Pyoderma gangrenosum – three fulminant cases and a review of treatment

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Introduction

Pyoderma gangrenosum (PG) is a rare, chronic, ulcerative skin disorder. It typically presents with a painful nodule or pustule which breaks downs to form a progressively enlarging ulcer.[1] It may present after apparently minor trauma or complicated surgical treatments. We present three aggressive cases of PG and their management.

Case 1

History and progress

Patient J is an 11-year-old boy who sustained minor trauma to the right knee while playing soccer. This developed into an open wound that had been debrided several times with no improvement before presenting to the wound clinic. He presented with a large, heavily exudative wound on the right leg with slough (Figure 1). Initial debridement and biopsies were done with no improvement of the wound. He was pyrexial with high C-reactive protein (CRP) (180), but cultures (blood and tissue) were negative. Histology was non-specific, with only a neutrophilic infiltrate. A clinical diagnosis of PG was made in conjunction with a dermatologist and paediatric rheumatologist. Treatment was commenced on prednisone and methotrexate, with a rapid resolution in clinical parameters – CRP and temperature normalised. There was improvement in the wound and granulation (Figure 2). The wound was closed with a skin graft and healed well (Figure 3). The patient was subsequently followed up and treatment tapered by the rheumatologist. The rheumatological work-up did not identify any underlying conditions.

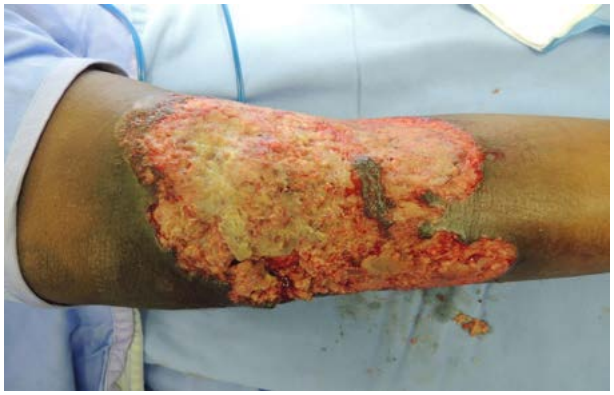

Figure 1: Heavily exudative wound on the right leg with slough

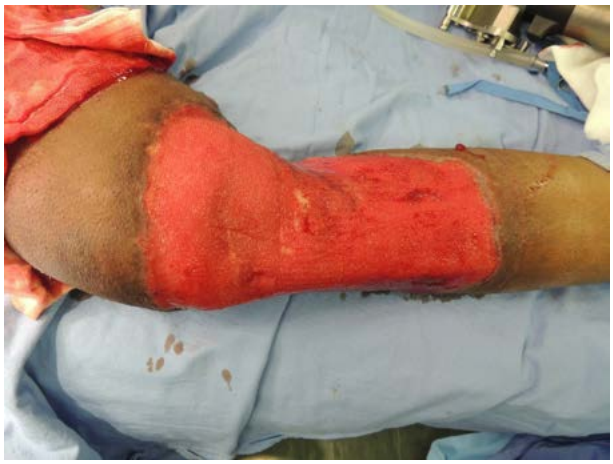

Figure 2: Wound improvement and granulation

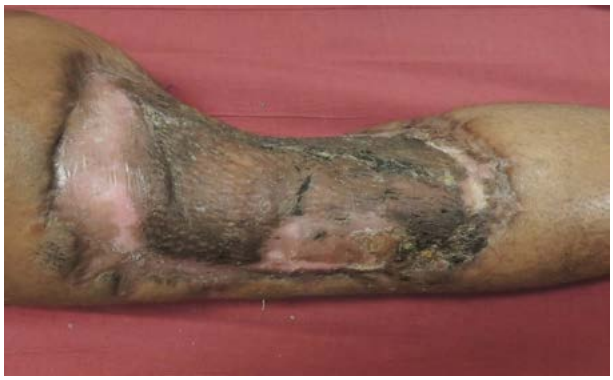

Figure 3: Wound closed with a skin graft and healed well

Case 2

History and progress

Patient N was referred by a gynaecologist 2 weeks after caesarean section for a non-healing lower abdominal wound after multiple

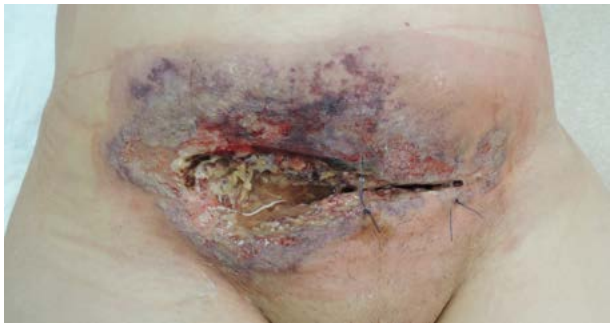

Figure 4: Large open wound, heavily exudative, with a noticeable violaceous border

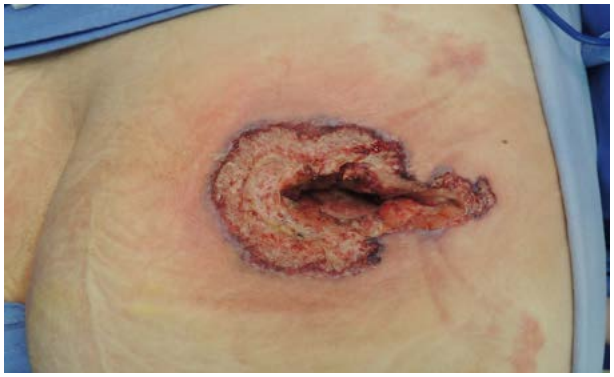

Figure 5: Smaller wound on the right buttock at IM injection site

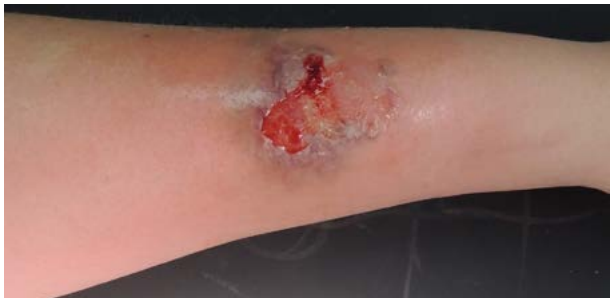

Figure 6: Developing wound on the right wrist at a drip site

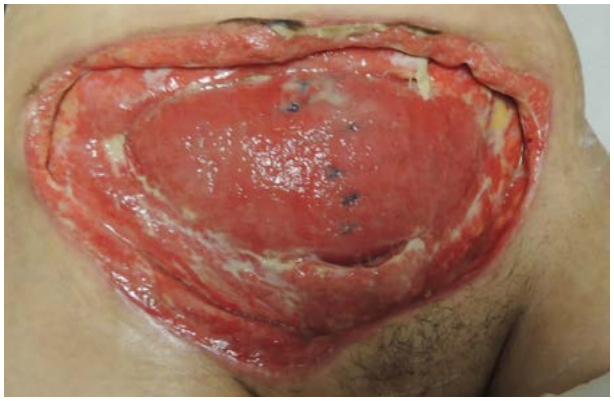

Figure 7: Wound rapidly granulated on negative pressure wound therapy

debridements. The patient was in ICU with high spiking temperatures and a CRP of 380 and required low-dose inotropic support. All cultures until then were negative. Examination showed a large open wound, heavily exudative, with a noticeable violaceous border (Figure 4). It was also interesting to note that there was a similar smaller wound on the right buttock where an IM injection had been given (Figure 5)

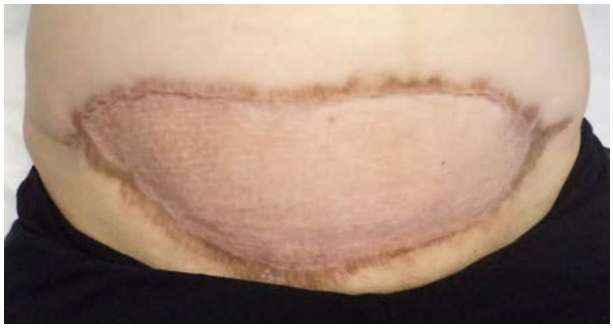

Figure 8: Skin grafted wound showing no further complications

and a developing wound on the right wrist at a drip site (Figure 6). The wound was debrided, and tissue biopsies sent. Histology showed a very marked neutrophilia of the tissue. No underlying rheumatological condition was identified. High-dose pulsed steroids were commenced and almost immediately improved all parameters. The wound rapidly granulated on negative pressure wound therapy (NPWT) (Figure 7) and was skin grafted with no further complications (Figure 8). An interesting development is that this patient subsequently fell pregnant again. The caesarean section and a lower abdominal wall reconstruction in the pattern of an abdominoplasty were performed uneventfully under the cover of prednisone.

Case 3

History and progress

Mrs T was a young lady referred for a lower abdominal wall reconstruction. She had a complicated caesarean section 2 years previously with a working diagnosis of necrotising fasciitis and loss of the lower abdominal wall. Her open abdomen had been skin grafted at that stage, leaving her with a large hernia (Figure 9).

Her abdominal wall reconstruction involved removing the skin graft, placing a mesh and closing the abdomen in an abdominoplasty fashion. The postop course was initially uneventful until day 4 when she developed pyrexia and high CRPs, and the entire wound became heavily exudative. A small wound developed on the right lower abdomen (Figure 10). Within 24 hours, this wound rapidly progressed (Figure 11), and the patient deteriorated to requiring inotropic support. All cultures

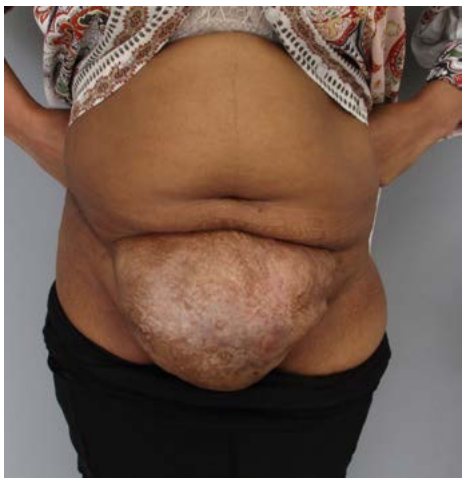

Figure 9: A large hernia visible after previous skin graft

Figure 10: Small wound developing on the right lower abdomen

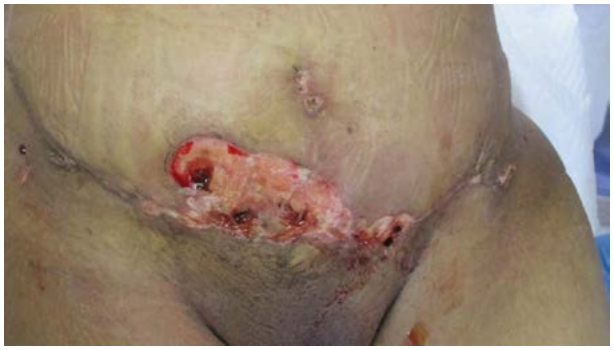

Figure 11: Rapidly progressing wound

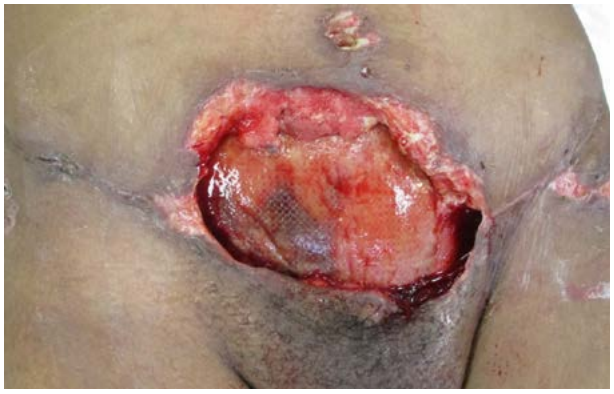

Figure 12: Enlarged wound

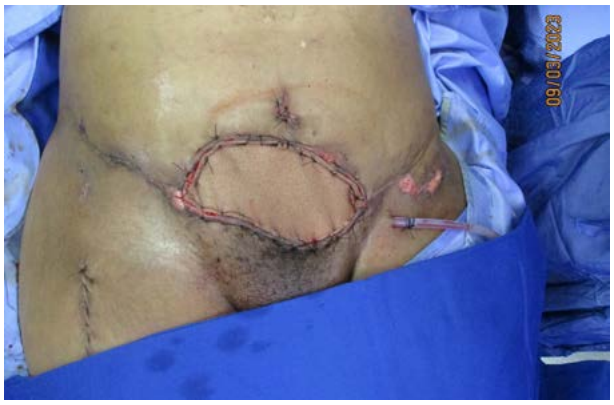

Figure 13: Secondary pedicled anterolateral thigh flap closing the lower abdomen

were negative. A diagnosis of PG was made and high-dose pulsed steroids were initiated. The patient responded well over the next 3 days, but by then, the wound had enlarged (Figure 12). With the patient's disease process under control, a secondary pedicled anterolateral thigh flap was done to close the lower abdomen (Figure 13). The rest of the treatment course proceeded uneventfully, and steroids were gradually tapered. The rheumatological work-up was negative.

Discussion

The aetiology of PG remains unknown; however, the notion that it has an infective origin has been dispelled in previous literature.[1] There is a strong association with systemic disorders such as inflammatory bowel disease, polyarthritis and lymphoproliferative disorders in at least 50% of cases.[2]

Although the pathogenesis is poorly understood, an inflammatory or immunologic abnormality is suspected. Pathergy (the development of new lesions or aggravation of existing ones in response to trivial trauma) would suggest an aberrant, exaggerated inflammatory response.[1] All three of the cases we managed displayed this pathergy. Numerous clinical forms have been described, i.e. classic, pustular, bullous, peristomal or genital, which all tend to behave aggressively. Vegetative PG is the only form that tends to be more localised and indolent. Histological features include a neutrophilic infiltration, tissue oedema, small vessel thromboses, liquefaction and necrosis—however, the hallmark is the presence of neutrophilic infiltrates.[1]

The diagnostic evaluation of PG remains two-fold, i.e. to exclude any other cause of cutaneous ulceration and to search for an underlying, treatable, systemic disorder. No specific serology is diagnostic of PG; instead, non-specific elevation of the inflammatory markers (white cell count, CRP and erythrocyte sedimentation rate) is seen. The natural progression of the disease remains variable. Some patients attain remission or a period of quiescence, whilst others follow a very fulminant course with mortality rates as high as 30% reported in previous literature.[3] Poor prognostic factors include male sex, old age at onset and a bullous variant, particularly when associated with a haematological disorder.

Treatment review

There are very few controlled trials of treatment for PG, perhaps due to the rare nature of the disease. Treatment is empiric and based on the severity of the disease. The treatment arms comprise a combination of local wound care and systemic medications. Local or topical treatment may be considered with milder disease not associated with systemic illness.

Systemic corticosteroids are often used as first-line therapy as they are the most predictable when used in effective doses and have an acceptable side effect profile. High doses are usually given until the inflammatory component of the pyoderma resolves, and then the dose is gradually tapered until full resolution occurs. Pulse therapy with large doses of methylprednisolone (500 mg–1 g/daily for 3–5 days) can be used to arrest disease progression in fulminant disease—prompt resolution of systemic symptoms such as fever, tachycardia and elevated septic markers is usually seen.[1-4] Alternative regimens are described

using dexamethasone; however, it seems that methylprednisolone is the most widely accepted.[2] Pulse therapy is reserved for fulminant cases due to the possibility of significant side effects such as worsening hypertension, increased risk of infection, electrolyte disturbances and mood/behavioural effects. Following pulse therapy, continued immunosuppression in the form of oral corticosteroid or sulfa drugs should be used.[1-3]

Cyclosporine is an alternative first-line agent which can be used as an oral therapy with or without steroids. Dosing ranges from 3–10 mg/kg/day; therapy is usually continued for up to four months. Side effects such as renal dysfunction and hypertension are possible and should be monitored for, but they are less common at these doses.[1,3] Cyclosporine has the additional benefit of being well-tolerated and the least myelosuppressive when compared to other disease-modifying agents (DMARDs). Dapsone and sulfasalazine are the most commonly used sulfa drugs, with sulfasalazine being the preferred agent even in those with no systemic disease. These drugs can be combined with systemic steroids to induce "remission" and then be continued longer term as part of a steroid-sparing strategy. Numerous other conventional DMARDS, e.g. cyclophosphamide, chlorambucil, azathioprine, daunorubicin, mycophenolate mofetil and methotrexate, have been employed with varying degrees of success in previous literature.

With the advent of more advanced medicine, other modalities such as plasmapheresis, intravenous immunoglobin therapy, hyperbaric oxygen therapy and biologic agents have been tested. One case series using infliximab showed promising results—however, routine use of this agent is still limited by cost and insufficient evidence.[2]

Conclusion

Whilst PG is rare, it will most likely be encountered by practitioners dealing with complex wounds at some stage. It presents a diagnostic challenge and is often confused with more common wound conditions. One must keep PG in mind as a differential diagnosis as it responds poorly to regular wound care and interventions, especially surgery, which can exacerbate the pathergy phenomenon. Once the correct immune modulating therapy is instituted, PG usually responds well, and surgical interventions can also be undertaken.

Conflict of interest
The authors declare no conflict of interest.

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Ethical approval
All patients consented to the use of information and images.

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