

# First presentation of pyoderma gangrenosum in a patient with partial immunoglobulin A deficiency

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## Abstract

We describe the case of a 58-year-old female with an intensely painful and rapidly enlarging necrotic cutaneous ulcer to the right shin on a background of partial immunoglobulin A deficiency (IgAD). She was seen by various healthcare professionals and managed with upscaling antibiotics for cellulitis requiring an inpatient hospital stay. The dermatology team made a clinical diagnosis of ulcerative Pyoderma Gangrenosum (PG) on assessing the patient 13 days post-onset of symptoms. The patient responded dramatically to steroids and oral tetracycline. This case highlights the unusually described association between PG and IgAD as well as the diagnostic challenge seen in patients presenting with PG.

## Keywords

Dermatology, immunology (including allergy), vasculitis, Rheumatology, haematology (incl blood transfusion)

## Lesson

In patients presenting with painful ulcerative dermatosis in whom Pyoderma Gangrenosum (PG) is suspected, consider adding serum immunoglobulins as part of your investigations. Involve your local Dermatology team for advice at the earliest opportunity where PG is suspected.

## Introduction

Pyoderma Gangrenosum (PG) is a rare neutrophil mediated inflammatory dermatosis that is neither infectious nor gangrenous in nature. It commonly starts as a sterile inflammatory pustule or erythematous nodule which rapidly develops into a painful ulceration with violaceous undermined borders.<sup>1</sup> PG can often be triggered or worsened by trauma, a phenomenon termed as pathergy.<sup>1</sup> The pathophysiology of the condition is not

fully understood, however its strong associations with diseases of autoimmunity as well as response to treatments like corticosteroids and immunomodulatory drugs support an immune mediated mechanism.<sup>2</sup> Up to 50% of patients presenting with PG are found to have an underlying systemic condition.<sup>3</sup> Commonly described comorbidities in the literature include inflammatory bowel disease, inflammatory arthritides, haematological malignancies and other haematological disorders.<sup>4</sup> Three of the largest studies looking at the associations between PG and comorbidities did not describe immunodeficiency disorders as an associated disease, stressing the rarity of this case and contributing to the diagnostic challenge faced.<sup>1–4</sup>

PG is often misdiagnosed, especially in clinical settings where there is low index of suspicion. Misdiagnosis of PG not only allows for rapid evolution of the lesion with concomitant pain but can expose patients to unnecessary antibiotic therapy or even more devastating interventions like debridement and limb amputation. We report the case of a patient with partial immunoglobulin A deficiency (IgAD) presenting with PG. The cases of PG that coexist with immunodeficiency disorders are rare and will be further discussed.

## Case

A 58-year-old white British female presented with a 7-day history of an intensely painful necrotic cutaneous lesion on the right shin. The lesion started as a small blood-filled blister with well-defined erythematous edges, which progressively increased in size with the development of mucopurulent discharge (Figure 1). Her past medical history included partial IgAD, which was incidentally identified when investigated for persistent fatigue several years ago. She remained under routine immunology follow up and was never noted to suffer from

**Figure 1.** Images demonstrating rapid progression of the necrotic cutaneous ulcer, 13 days after treatment with oral antibiotics.

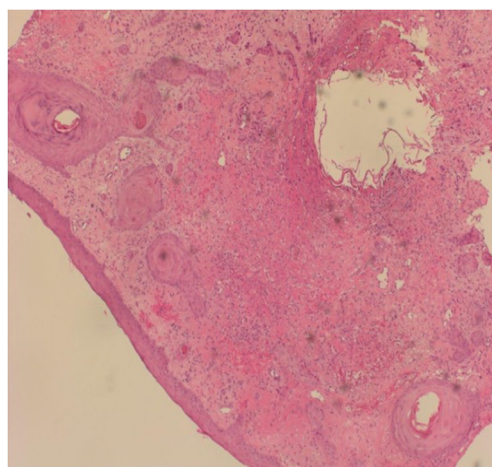


recurrent infections or inadequate test immunisation response. Her hypogammaglobulinemia was felt to be primary following extensive investigations to rule out secondary causes. On assessment of her ulcer, she denied any history of preceding trauma, and there were no systemic symptoms. She was seen by various health-care professionals including her GP and A&E doctors, and managed with upscaling penicillin antibiotics as presumed cellulitis/infected insect bite. After 5 days of worsening pain at the site and an increase in the size of the ulcer, the patient was admitted for intravenous (IV) antibiotics. She received 13 days of IV antibiotics with no significant improvement (Figure 1).

Her laboratory tests revealed anaemia of chronic disease which had been extensively investigated by the Haematology and Gastroenterology team and was attributed to her longstanding partial IgAD. Her IgA level on admission was 0.61 g/L (0.8–4.0 g/L) and IgG was 5.7g/L (5.5–16.5 g/L). Her inflammatory markers were raised with a CRP on admission of 239 mg/L (< 3mg/L). Lyme serology and auto immune screen were negative. Wound swab microscopy and culture was negative. An ultrasound doppler scan of the right leg demonstrated good flow. MRI of the right leg with contrast showed diffuse non-specific cutaneous and subcutaneous thickening/induration and enhancement within the right mid and distal calf on its lateral aspect with no evidence of osteomyelitis.

Clinical diagnosis of ulcerative PG by the Dermatology team was made 13 days following admission to hospital. The Dermatology team advised starting patient on IV hydrocortisone 200mg three times daily and 100mg of oral doxycycline once daily. Inpatient 4mm punch biopsy was carried out which showed pseudoepitheliomatous hyperplasia of squamous epidermis, collagen degeneration and haemorrhage (Figure 2).

**Figure 2.** Skin punch biopsy from leg shows pseudoepitheliomatous hyperplasia of squamous epidermis, collagen degeneration and haemorrhage.



Strict foot elevation was advised, and the ulcer was managed with saline soaks for 30–60 minutes 3 times daily and topical emollients. After 7 days, hydrocortisone was switched to high dose oral prednisolone (40mg) for 8 weeks which was gradually weaned by 5mg every week. Our patient completed a total of 3 months weaning dose of prednisolone and doxycycline with full resolution of the skin lesion (Figure 3).

## Discussion

To this date there is no widely adopted diagnostic criteria for PG as it remains largely clinical. Diagnostic skin biopsies are carried out to primarily to exclude other causes of

**Figure 3.** Shows improvement of cutaneous ulcer following 3 months of treatment with steroids and oral doxycycline.



ulcerative lesions rather than to confirm the diagnosis. Common differentials include infectious processes such as a deep fungal, bacterial, mycobacterial and parasitic infestations. Venous and arterial insufficiency can also present with ulcers over the extremities. Autoimmune diseases such as Systemic Lupus Erythematosus, Behcet's Disease, Granulomatosis with Polyangiitis and Polyarteritis Nodosa are rare but can often present as cutaneous ulcers. Insect bites (brown recluse spider), Dermatitis Artefacta (skin lesions that are self-inflicted) and drug induced ulceration (nicorandil, hydroxyurea) can have similar presentations.<sup>5,6</sup>

Classical histopathological features include neutrophilic infiltrates in the dermis, ulceration, epidermal and superficial dermal necrosis and intradermal abscess formation.<sup>6</sup> The histopathological results in our case were not in keeping with that of PG and this could be explained by the fact that our patient had 7 days of high dose steroids and oral doxycycline prior to the biopsy being obtained.

Our patient did not fit the criteria for CVID or selective IgA deficiency and was therefore diagnosed with partial IgA deficiency. A literature search yielded a few cases published showing an association between PG and immunodeficiency disorders. Bergler-Czop *et al.* published a case report of a 22-year-old man with PG that co-existed with Common Variable Immunodeficiency Disorder (CVID) and responded well to IV steroids.<sup>7</sup> Paller *et al.* presented two children with a background of congenital immunodeficiency who went on to develop PG.<sup>8</sup> Simsek *et al.* presented a case of a male patient with a history of recurrent abscess formations in which one of them transformed into a growing ulcer after incision and drainage and a diagnosis of PG was made supported by histology.<sup>9</sup> He was also consequently diagnosed with CVID. Joseph *et al.* described a novel mutation in a patient with CVID and facial PG.<sup>10</sup> The oldest article links IgA deficiency to PG found by the authors dates to 1984. Bundino *et al.* described the case of a previously fit and well 4-year patient who presented with a severe scattered ulcerative dermatosis and was found to have

undetectable IgA serum levels. Diagnosis of both PG and IgAD was made, and there was an excellent response to treatment with prednisolone and clofazimine.<sup>11</sup>

Our case highlights the importance of suspecting a diagnosis of PG in patients with immunodeficiency disorders presenting with ulcerating skin lesions as well as the need to include serum immunoglobulin levels when investigating patients with suspected PG. The cases of immunodeficiency disorders that coexist with PG are relatively uncommon and further work is needed to understand the basis behind this association.

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**Guarantor:** SD and MS.

**Contributorship:** SD, MS and MP wrote the manuscript. KM was responsible for patient care and reviewing the text. All authors have seen and approved the final version of the case report.

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