

Case Report

Pyoderma gangrenosum presenting with acute generalised haemorrhagic bullae

壞疽性膿皮病表現為急性泛發型血疱

YH Chan 陳耀海, WYM Tang 鄧旭明, WY Lam 林永賢

A 31-year-old Chinese man presented with acute generalised bullous eruption followed by painful ulcers formation with bluish edge. The skin biopsy was consistent with the clinical diagnosis of pyoderma gangrenosum. Subsequent workup did not identify any underlying or associated medical disorders. His skin condition was controlled with non-adhesive dressing care and analgesic intervention, high dose systemic steroid, cyclosporine and topical 0.1% tacrolimus.

報導一例三十一歲中國男子表現為急性泛發型血疱。皮膚切片檢查與臨床診斷壞疽性膿皮病吻合。隨後的有關檢查並無發現相關的內臟疾病。其皮膚情況在非黏性敷料護理，並給予止痛藥，高劑量皮質激素，環孢素及局部外用0.1%他克莫司後得到控制。

Keywords: Chinese, haemorrhagic bulla, pyoderma gangrenosum

關鍵詞：中國人，血疱，壞疽性膿皮病

Introduction

Pyoderma gangrenosum (PG) is an uncommon destructive ulcerative dermatosis. Up to 50% cases

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of PG are associated with concurrent medical illness. Prompt diagnosis with exclusion of other causes of ulceration can facilitate early treatment with steroid and immunosuppressant, and detailed investigation is warranted to identify any underlying medical disorder. The following is a case report of a 31-year-old Chinese male patient with PG.

Case report

A 31-year-old Chinese man was admitted to the medical ward and presented with three days' sudden onset of erythematous papules on the thighs and buttock (Figures 1 & 2). The lesions

rapidly enlarged to form plaques and evolved to haemorrhagic blisters. Rupture of blisters gave rise to painful erosion and ulcers (Figure 3). New lesions developed sequentially on the elbows,

upper arms, shoulders, back, ears and scrotum. The patient also had transient high fever (39°C) but no other systemic symptoms. He enjoyed good past health with no significant medical illness. On



Figure 1. Multiple ulcers of pyoderma gangrenosum over buttock.



Figure 2. Multiple ulcers of pyoderma gangrenosum over right leg.



Figure 3. An ulcer of pyoderma gangrenosum .

physical examination, the patient had multiple flaccid and haemorrhagic blisters. Tender erosions and ulcers with tender bluish edge on the thighs, buttock, arms, back, fingers, ears and scrotum were noted. Differential diagnoses included pyoderma gangrenosum, ecthyma gangrenosum, bullous pemphigoid, pemphigus vulgaris, vasculitis and cryoglobulinaemia.

Full blood count revealed marked neutrophilia with normal haemoglobin and platelet count. C-reactive protein and ESR were elevated. Ulcer swab and blister fluid were negative for bacterial, viral and fungal culture. Sepsis and autoimmune workup were unremarkable. HIV and syphilis serology were negative. Immunoglobulin analysis was normal and anti-skin antibody was negative. Skin biopsy of an intact blister from his left thigh showed mixed pattern of neutrophilic infiltration in the epidermis with congested dermis (Figures 4-6). Viral inclusions, fungal hyphae and bacteria were not found, and immunofluorescence was negative. These features supported the diagnosis of PG.

The patient was treated with non-adherent dressings, analgesics, high dose prednisolone commencing at a dose of 30 mg twice daily and later stepped up to 50 mg twice daily and cyclosporine 150 mg twice daily. Topical tacrolimus 0.1% ointment was applied on the lesions after wound dressing. Complete remission was achieved after three months' therapy. Unfortunately, he had a relapse five weeks after cessation of systemic therapies.

Discussion

PG is an uncommon, destructive cutaneous ulceration which was first described by Brunsting et al in 1930.¹ It usually occurs in patients between 25-54 years with peak at the fifth decade. Equal sex ratio was described in

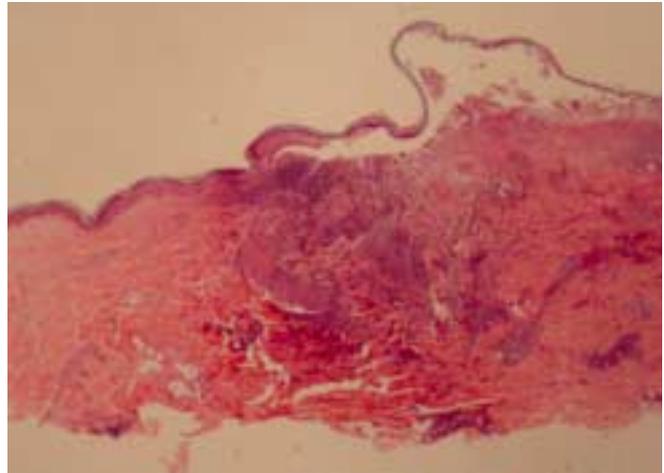


Figure 4. There is a dermal inflammatory infiltrate in nodular array with overlying devitalised epidermis (X10).

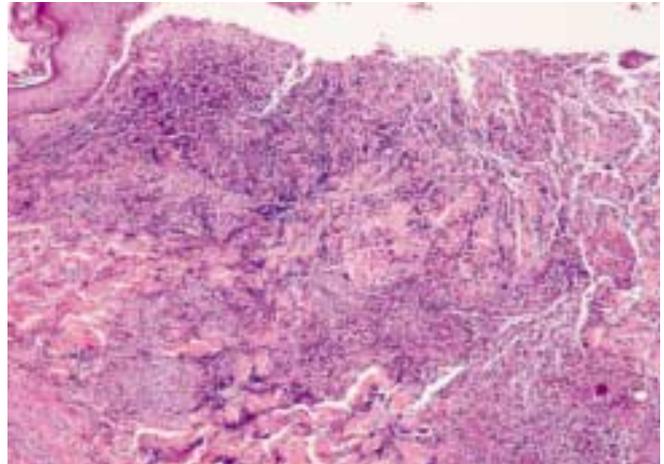


Figure 5. Medium magnification reveals the inflammatory nodules are composed predominantly of neutrophils. There are no leucocytoclasia nor obvious vasculitis (X40).

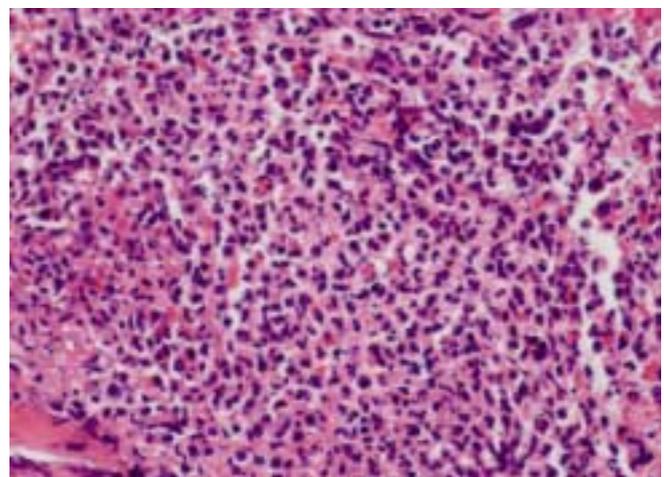


Figure 6. High magnification showing neutrophils in the inflammatory nodules (X200).

most series of case reports but there are few exceptions with female predominance.² The most commonly affected areas are the legs especially the shins.

Acute generalised eruptive PG is exceedingly rare, especially in Chinese. One more unusual feature in our case was the initial haemorrhagic bullous formation before progression to ulcerative PG. Differential diagnoses of acute generalised PG includes vasculitis, ecthyma gangrenosum, antiphospholipid syndrome, cryoglobulinaemia, bullous pemphigoid and pemphigus vulgaris.

Up to 50% cases of PG are associated with concurrent medical illness. Commonly associated diseases include inflammatory bowel disease, either ulcerative colitis or Crohn's disease; a polyarthritis that is usually symmetrical and may either be seronegative or seropositive; and haematologic disorders such as leukaemia or preleukaemic states, predominantly myelocytic in nature or monoclonal gammopathies especially IgA. None of these disorders were present in our patient.

The histopathology of PG is nonspecific and varies according to stage, variant, and biopsy location. Suggestive findings include ulceration with capillary and venous thrombosis, dense polymorph infiltration and sterile abscess formation. Frank vasculitis is rarely reported in areas of maximal tissue destruction. Biopsy of the erythematous leading border may show lymphohistiocytic infiltration. Culture of biopsy specimens is advisable to rule out infection due to bacteria, acid fast bacilli, atypical mycobacteria and fungi.

Systemic steroid either high dose oral therapy or administered in pulses, in combination with wound care and adequate analgesia constitute the mainstay of treatment for severe PG.³ Other agents reported to be useful in severe PG include cyclosporine,⁴ tacrolimus,⁵ cyclophosphamide,⁶ mycophenolate mofetil⁷ and intravenous

immunoglobulin.⁸ Cyclosporine and tacrolimus are members of the macrolide family of immunosuppressive antibiotics. They have their effect mainly by an action on T lymphocytes. After complex formation with cytosolic binding proteins, they interfere with the activation of the transcription factor NF-AT (nuclear factor of activated T cell) and inhibit the transcription of proinflammatory cytokine genes including interleukin-2, interleukin-4, interferon- γ and tumour necrosis factor- α . Topical tacrolimus is said to be effective in treatment of early lesions of pyoderma gangrenosum and it may be beneficial in combination with systemic cyclosporine in the treatment of advanced PG.⁹ Such combination allows a reduction of cyclosporine dose and treatment time. Our patient showed marked improvement to the combination of high dose systemic steroid, cyclosporine and topical tacrolimus with complete remission achieved by three months. However, the relapse of PG shortly after cessation of systemic therapy might indicate the need of longer period of maintenance immunosuppressant therapy.

In conclusion, acute generalised eruptive pyoderma gangrenosum should be treated with systemic immunosuppressive therapy once infectious causes have been excluded. The experience in our case suggested that combination of high dose systemic steroid, cyclosporine and topical tacrolimus work well in extensive case of PG but longer maintenance therapy may be required to prevent early relapse. Any associated medical illness should be looked for and treated accordingly. PG usually follows a refractory course with a reported recurrence rate of 46-50%.¹⁰ Long term follow up is therefore necessary.

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