

## Good Response of Acne Conglobata to Adalimumab in Two Patients with Hidradenitis Suppurativa

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### Introduction

Acne conglobata is a form of nodulocystic acne characterized by abscesses, sinuses and large comedones that can lead to hypertrophic and atrophic scarring. The condition may result in marked disfigurement and a significant effect on the quality of life. It frequently affects the back, chest, shoulders, upper arms, thighs and the face. Acne conglobata may occur as a recurrence of previously dormant

acne or as a result of a sudden deterioration in existing papular or pustular acne. It is usually associated with Follicular Occlusion Syndrome in particular Hidradenitis Suppurativa, dissecting folliculitis and pilonidal sinus. Treatment can be challenging with options including antibiotics, oral steroids, intralesional steroids and oral isotretinoin. There is evolving evidence that anti-TNF  $\alpha$  therapy is effective in the management of severe recalcitrant inflammatory acne [1]. We report two cases of good response of acne conglobate in two patients with HS treated with adalimumab.



**Figure 1:** Resolution of patients' acne conglobata on Adalimumab at 12 week follow up.

### Report

The first patient was a 44 year old male who has had a long standing history of painful, nodulocystic acne since the age of 12 mainly affecting his back. He received two course of oral isotretinoin at the age of 20 and 30. In his 20s he developed psoriasis that was managed with topical treatment only. Ten years later he began to develop painful boils intermittently in his groin and axillary areas. At the age of 40, he had a recurrent flare up of his acne requiring referral to the Dermatology Department for further management.

At presentation, he had moderately severe nodulocystic acne with atrophic scarring on his back. He had erythematous nodules in his groin and axillary areas with double comedones consistent with Hidradenitis Suppurativa. There were psoriatic plaques in groin area as

well as evidence of pitting on the right finger nails. His PASI score was 10.4.

Failing multiple lines of antibiotics including Rifampicin and Clindamycin combination, as well as Isotretinoin, he was commenced on Adalimumab at 80 mg loading dose followed by 40 mg every other week as a monotherapy. At his 12 week follow up, he had made a significant improvement in his acne conglobata and Hidradenitis Suppurativa with minimal activity and flare ups (Figure 1). His PASI score was 4.2.

The second case is a 55 year old gentleman with a long history of severe nodulocystic acne affecting his face and back and a 25 year history of Hidradenitis Suppurativa. Previous failed treatment for his acne includes trimethoprim, minocycline and isotretinoin at a dose of 0.75 mg/kg. He was commenced on Rifampicin and Clindamycin combination therapy for his recurrent flare ups of Hurley Stage 2 Hidradenitis Suppurativa but had suboptimal response to after 10 weeks. He was then commenced on Adalimumab at 80 mg loading dose followed by 40 mg fortnightly as a monotherapy mainly for his Hidradenitis Suppurativa. At his 1 year follow up, his Hidradenitis

Suppurativa was quiescent and his acne conglobata had simultaneously improved with minimal flare ups or activity (Figure 2).

## Discussion

Isolated case reports in the literature have shown that anti-TNF $\alpha$  therapies are effective in treatment of acne conglobata presenting in isolation or as part of systemic inflammatory conditions including synovitis, acne, pustulosis, hyperostosis and osteitis (SAPHO syndrome) [2].

To our knowledge, there has only been one other case reported in the literature to date which describes successful treatment of refractory acne conglobata with Adalimumab as monotherapy [3]. This case reported by Sand et al. describes an 18 year old man who had severe acne conglobata which was unresponsive to doxycycline, isotretinoin, prednisolone and dapsone. Adalimumab was initiated as a monotherapy with a loading dose of 80 mg, followed by 40 mg twice monthly subcutaneously which resulted in a marked decrease in the size and degree of inflammation of the nodular lesions at 4 weeks after commencement of treatment with a sustained efficacy for 12 months with no recurrence of acne lesions.



Figure 2: Atrophic scarring on face and back of patient 1 year after treatment of acne conglobata with Adalimumab.

The most recent case reported in the literature by Yiu et al. describes a 26 year old gentleman with isolated acne conglobata who had failed multiple lines of treatment including rifampicin and clindamycin in combination, minocycline, isotretinoin, dapsone, trimethoprim and prednisolone. He was commenced on subcutaneous Adalimumab at 80 mg loading dose followed by 40 mg every other week in combination with 15 mg of prednisolone. This combination had resolved most of

the inflammatory nodules within 4 weeks of commencing Adalimumab with good response maintained at the 12 week follow up.

A further case report using Adalimumab at a dose of 40 mg every week for 4 weeks followed by a maintenance dose of 40 mg every other week in combination with low dose (0.5 mg/kg) Isotretinoin was reported in a patient with acne conglobata associated SAPHO

syndrome. This regime was commenced after patient had relapsed with cessation of Isotretinoin and prednisolone. Patient achieved complete resolution at 48 weeks with remission of cutaneous disease maintained at 24 months.

Both Etanercept and Infliximab have also been reported in the literature in several cases to be effective therapies in patients with severe nodulocystic acne, both in isolated cutaneous disease and in association with SAPHO syndrome [4-8].

Acne is an inflammatory condition characterized by significant elevations in *Propionibacterium acnes* that subsequently triggers keratinocytes to produce particular cytokines including tumour necrosis factor (TNF $\alpha$ ) and interleukin (IL)-1 $\alpha$  [9]. Furthermore, a study by Cailion et al. showed that *P. acnes* stimulated significantly higher levels of TNF  $\alpha$  and IL-8 compared to controls explaining the benefit of anti-TNF therapies in inflammatory conditions such as acne conglobata by the blockage of this inflammatory cascade [10].

It is however an unusual but well acknowledged phenomenon that anti-TNF therapies can trigger inflammatory skin conditions with a common one being psoriasiform skin eruptions. This appears to be paradoxical as TNF  $\alpha$  is a pivotal molecule in the pathogenesis of psoriasis. There have been several case reports also describing acne being triggered by anti-TNF therapies suggesting that the delicate balance between cytokines may be important for the induction of disease and for the response to treatment [11].

## Conclusion

In conclusion, Adalimumab appears to be an effective treatment option in patients with severe acne conglobata resistant to conventional therapies based on the two cases we have reported in addition to cases described in the literature thus far. Although both our patients maintained response to treatment at 12 weeks and 1 year, the durability of remission is unknown. Interestingly both patients had a good response at the lower dosage regimen of 40 mg once fortnightly than 40 mg once weekly as is recommended for HS. Therefore, larger scale, double-blinded, randomized, placebo-controlled and long term

follow up studies are essential to elucidate the efficacy and safety of anti-TNF therapies in the treatment of acne conglobata as well as its durability of remission.

## References

1. Yiu ZZ, Madan V, Griffiths CE (2015) Acne conglobata and adalimumab: use of tumour necrosis factor- $\alpha$  antagonists in treatment-resistant acne conglobata, and review of the literature. *Clin Exp Dermatol* 40: 383-386.
2. Garcovich S, Amelia R, Magarelli N, Valenza V, Amerio P (2012) Long-term treatment of severe SAPHO syndrome with adalimumab: case report and a review of the literature. *Am J Clin Dermatol* 13: 55-59.
3. Sand FL, Thomsen SF (2013) Adalimumab for the treatment of refractory acne conglobata. *JAMA Dermatol* 149: 1306-1307.
4. Campione E, Mazzotta AM, Bianchi L, Chimenti S (2006) Severe acne successfully treated with etanercept. *Acta Derm Venereol* 86: 256-257.
5. Su YS, Chang CH (2015) SAPHO syndrome associated with acne conglobata successfully treated with etanercept. *J Formos Med Assoc* 114: 562-564.
6. Shirakawa M, Uramoto K, Harada FA (2006) Treatment of acne conglobata with infliximab. *J Am Acad Dermatol* 55: 344-346.
7. Schuttelaar ML, Leeman FW (2011) Sustained remission of nodular inflammatory acne after treatment with infliximab. *Clin Exp Dermatol* 36: 670-671.
8. Burgemeister LT, Baeten DL, Tas SW (2012) Biologics for rare inflammatory diseases: TNF blockade in the SAPHO syndrome. *Neth J Med* 70: 444-449.
9. Graham GM, Farrar MD, Cruse-Sawyer JE, Holland KT, Ingham E (2004) Proinflammatory cytokine production by human keratinocytes stimulated with *Propionibacterium acnes* and *P. acnes* GroEL. *Br J Dermatol* 150: 421-428.
10. **Cailion F, O'Connell M, Eady EA, Jenkins GR, Cove JH, et al. (2010) Interleukin-10 secretion from CD14+ peripheral blood mononuclear cells is downregulated in patients with acne vulgaris. *Br J Dermatol* 162: 296-303.**
11. Fernández-Crehuet P, Ruiz-Villaverde R (2015) Acneiform eruption as a probable paradoxical reaction to adalimumab. *Int J Dermatol* 54: e306-308.