Pyoderma Gangrenosum

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SUMMARY
Pyoderma Gangrenosum (PG) is a non-infective, necrotising neutrophilic dermatosis. Many diseases may mimic PG. It may be idiopathic or may be associated with a systemic disorder. We report a case of PG in association with ulcerative colitis.

KEYWORDS:
Pyoderma Gangrenosum, Inflammatory bowel disease

INTRODUCTION
Pyoderma Gangrenosum (PG) is a destructive necrotizing, non infective ulceration of the skin which presents as a furuncle-like nodule, pustule or haemorrhagic bullae. PG can develop before, during or after the onset of systemic disease.

CASE REPORT
Mr. S, a 74 year old Malay male, was admitted to Penang Hospital with complaint of painful, non healing ulcers over the right medial malleolus and left buccal mucosa of ten days duration. The ulcers were associated with fever, loss of appetite and loss of weight.

On further questioning, he claimed that he had intermittent diarrhoea for the past two years. The diarrhoea were associated with blood and mucus occasionally. There were no significant past medical or surgical history. He did not give a family history of bowel malignancy or bowel problems. Abdominal examination revealed no organomegaly and no lymphadenopathy. Peripheral pulses were normal. Digital rectal examination revealed soft mucoid bloody stool but no masses.

A provisional diagnosis of pyoderma gangrenosum associated with inflammatory bowel disease (most likely ulcerative colitis) was made. He was referred to the surgical team for colonoscopic examination and biopsies (leg, oral and bowel biopsy). Colonoscopic examination showed diffuse severe mucosal inflammation with area of superficial ulceration and multiple sessile pseudopolyps especially at the caecum and ascending colon. Terminal ileum appeared normal. Findings were consistent with severe ulcerative colitis.

All tissue cultures (bacterial/fungal/AFB) were negative. Mantoux test was negative. Chest x-ray was normal. Ultrasound of the abdomen revealed no focal liver lesions or lymphadenopathy. Laboratory tests were performed. Erythrocyte Sedimentation Rate was elevated (111mm/hr). Antinuclear Factor, Rheumatoid Factor and Antinuclear Cytoplasmic Antibody were negative. C3, C4 level were within normal range. HIV, Hepatitis B surface antigen and Hepatitis C screening were non reactive; coagulation profile and fasting blood sugar level were normal.

Colonoscopic examination showed multiple fragments of benign large bowel mucosa, with focal ulceration, focal acute cryptitis and a few crypt abscesses. Lamina propria was diffusely infiltrated by lymphoplasmacytic cells, neutrophils and eosinophils. No granuloma or malignancy was noted. The impression was of a chronic active colitis with features suggestive of ulcerative colitis.

Biopsy of right lower leg ulcer showed benign inflamed skin with extensive ulceration and necrosis; there was no granuloma and no evidence of malignancy.

Subsequently, patient was started on oral prednisolone 60mg daily (1mg/kg of body weight/day). Oral sulphasalazine 500mg 8 hourly was started at the same time. Dressing of the ulcer with normal saline was done twice a day. He was also put on stress ulcer prophylaxis and oral analgesics. A repeat colonoscopic examination after two months of treatment showed marked improvement.

The prednisolone was tapered by 5mg every two week. He was given oral prednisolone for a total of four months before it was stopped. His condition is currently stable with no recurrence of gastrointestinal or cutaneous symptoms. He is still under dermatology and gastroenterology clinic follow up.

DISCUSSION
IBD affects 0.37% of the population. It has two subtypes: Ulcerative Colitis (UC) and Crohn’s Disease (CD). IBD commonly presents as diarrhoea, per rectal bleeding, weight loss and signs of malnutrition. It is associated with a wide range of extraintestinal manifestations like cutaneous, metabolic, ocular, hepato-biliary and musculo-skeletal symptoms and signs. Approximately one third of IBD
patients have extraintestinal manifestation. Of those patients, 1/3 will have cutaneous manifestations. Cutaneous manifestation is usually related to the activity of the bowel disease but may have an independent course.

Common cutaneous manifestations are PG, erythema nodosum and oral lesions like aphthous stomatitis, mucosal nodularity and pyostomatitis vegetans.

PG is a severe ulcerating non infective neutrophilic dermatosis. Incidence of PG is low. However, a literature review revealed that 50%-70% of PG cases were associated with systemic diseases like IBD, rheumatological disorder and hematological malignancy (myeloproliferative or myelodysplasia). UC is the most common underlying disease associated with PG in adults. Male and female are equally affected with a peak incidence between 25-54 years.

Classically PG begins as an acute onset painful haemorrhagic pustule or painful nodule either de novo or following minimal trauma (Pathergy sign). PG is characterized by the presence of painful, irregular, boggy, bluish-purplish, rapidly enlarging necrotic ulcers with undermined borders, surrounded by an advancing active zone of erythema. Course of the disease varies. If left untreated, it may last for months to years or ulceration may extend rapidly within days. Healing occurs centrally with peripheral extension. When healed it often produce cribriform scars. New lesion may appear as older lesions resolve. PG most commonly involves the lower limb but it can occur on any part of the body.

PG is a diagnosis of exclusion because many diseases can mimic PG. We should always exclude infective causes of non healing ulcers like fungal/mycobacteria/bacterial infection.

Mr. S had a rapidly evolving irregular, bluish-purplish ulcer at his right leg which is consistent with the classical description of PG. Repeated tissue and swab cultures failed to yield any infective organism. A detailed history taking and physical examination revealed an association with Ulcerative Colitis, which was confirmed by a colonoscopic examination and biopsies. He was given oral prednisolone and sulphasalazine with satisfactory responses in both his cutaneous and gastrointestinal symptoms.

At this time, there is no specific laboratory or histopathological tests for PG. Classical histopathological description of ulcerative PG is neutrophilic infiltration in the center of the ulcer and lymphocytic infiltration in the peripheries. Skin biopsy only helps to rule out conditions that may mimic PG.

It has been demonstrated that both the type and severity of associated systemic diseases are important prognostic factors of PG. Poor response to treatment of the associated disease is often associated with a poor prognosis of the skin condition.

Treatment should be directed at both the cutaneous and the underlying systemic condition. Moist wound management with emphasis on preventing secondary infection is crucial. Minimal operative handling and non surgical management is recommended in the treatment of PG.

Prednisolone is generally considered the drug of choice. Usual dose ranges from 1 to 2 mg/kg of body weight /day. Cyclosporine at doses of 3 to 5 mg/kg/day has also been shown to be effective either as monotherapy or combination therapy especially in refractory cases. Average length of treatment with systemic agent was 11.5 months and most of the lesions healed within one year. Surgery can aggravate PG. If it must be performed, it must be done in conjunction with immunosuppressive therapy in patients with remitted or stable disease.

Systemic immuno-suppressants are the mainstay of treatment for PG. But prolonged therapy is usually associated with significant side effects. Treatment strategies should include proper monitoring and prevention of adverse effects. In steroid-refractory PG, Cyclosporin, dapsone, azathioprine, thalidomide, mycophenolate mofetil and infliximab need to be considered. There have been report of success with treatment with intravenous immunoglobulin. Adequate analgesia is warranted in PG management especially during
wound dressing’. Supportive treatment like bed rest, stress ulcer prophylaxis, and nutritional support may help.

In conclusion, cutaneous manifestations of IBD are common. Patients presenting with IBD should be examined for cutaneous manifestations. In the management of PG, associated diseases should be sought. Management should focus on both the cutaneous and underlying systemic disease.

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REFERENCES