

Introduction

- Pyoderma gangrenosum (PG) is an inflammatory neutrophilic dermatosis characterised by rapidly enlarging, deep and painful ulcers and is estimated to affect 3-10/million per year.¹
- The management of recalcitrant severe PG in patient unresponsive to or intolerant of systemic steroids can pose a significant therapeutic challenge.
- Adalimumab, a fully human anti TNF α monoclonal antibody, has been reported to be effective in the management of recalcitrant Pyoderma Gangrenosum.²
- A recent open-label, phase 3, multi-centre study of patients with PG treated with adalimumab demonstrated a Pyoderma gangrenosum area reduction 100 (PGAR 100) in 3 patients (13.6%) at week 6 and 12 patients (54.5%) at week 26.³
- Adalimumab represents a much-needed advance in treatment however further therapeutic options are needed for patients who do not respond to current dosing recommendations.
- We present a case series of two patients successfully treated with dose intensification of Adalimumab from 40mg to 80mg weekly.

Case 1

- Patient one is a 32-year-old male who developed ulceration of the left knee and right heel in 2015.
- Treatment with oral steroids, minocycline and cyclosporin was ineffective.
- The patient has cerebral palsy and infliximab was not considered an appropriate option due to high infection risk.
- Humira 40mg subcutaneously alternative weeks was initiated in combination with 25mg oral prednisolone in April 2016.
- Adalimumab dose was escalated to 40mg weekly, then 80mg weekly in August 2016 due to poor control. The patient remains in remission.

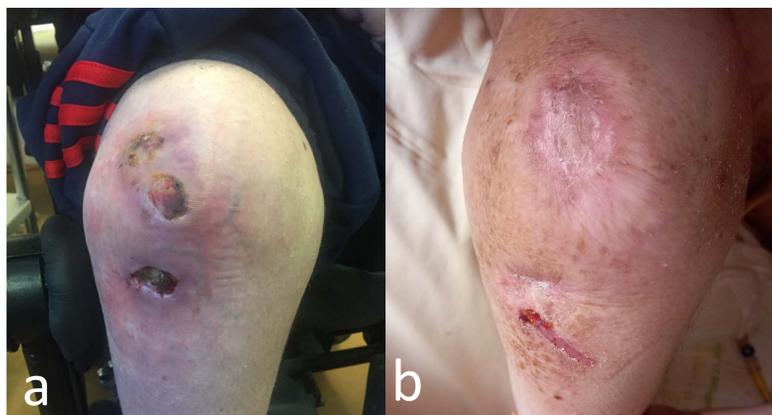


Image a) Ulceration right knee prior to commencing adalimumab. b) Right knee October 2021 with complete re-epithelialization. Superficial excoriation due to unconnected Trauma.

Case 2

- Patient two is a 61-year-old woman who developed painful severe ulceration of the left breast and right medial malleolus in 2015.
- Adalimumab 40mg weekly was commenced in 2016.
- There was an initial improvement, however, despite ongoing treatment the right medial malleolus ulcer deteriorated.
- Further treatment with intralesional steroids, dapsone, methotrexate, rituximab, mycophenolate mofetil, cyclosporin, IVIG, infliximab and acitretin was ineffective.
- Adalimumab 40mg weekly was recommenced in January 2021. The dose was escalated to 80mg weekly in April 2021 with rapid improvement.
- At last review in October 2021 the ulcer continues to reduce in size with almost complete re-epithelialisation.



Images: a) Ulceration right medial malleolus prior to commencing adalimumab. b) Ulceration October 2021 after 6 months of adalimumab 80mg weekly

Discussion

- The management of recalcitrant PG is challenging. An enhanced level of effectiveness was demonstrated in both patients treated with adalimumab dose intensification (80mg/week subcutaneously).
- Larger studies are required to establish its place in the current treatment armamentarium.

References

1. Binus AM, Qureshi AA, Li VW, Winterfield LS. Pyoderma gangrenosum: a retrospective review of patient characteristics, comorbidities and therapy in 103 patients. *Br J Dermatol* 2011; 165:1244–50.
2. Partridge, A. C. R., Bai, J. W., Rosen, C. F., Walsh, S. R., Gulliver, W. P., & Fleming, P. (2018). Effectiveness of systemic treatments for pyoderma gangrenosum: a systematic review of observational studies and clinical trials. *British Journal of Dermatology*. doi:10.1111/bjd.16485
3. Yamasaki, K., Yamanaka, K., Zhao, Y., Iwano, S., Takei, K., Suzuki, K., & Yamamoto, T. (2020). Adalimumab in Japanese patients with active ulcers of pyoderma gangrenosum: Twenty-six-week phase 3 open-label study. *The Journal of Dermatology*. doi:10.1111/1346-8138.15533