Treatment of resistant aphthous ulceration with thalidomide in patients positive for HIV antibody

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Mouth ulceration is common in patients infected with HIV and is mainly due to malignancy, herpes simplex virus, or fungal infection.[1] Some patients positive for HIV antibody have recurrent mouth ulcers that are not caused by obvious infection but are histologically similar to the giant aphthous ulcers seen in Behçet's syndrome. No prospective studies of the prevalence of such ulcers have been performed, but they are often painful and unresponsive to treatment.

Thalidomide, first used as a good hypnotic and sedative, was withdrawn from the market in 1961 because of its teratogenic effects—namely, phocomelia.[2] The drug has been reported to be therapeutic in oral and genital ulceration.[3,4] Adverse reactions of nausea and drowsiness and dose related irreversible neurotoxicity, however, tempered enthusiasm for its use. We investigated its effect in patients with aphthous ulcers who were positive for HIV antibodies.

Patients, methods, and results

We studied seven patients positive for HIV antibody who had had recurrent mouth ulcers for more than two months (table). A biopsy specimen taken from one patient (case 1) showed histological changes suggestive of aphthous ulceration. Swabs of ulcers were taken from all seven patients and cultured for herpes simplex virus and fungi with negative results. The patients were treated with acyclovir 200 mg five times daily for at least 10 days and also used steroid based creams or lozenges without benefit. They all received courses of antibiotics, and five of them used topical tetracycline, without healing of the ulcers. OKT4 cell counts were measured with the Becton-Dickinson Simultest kit.

Thalidomide 100 mg was given at night for two weeks, and thereafter a maintenance regimen of 100 mg every fifth day was followed. Treatment was stopped after six weeks in cases 1, 4, and 5 but was given continuously for three to six months in cases 2, 3, 6, and 7. The mouth ulcers healed rapidly in all seven patients. In three cases treatment was initially associated with drowsiness, and the dose was reduced to 50 mg. In the patients who received only six weeks' maintenance treatment the ulcers recurred between one and five months after the end of treatment. In the four patients whose treatment was continued no relapses were noticed. No serious adverse effects were seen, and in particular no signs of peripheral neuropathy, during follow up of between three and six months. Two patients took zidovudine before thalidomide and four others subsequently took it with no adverse interactions. No appreciable changes in OKT4 cell count were seen during treatment with thalidomide (table).

Clinical and immunological details of patients positive for HIV antibody with mouth ulceration treated with thalidomide

Case No	Sex	Age (years)	Diagnosis	No of OKT4 helper cells: Before treatment	No of OKT4 helper cells: During treatment	Duration of recurrent ulcers (months)	Time to complete healing of ulcers (weeks)	Time to relapse after treatment stopped (months)
1	M	35	Persistent generalised lymphadenopathy		372	14	2	1
2	M	33	Persistent generalised lymphadenopathy	270	280	4	1	
3	M	32	*Pneumocystis carinii* pneumonia	6	15	17	6	
4	M	38	Cytomegalovirus encephalitis (died after treatment)	7	4	26	2	3
5	M	43	*Pneumocystis carinii* pneumonia		100	1	1	5
6	F	30	*Pneumocystis carinii* pneumonia, cytomegalovirus oesophagitis	9	4	2	1	
7	M	34	Oesophageal candidiasis	55	76	6	1	

Comment

There is no diagnostic test for aphthous ulcers, but these ulcers all had the typical punched out appearances of aphthous ulcers and responded dramatically to thalidomide after failing to respond to conventional treatment.

Thalidomide has been shown to have a beneficial effect in several conditions such as erythema nodosum leprosum, Behçet's disease, actinic prurigo, and graft versus host reactions. The mechanism is obscure, although immunomodulation has been suggested.[5] Thalidomide seems to have a place in the treatment of resistant aphthous ulceration in patients positive for HIV antibody, but its use in women of childbearing age is totally contraindicated. At present supplies of thalidomide in the United Kingdom are limited, but with its increasing range of therapeutic uses it should become more widely available.

1 Barr CE, Torosian JP. Oral manifestations in patients with AIDS or AIDS-related complex. *Lancet* 1986;ii:288.
2 Burley D. Is thalidomide to blame? *Br Med J* 1961;i:130.
3 Grinspan D. Significant response of oral aphthosis to thalidomide treatment. *J Am Acad Dermatol* 1985;**12**:85-90.
4 Torras H, Lecha M, Mascaro JM. Thalidomide treatment of recurrent necrotic giant mucocutaneous aphthae and aphthosis. *Arch Dermatol* 1982;**118**:875.
5 Moncada B, Baramda ML, Gonzalez-Amaro R, Urbina R, Loredo CE. Thalidomide—effect on T cell subsets as a possible mechanism of action. *Int J Lepr Other Mycobact Dis* 1985;**53**:201-5.

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Correction

Spacer device with face mask attachment for giving bronchodilators to infants with asthma

An editorial error occurred in this article by Dr C O'Callaghan and others (21 January, p 160). In the Patients, methods, and results section ipratropium bromide 50 mg should have been 10 μg released into the spacer, so that five repetitions resulted in a total dose of 100 μg (not 200 mg).