The Use of Thalidomide in the Treatment of HIV-Related Oral Ulceration

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Introduction

The prevalence of HIV-related oral ulceration varies from 5-10% globally. Thalidomide has been used as an off-licence medication in the management of HIV-related oral ulceration since the late 1990s. Whilst the exact mechanism of action of thalidomide is unknown, modulation of the inflammatory cascade and interaction with various cytokines, such as tumour necrosis factor-α are believed to be involved. Thalidomide is used in the management of recalcitrant ulceration that has failed to respond to alternative systemic and topical therapies. The adverse effects include teratogenicity, peripheral neuropathy and thromboembolic disease, limiting its use. [1,2,3,4] Here we present two cases of HIV-related oral ulceration treated with thalidomide.

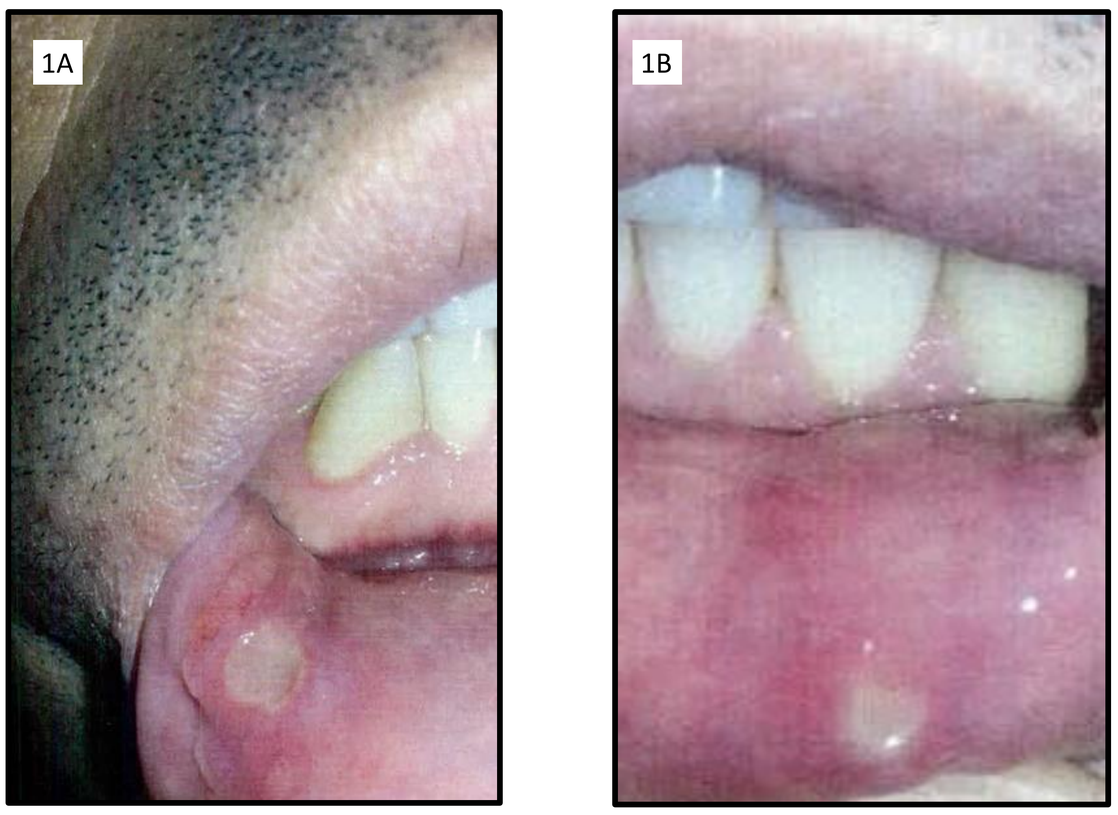
Presentation

Case 1

A 35-year-old male was referred with a 14 year history of HIV-related oral ulceration. The Ulcer Severity Scores (USS) at presentation was 38. The patient failed to respond to a number of topical and systemic agents over an 8-month period. Baseline nerve conduction study was normal. The patient was never ulcer free at baseline and Figures 1A & 1B illustrate the type of ulcers prior to thalidomide treatment. He was treated with thalidomide (varying dosing regimens) over a 5 year period, with spontaneous resolution of ulceration eventually reported. The USS 3 and 6 months after thalidomide therapy was 10 and 0, respectively (Figure 2).

Case 2

A 56-year-old female was referred with 1-year history of HIV-related oral ulceration. The USS at presentation was 28. The patient failed to respond to topical therapy for 1 year. The patient had baseline neuropathy of her lower limbs on nerve conduction study. The USS reduced to 0 three months after commencing thalidomide (50mg once daily for one week and one week off) (Figure 2). Treatment was stopped after 3 months due to worsening neuropathy.



Figures 1A & 1B: Both from Case 1, at baseline prior to thalidomide therapy. 2A showing a large ulcer (5x5mm) on the lower right labial mucosa and 2B showing a similar sized ulcer (4x5mm) on the lower left labial mucosa

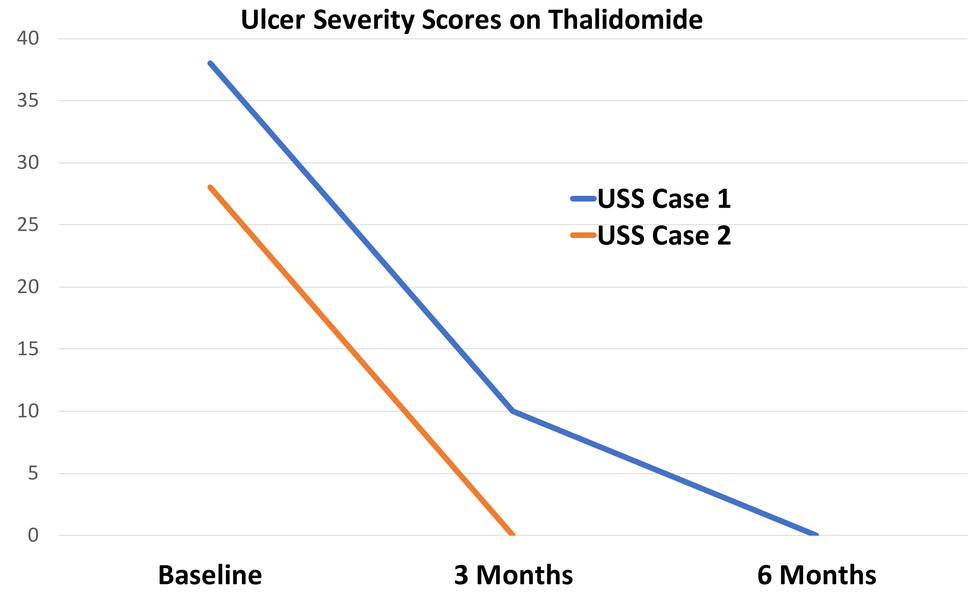


Figure 2: Ulcer severity scores for both cases (Case 1; Blue/ Case 2; Yellow). At 6 months the Ulcer Severity Score was 0 in case 1 and 0 at 3 months in case 2, treatment was stopped at 3 months due to worsening of an existing neuropathy.

Discussion

Thalidomide in used in the management of oropharyngeal ulceration, which may be a manifestation of systemic disease such as Bechet's Disease and HIV. Additionally, thalidomide has been shown to be efficacious in erosive lichen planus and other dermatological conditions. In the 1990s thalidomide was typically prescribed at a dose of 100mg per day, this was reduced as similar efficacy was found at lower doses with less adverse effects reported. A dose of 50mg per day is therefore typically used. [1,2,3]

Clinicians should be aware of the risk of worsening neuropathy by co-prescribing thalidomide in HIV patients. It has been suggested that thalidomide should not be used in those with pre-existing HIV-related peripheral polyneuropathy or polyradiculopathy. A number of randomised trials suggest that thalidomide treatment should not be continued after healing of ulceration in HIV-infected patients to minimise the risk of adverse effects.

Our case series suggests thalidomide should be used in caution in patients with pre-existing neuropathy and emphasises the need for regular nerve conduction studies in monitoring.[1,2,3] In addition, studies have shown thalidomide to elevate HIV RNA to some extent.[1]

Conclusion

These two cases highlight the usefulness of thalidomide in HIV-related oral ulceration, whilst also demonstrating the adverse effects associated with its use. Thalidomide may be the preferred choice of drug in recalcitrant cases over traditional immunosuppressive agents. Clinicians should be aware of the risk of worsening neuropathy by co-prescribing thalidomide in HIV patients. It has been suggested that thalidomide should not be used in those with pre-existing HIV-related peripheral polyneuropathy or polyradiculopathy. Regular clinical review, EMG and haematological investigations facilitate the safe use of thalidomide. This series also highlights the benefit of the Ulcer Severity Score as a clinical tool in monitoring response to treatment.

References:

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