Case Report

Multifocal Pyoderma Gangrenosum Complicated by Multiple Organ Dysfunction

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Abstract

Background : A 21-year-old male with cardiomyopathy presented to our clinic with symptoms consistent with Dermatitis Herpetiformis. Despite a favourable clinical response, dapsone initiated for treating dermatitis herpetiformis had to be discontinued following the development of hepatic dysfunction. The lesions ulcerated following treatment cessation, exhibiting characteristics consistent with Pyoderma Gangrenosum as defined by the Delphi diagnostic criteria. Since traditional first-line treatments could not be used for pyoderma gangrenosum due to the underlying cardiac dysfunction, the patient was started on oral cyclophosphamide. However, a rapid decline in renal function ensued, forcing us to withdraw cyclophosphamide. Eventually, the patient was started on low-dose prednisolone. This led to clinical improvement; however, cardiac failure eventually occurred, leaving us searching for alternatives. The patient was counselled about administering biologicals, but he succumbed to cardiac arrest before a decision was made. The lack of proper guidelines for immunosuppressive therapy in multiorgan dysfunction made managing this case extremely challenging.

Key words : Pyoderma Gangrenosum, Multiple Organ Dysfunction, Cardiomyopathy.

Pyoderma Gangrenosum (PG), an acute necrotising neutrophilic dermatosis, is characterised by painful ulcers with raised, undermined, violaceous borders and surrounding erythema. Most ulcers are preceded by nodules, plaques, or pustules and eventually resolve with cribriform scarring[1]. The absence of any discernible infection is a hallmark of this disease, suggesting that autoinflammatory processes may be involved. Autoactivation of key Interleukins (IL) and cytokines, such as IL-1, IL-17, IL-18, IL-33 and IL-36, propel the inflammatory pathway. This stems from an autonomous inflammasome activity, which cleaves inactive cytokine precursors into their active forms[1]. Another interesting caveat of this disease is the presence of the pathergy phenomenon, wherein minor trauma can further propagate the disease mechanisms and lead to extensive ulcers. Hence, surgical debridement and suturing are not viable therapeutic options in PG.

Case Presentation

A 21-year-old man of Uzbek descent, with an underlying non-ischaemic dilated cardiomyopathy and left ventricular systolic dysfunction was awaiting cardiac transplantation. He presented to the clinic with complaints of multiple bilaterally symmetrical, erythematous, pruritic papules and pustules over the face, arms, back, buttocks, and knees which had appeared over the past 10 days. A provisional clinical diagnosis of Dermatitis Herpetiformis (DH) was made, for which the patient was started on tablet dapsone 100 mg and advised a gluten-free diet. There was immediate improvement, but three days later, serum bilirubin levels were found to be significantly elevated, preventing further use of dapsone. The patient was maintained on mid-potent topical steroids and mupirocin[2-4].

Editor's Comment :

- Pyoderma gangrenosum is a recalcitrant autoinflammatory ulcerating dermatosis, which often requires months of immunosuppressive therapy. When complicated by multiple organ dysfunction, especially in a patient with non-ischaemic dilated cardiomyopathy, low dose prednisolone and secukinumab may be the only medication with a favourable adverse effect profile that can manage the disease without precipitating cardiovascular decompensation.

However, the lesions progressed and eventually ulcerated, becoming painful, purulent, and punched out with violaceous margins and surrounding erythema (Fig 1). Infection was ruled out after a negative pus culture report, and the diagnosis was revised to Pyoderma Gangrenosum (PG) based on the morphology as well as the histopathology of the new lesions (Table 1). Systemic corticosteroids and cyclosporine were deemed unsuitable as treatment options by the Cardiologist. Tablet cyclophosphamide, 50 mg OD, along with topical tacrolimus 0.1% ointment, was thus started[5]. However, five days later, there was a significant elevation of serum Creatinine, necessitating the stoppage of cyclophosphamide and worsening his symptoms again. As the ulcers progressed to increase in size and become more painful, it was imperative that systemic steroids in low doses be started to improve his Quality of Life[5-7]. The patient was started on prednisolone, with the dosage limited to 20 mg OD to prevent cardiac decompensation. The symptoms improved, and the patient was discharged. Unfortunately, the patient returned a month later with severe shortness of breath and signs of cardiac failure, forcing us to withhold prednisolone. This improved his cardiac symptoms but worsened the skin lesions. As a last resort, the patient was counselled for secukinumab administration; however, before he could make up his mind, he passed away due to cardiac arrest[8].

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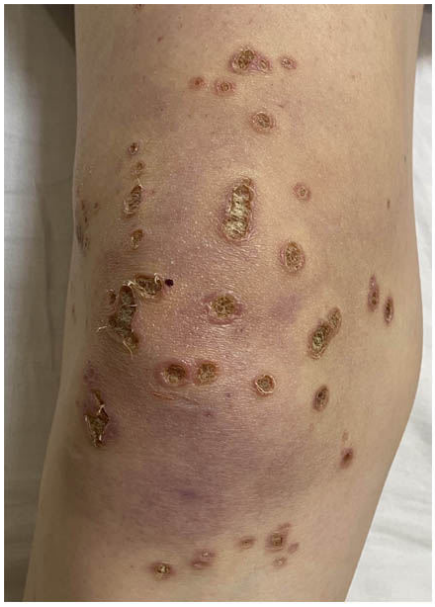

Fig 1 — Multiple well-defined punched-out ulcers with violaceous margins, yellow crusts on the floor and surrounding erythema over the right knee.

Discussion

PG remains a major diagnostic and therapeutic dilemma, especially in the early stages of the lesions. Although the Delphi diagnostic criteria aids in confirming the diagnosis, most of the essential components of this criteria can only be fulfilled after the lesions completely ulcerate. Furthermore, PG ulcers have often been confused with ulcers of infective aetiology which prompts most doctors to debride these lesions before receiving the culture and sensitivity reports[7]. This error can lead to a worse prognosis due to the pathergy phenomenon. While the precise aetiology of PG remains unknown, several cytokines, such as tumour necrosis factor-alpha and IL-1β, have been suggested to play a role in its pathogenesis. Hence, immunosuppressants, such as oral corticosteroids and cyclosporine, remain the cornerstone of treatment[5]. However, both drugs were ruled out due to their tendency to worsen heart failure. Further, dapsone and cyclophosphamide had to be discontinued due to an increase in bilirubin and creatinine levels, respectively[5,6]. Biologics like Infliximab could not be infused due to the risk of volume overload, whereas Adalimumab was contraindicated due to its risk of precipitating new-onset cardiac failure. Finally, after exhausting all other treatment options, the administration of low-dose prednisolone led to some clinical improvement but eventually exacerbated the Heart failure and had to be discontinued, sending us back to square one[5,6]. Thus, we were left searching for alternative therapeutic options for managing this case of cardiac failure, complicated by drug-induced hepatic and renal dysfunction.

Conclusion

The unique challenges faced during our patient's treatment prompted us to scour the literature in search of immunosuppressants with superior adverse effect profiles to effectively control the disease and improve the patient's Quality of Life. We believe secukinumab is particularly safe in the background of cardiac dysfunction as there are no reported cases of this drug precipitating cardiac events[8,9]. More research and guidelines on immuno-suppressive treatment ladders for individuals with multiorgan dysfunction would help guide clinicians in managing similar cases more efficiently.

Table 1 — *A summary of the essential laboratory reports*

y parameters	Day 01	Day 04	Day 09	Day 42
Haemoglobin	11.90	11.90	10.20	11
Total Leukocyte Count	11,000	10,000	8,500	10,200
Platelets	5,67,000	5,40,000	3,49,000	3,21,000
Urea	83	75	89	104
Creatinine	1.17	1.21	1.66	1.58
Total Bilirubin	3.65	6.01	5.57	2.34
AST/ALT/ ALP	27/19/136	23/18/167	23/16/145	28/18/159

Histopathology Report : The sections show epidermis with ulceration and inflammatory infiltrate at the base composed predominately of neutrophils. Vessel wall shows endothelial cell thickening nut fibrinoid degeneration and nuclear dust is not seen. Papillary microabcess, eosinophils, frank vasculitis, thrombus formation, granulomas or dysplasia are not evident in this section. In appropriate clinical settings, the histological findings raise the possibility of Pyoderma Gangrenosum.
Anti-TTG antibody : Negative.
Swab from the ulcer floor sent for culture and sensitivity : No organisms detected
AST - Aspartate Transaminase; ALT - Alanine Transferase; ALP - Alkaline Phosphatase; Anti-TTG antibody – Anti-tissue Transglutaminase antibody.

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Conflict of Interest : None.

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