence of this disease is uncertain. It is estimated to be 3-10 patients per million population per year. The peak incidence occurs between the ages of 20-50 years with a possible slight female preponderance, and approximately 4% of patients are children. Approximately 50% of patients with PG have an associated systemic disease. These diseases may precede, follow or occur simultaneously. Parainflammatory (paraimmune) (associated with IBD, collagen vascular diseases, arthritis, etc.), Paraneoplastic (associated with malignancy), Hematologic (leukemias, polycythemia), drug induced and idiopathic. The most common associations are IBD, arthritis, and hematologic diseases. PG associated with IBD is characterized by ulcerative or pustular PG. In patients with HIV infection, perineum is the most common site of involvement and ulcers are often secondarily infected with bacterial organisms. In our case the above conditions are ruled out and is labelled as idiopathic variety and conservative management is done.

PG of the head and neck is very rare, with an estimated incidence of 5% among all PG cases. Till date, very few cases of nasal septal involvement have been reported in the literature, one of which was associated with IBD. Its association with bilateral pinna erosion, multiple keloids, multiple digital amputation, sub-mucus cleft palate makes it probably a rare case association in the literature. This is a rare case report of PG, in the absence of inflammatory bowel disease, autoimmune disease, or hematologic malignancy. The attendants were counselled regarding the reconstructive options of the pinna, septum and a need for septo-rhinoplasty in the future and the other conditions like keloid management by surgical department, skin lesions by dermatology and digital amputation by plastic surgeon, sub mucus cleft palate by maxilla-facial surgeon were explained. Patient is in regular follow up with the concerned specialists and is under conservative management.

REFERENCES