

## **Pyoderma gangrenosum: A clinico- therapeutic profile of patients attending a tertiary care hospital in Nepal**

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### **Abstract**

Pyoderma gangrenosum (PG) is a primarily sterile inflammatory neutrophilic dermatosis characterized by recurrent cutaneous ulcerations with mucopurulent or hemorrhagic exudate. In many cases, PG is associated with inflammatory bowel disease, rheumatic disorder or neoplasia. The peak of incidence occurs between the ages of 20 to 50 years with women being more often affected than men.

To study the clinical and therapeutic profile of patients with pyoderma gangrenosum.

All patients diagnosed as pyoderma gangrenosum in the department of dermatology from July 14<sup>th</sup> 2003- July 12<sup>th</sup> 2008 were included in the study. Demographic profile, clinical features as well as relevant investigations, treatment and follow-up were noted.

A total of 8 patients with pyoderma gangrenosum were diagnosed over a 5 year period. There were 3 males and 5 female patients whose ages ranged from 32 to 80 years. Lower limbs were the commonest site to be involved in 6 patients (75%). Recurrent episodes were noted in 4 patients (50%) and among them 3 patients (75%) had multiple ulcers. Histopathological confirmation of the diagnosis was done in 7 patients (87.5%). Association with ulcerative colitis was seen in 2 patients (25%). All patients were treated with dapsons and systemic steroids which showed resolution of the lesions in all patients.

Pyoderma gangrenosum was seen more frequently in females and association with ulcerative colitis was seen in 25% of the patients.

**Key words:** Clinical features, pyoderma gangrenosum, treatment.

### **Introduction**

Pyoderma gangrenosum (PG) is primarily a sterile inflammatory neutrophilic dermatosis characterized by

recurrent cutaneous ulcerations with mucopurulent or hemorrhagic exudates and a rapid evolution. In many cases, PG is associated with inflammatory bowel disease (ulcerative Colitis and Crohn's disease), rheumatic and immunological disorders (seropositive

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arthritis, collagenoses, Behcet's disease, Wegener's Granulomatosis, Takayasu's arteritis, Sjogren's syndrome), neoplasia (myeloproliferative disorders), hepatitis and AIDS<sup>1-5</sup>. PG has also been found to be associated after surgical operations<sup>6-10</sup>. The peak incidence of disease occurs between the ages of 20 to 50 years with women being more often affected than men<sup>4</sup>.

PG is an uncommon disease with an uncertain etiology. Initially people thought that it was caused by streptococcal infection leading to cutaneous gangrene, thus its name PG is a misnomer<sup>4</sup>. There are no precise diagnostic criteria. The clinical features of this disease supported by histopathological findings plus serological tests to exclude auto-immune disorders makes this disease a diagnosis of exclusion. There are four varieties of PG- ulcerative, pustular, bullous and vegetative- and the diagnosis is solely based on clinico-histopathological features. The most common type of PG is an ulcerative (classic) variety which is very painful and has a large ulceration with a purulent base and undermined borders<sup>1,4</sup>.

The clinical course of PG can be worsened by a non-specific external stimulus such as trauma or surgery. This condition known as pathergy, if not conscious, can lead to a vicious cycle of debridement of the lesion and clinical worsening of PG.

Till date, in Nepal there has been no published study which has highlighted the clinical and therapeutic profile of this difficult-to-diagnose disease. This study aims to bring forth various clinical features of PG in a number of patients attending a tertiary care hospital in eastern Nepal and the patients' response to the treatment offered.

It is important to differentiate PG from infectious causes because of the nature of treatment that entails giving immunosuppressive therapy which would cause an aggravation of the condition if wrongly given to patients with an infectious etiology. Therefore, if one misses the diagnosis of PG, the ulceration continues relentlessly but if the diagnosis is made correctly and an appropriate therapy instituted then one can achieve a dramatic response. This study was conducted to make ourselves vigilant about the presence of this rare and difficult-to-diagnose disease in Nepal and the importance of making a right diagnosis at the right time.

## **Materials and methods**

Patients attending the B.P Koirala Institute of Health Sciences, a tertiary care hospital in eastern Nepal for a period of five years (14 July 2003- 12 July 2008) were recruited in the study. The study was conducted in the Department of Dermatology, Venereology and Leprology. All patients whose final diagnosis was PG during the study period were included in the data analysis at the end.

The data for individuals were recorded in a format in which the first section consisted of demographic profile including age, sex and duration of illness. The second section consisted of clinical features including the symptoms (pain, itching and type of early lesion), number of episodes (primary or recurrent), site of lesions, number of lesions and type of lesions (ulcerative, pustular, bullous and vegetative). The third section consisted of findings of serological tests and histopathology. The fourth section consisted of any associated systemic diseases. The final section

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The diagnosis of PG was made only after a careful deliberation by discussion among the consultant dermatologists on the basis of clinical features, histopathological support and rigorous laboratory exclusion of other similar diseases. Patients were subjected to a battery of serological tests including ANA, ds-DNA, RF and haemoglobin, total leucocyte count and liver function tests. They also underwent urinalysis and swab culture from the lesion. Biopsy was taken from the lesion in patients who agreed to undergo the minor operative procedures. Patients were also evaluated for the presence of any systemic medical or surgical conditions associated with the disease.

The patients were then prescribed a various combinations of dexamethasone/ prednisolone, mesalamine, dapsone and clofazimine based on the severity of the disease and the response to previous treatment. They were followed up for a period of 4 to 8 weeks. The patients' responses were evaluated for the treatment given. A patient was regarded to have a complete response when there was a complete healing of the skin lesion and a partial response when the lesion stopped growing and healed partially.

## **Results**

There were a total of 8 patients who were finally diagnosed to have pyoderma gangrenosum during the five years period. There were 3 males and 5 females with a male female ratio of 1: 1.7. The median age of the patients was 50.5 years (range from 32 to 80 years). The median duration of illness was 4.5 months with a huge range from 1 month to 360 months.

## **Clinical profile**

Majority of the patients (75%) had pustular lesions as an early feature. Of the remaining two, one patient started with a bullous lesion and the other with vesicular lesion. Most of the patients (62.5%) had an ulcerative variety of PG and the rest had a bullous variety. The lesions were present on legs in half of the patients and on thigh on 2 patients and on check in one and on hand in the other. Four patients presented with a recurrent episode while the remaining presented with the first attack. Among those who suffered from recurrent episodes, 3 patients had multiple lesions. Almost all patients who had the lesion presented with pain, except one who presented with itching.

## **Systemic conditions**

There were four patients who also had some systemic medical and surgical conditions associated with PG in this study. Two of them suffered from Ulcerative Colitis, one was diagnosed to have Pott's spine and the fourth patient had varicose veins.

## **Histopathological and microbiological findings**

Seven out of eight patients underwent minor operations to obtain tissue for biopsy. One patient declined for tissue biopsy. Skin biopsy from the border of the ulcerations revealed non-specific inflammation and showed mixed cellular infiltrates with neutrophilic predominance. Tissue biopsy from these lesions ruled out other causes of ulceration like malignancy, infection and vasculitis. However, direct immunofluorescence studies on these biopsy specimens were not done due

to lack of such technological facilities. Swab cultures from the wound were sterile after 48 hours of culture for aerobic bacteria.

### Treatment and therapeutic response

Most patients received a combination of prednisolone and dapsone. Two recurrent cases were given

clofazimine considering their treatment which they received earlier. One recurrent case was treated with a pulse dexamethasone with mesalamine (Table 1). The patient who had Pott's spine was prescribed anti-tuberculosis treatment in addition to the above treatment.

**Table 1: Clinical and Therapeutic profile of patients**

Pt no	Episode	Association	Site	Treatment	Outcome
1.	Recurrent	Ulcerative colitis (UC)	Leg	Dexona pulse therapy mesalamine	Partial remission (PR) in 6 weeks
2.	Recurrent	Varicose veins	Leg	Dapsone clofazimine	Complete remission(CR) in 8 weeks
3.	Primary	None	Thigh	Prednisolone dapsone	CR in 8 weeks
4.	Primary	None	Thigh	Prednisolone dapsone	PR in 6 weeks
5.	Recurrent	UC	Hand	Prednisolone dapsone	CR in 10 weeks
6.	Primary	Pott's spine	Cheek	Prednisolone dapsone ATT	PR in 8 weeks
7.	Primary	None	Leg	Prednisolone dapsone	CR in 8 weeks
8.	Recurrent	None	Leg	Prednisolone dapsone clofazimine	PR in 4 weeks

\*PR- Partial response \*CR- Complete response

**Figure 1: PG in a leg. Before Treatment**



**Figure 1: PG in a leg. After Treatment**



At follow up, half of the patients had a partial response to the treatment given while the rest had a complete cure of the initial lesions. The pictures of a patient before and after treatment are shown in Figures 1 and 2.

## Discussion

The first objective of this study was to describe the clinical profile of the patients who were diagnosed of pyoderma gangrenosum. PG has been shown to have a higher preponderance to females in studies including ours.<sup>11-13</sup> It is not clearly evident why females outnumber males but the possible reason may be its immunological nature as we know that auto-immune disorders are more prevalent in females.

In our study all the patients were young adults and adults with one patient at 80 years of age. Adults are predominantly affected by PG.<sup>2, 12-16</sup> In studies which had a fairly good number of cases, the average age of the patients have been shown to range from 34.4 years to 52.2 years.<sup>2, 12-14, 16</sup> Although adults are more affected than children, PG can be found even in children and infants<sup>2,4,17</sup>, so a high index of suspicion should be exercised in children and infants with recalcitrant ulcers. The clinical appearance and distribution of PG in children are often similar to that in adults but PG of head and face appears to be more common in children. Infants, on the other hand, have perianal and genital lesions.<sup>17</sup>

The body part which was more commonly affected by PG in patients of our study was lower extremity. Four out of eight patients had lesions on their legs and two had lesions on their thigh. Our finding is in agreement with the data published in large case series and review

literatures<sup>11, 12, 15, 18</sup> of PG. However, we should note that one of our patients had the lesion on her cheek, an atypical site for the typical ulcerative type of lesion.

Ulcerative Colitis and Crohn's Disease are one of the commonest associations seen in patients with PG.<sup>12, 14, 15, 18</sup> Studies have shown that peristomal PG can be an unrecognised complication in patients with these inflammatory bowel diseases and who have undergone some sort of colostomy operations.<sup>13, 19</sup> Our study also had two out of four patients (50%) patients who had associated systemic conditions. These patients suffered from Ulcerative Colitis but neither had undergone any stomal operations and the lesion was present on the leg in one patient and on the hand in the other.

Our study showed a slight preponderance of typical (ulcerative) type over atypical (bullous) type of PG with a ratio of 5:3. The ulcerative variant of PG is the most common type with which a patient presents<sup>2, 11, 16</sup>. It is typically characterised by a rapidly enlarging ulcer with an undermined edge, a necrotic purulent base and a surrounding bright ring of erythema. The three bullous variants of PG in our study started with an initial lesion of pustule, vesicle and bulla which rapidly enlarged into bullae with central necrosis and a surrounding halo of erythema. These two variants require aggressive systemic therapy for control.<sup>4</sup>

Since the variants of PG in our study belonged to aggressive type, we treated them with a systemic immunosuppressive therapy with a various combination of corticosteroids, dapsone, mesalazine and clofazimine. Immunosuppressive therapies like above and others (e.g. methotrexate, mycophenolate mofetil, azathioprine, cyclosporine and infliximab)<sup>11, 16</sup> are the

cornerstones of treatment of PG once the diagnosis has been established. Because of the severity of the disease, intermittent pulse dexamethasone was supplemented with a maintenance dose of prednisolone in one of our patients to prevent relapse. The treatment was only efficacious for 50% of the patients in the present study during the follow up made, although nothing was known of the patients who had shown partial response and were asked to continue the same drugs. This was one of the limitations of the study as the follow up period was very short.

The study outcome is limited by the number of patients that could be enrolled to find out the clinico-therapeutic profile of PG. However, it is not surprising to see that we could only have 8 patients in the five years given the rare nature of this disorder. We should make sure in the future that this rarity does not make PG as a disorder of omission because of the grave consequences that can happen if the disease is not recognized at the right time.

## **Conclusion**

This study has highlighted the salient features of PG, a rare disorder, in the context of Nepal. A high index of suspicion and identification of relevant clues like the location of the ulcers in the legs and associations with inflammatory bowel diseases after ruling out other causes of ulceration can lead to the diagnosis of PG. A careful assessment of the lesions and appropriate and timely treatment can avert aggressive debridement and even amputation of limbs.

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