

**LICHENOID ERUPTION OF ORAL MUCOSA AND SKIN  
FROM METHYLDOPA AND CHLORPROPAMIDE :  
A CASE REPORT**

**Kobkan Thongprasom<sup>\*</sup>, Wanee Thaweasap<sup>\*\*</sup>, and Surasak Cheerat<sup>\*\*\*</sup>**

<sup>\*</sup>Department of Oral Medicine, <sup>\*\*</sup>Department of Pharmacology,

<sup>\*\*\*</sup>Department of Oral Pathology, Faculty of Dentistry, Chulalongkorn University,

Bangkok 10330, Thailand.

*A 46-year-old Indian woman had been treated with methyldopa for three months, had the erosive lesions on the buccal mucosa. This patient was then treated with amoxycillin in concomitant with the antihypertensive drug, methyldopa. However, the erosive lesions were still there. She was referred to the Oral Medicine Department, Faculty of Dentistry, Chulalongkorn University by her physician. The lesions were diagnosed to be erosive lichen planus and were treated with 0.1 percent solution of fluocinolone acetonide. It has been documented that methyldopa could induce intraoral membrane reactions; therefore the recommendation to change the antihypertensive drug from methyldopa to be a beta adrenergic blocking drug, atenolol, was given to her physician. After this treatment regime, the erosive lichen planus was gradually disappeared within a period of 2 months. Later, the same patient underwent medical treatment with the oral hypoglycemic drug, chlorpropamide. Following 3 months after treatment, the marked intraoral lesions with generalized skin lesions of lichen planus were aggressively flared up. Together with a dermatologist of Chulalongkorn hospital, both skin and oral lesions were treated and improved within one year. It is suggested, therefore, that the precaution should be taken on the treatment of hypertensive and diabetic patient with*

*methyldopa and chlorpropamide. If it is possible, the changing of these drugs to the others is recommended whenever the oral lesions occur from their side effects. Moreover, lichenoid eruption of oral mucosa due to methyldopa and chlorpropamide has never been reported in Thai patients.*

**KEY WORDS :** oral lichenoid, methyldopa, chlorpropamide, fluocinolone acetonide

### INTRODUCTION

Although the exact etiology of oral lichen planus (OLP) is still unknown, various drugs may induce lichenoid reactions that are clinically and histopathologically identical to the oral lichen planus.<sup>(1,2)</sup> Diverse exogenous drugs such as methyldopa,<sup>(3,4)</sup> chlorpropamide<sup>(5)</sup> and nonsteroidal anti-inflammatory drugs (NSAIDs)<sup>(6)</sup> have been reported to precipitate and exacerbate this condition. Recent studies have confirmed that the T-lymphocytes play the role of cell-mediated immunological disease mechanisms and are involved in the pathogenesis of OLP.<sup>(7)</sup> So these drugs may implicate the initial onset and exacerbations of lichenoid eruption.

The purpose of this case report was to demonstrate both lichenoid eruption of

oral and skin lesions after the administration of antihypertensive and oral hypoglycemic drugs. This report may be useful for the physician to consider before treatment the patients with hypertension and diabetes mellitus. Treatment and management of patients with oral lichenoid lesions were discussed.

### CASE REPORT

A 46-year-old Indian woman with a history of hypertensive (180/110 mm Hg) and fasting blood sugar 119 mg% had been treated with methyldopa 250 mg (Aldomct<sup>®</sup>) by her physician since January 1993. Three months after an initiation of treatment, she complained about severe painful ulceration on the left buccal

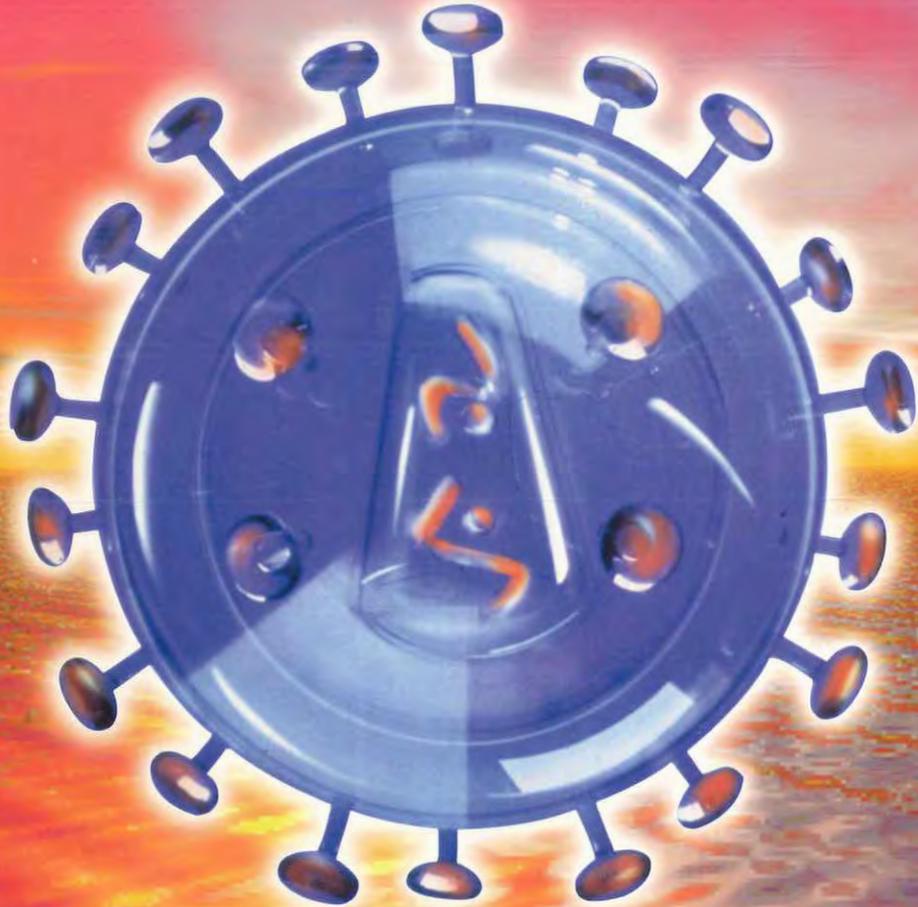
mucosa. An exfoliative cytology examination from the oral lesion showed no abnormality of the cells. This patient had still been treated with methyldopa and amoxicillin (Ibiamox<sup>®</sup>) 500 mg four times a day but there was no improvement. In June 1993, she was referred to the Oral Medicine Department, Faculty of Dentistry, Chulalongkorn University.

By clinical examination, no skin lesion was found. Oral lesions were erosive on both right and left buccal mucosa with white striae size ~5x3 cm (Fig. 1). She complained of severe pain, difficulty in chewing and bleeding when brushing. Biopsy specimen was taken from the left buccal mucosa and histopathologic examination confirmed the diagnosis of erosive lichen planus. Then the other antihypertensive drug was recommended to her physician instead of methyldopa. After that, atenolol (Tenormin<sup>®</sup>) 50 mg daily had been used to treat this patient and at the same time topical steroid-fluocinolone

acetone 0.1% solution was used for treatment of oral lesions. In August 1993, the right and left buccal mucosa were improved and healing was almost complete (Fig. 2). Unfortunately, her blood sugar elevated and chlorpropamide (Diabenes<sup>®</sup>) was administered 250 mg daily by her physician. In July 1993, skin lesions were first recognized as dusky pink itchy papules with white scale at the wrist of hands and the soles. In December 1993, the oral lesions were severely flared up with extensive erosive area, white striae and some pseudomembrane covered on the surface of the lesion (Fig. 3). Skin lesions aggressively developed on both arms, legs, buttocks and back (Fig. 4,5). The patient was referred to the dermatologist at Chulalongkorn Hospital for skin biopsy and treatment. Skin lesions were diagnosed as lichen planus. One year after treatment both skin and oral lesions had improved and the patient dropped out from the clinic.

# HIVID<sup>®</sup>

zalcitabine, ddC



**Roche : Helping people with HIV**

*Further information is available on request*



**Roche Thailand Ltd.**

19th floor Rasa Tower, 555 Phaholyothin Rd., Ladyao, Chatuchak, Bangkok 10900.

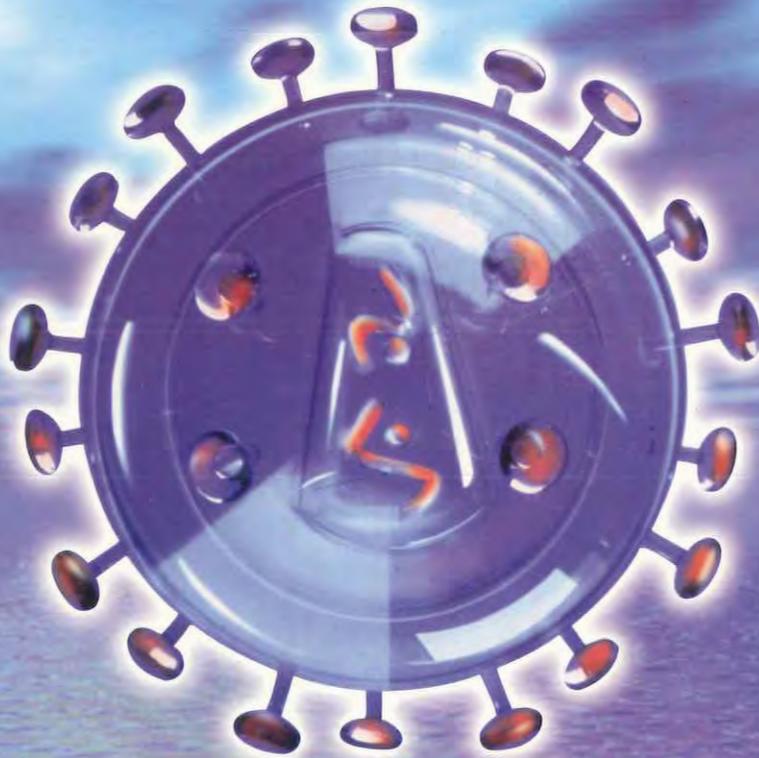
Tel. 937-0444 Fax. 937-0383

*For medical profession only*

# **INVIRASE<sup>®</sup>**

(saquinavir)

## **A Proteinase inhibitor**



## **An Advance in HIV Treatment**

*Further information is available on request*

**Roche**

**Roche Thailand Ltd.**

19th floor Rasa Tower, 555 Phaholyothin Rd., Ladyao, Chatuchak, Bangkok 10900.  
Tel. 937-0444 Fax. 937-0383

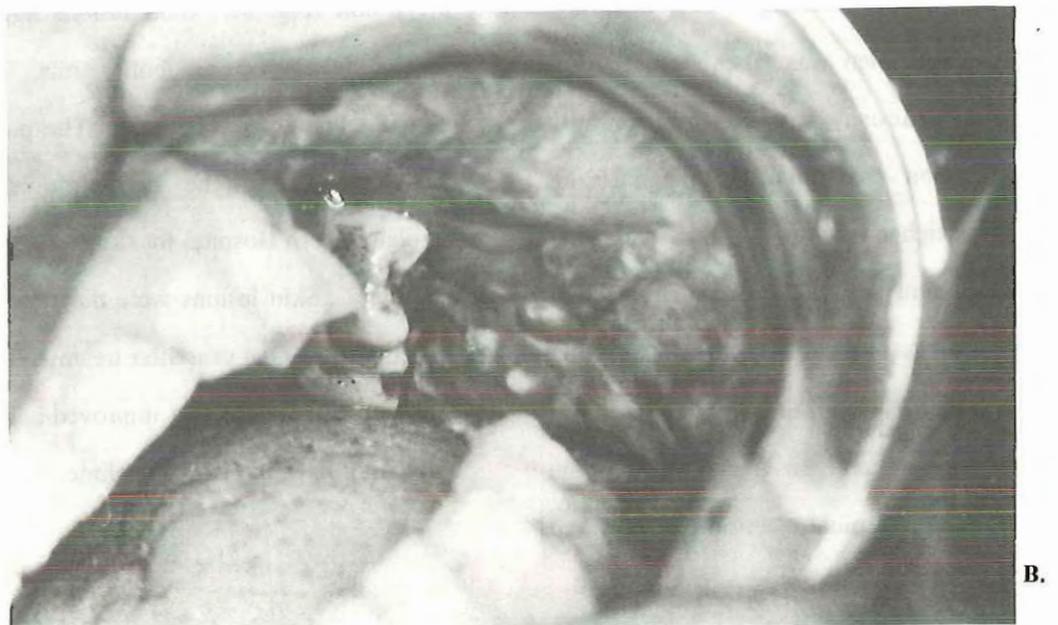
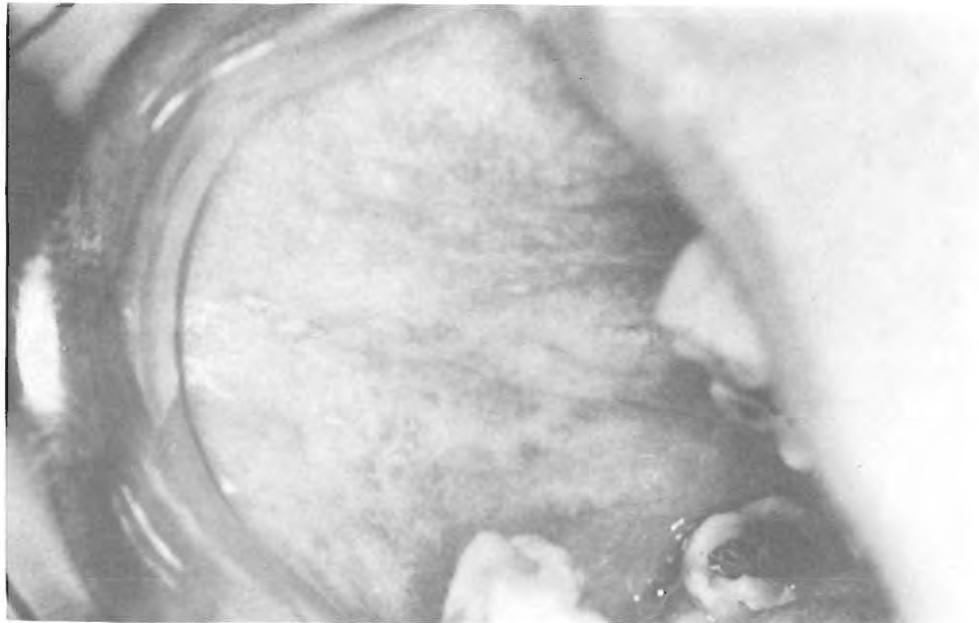


Fig. 1 Erosive area surrounded with keratotic white lesion on the right (A) and left buccal mucosa (B).

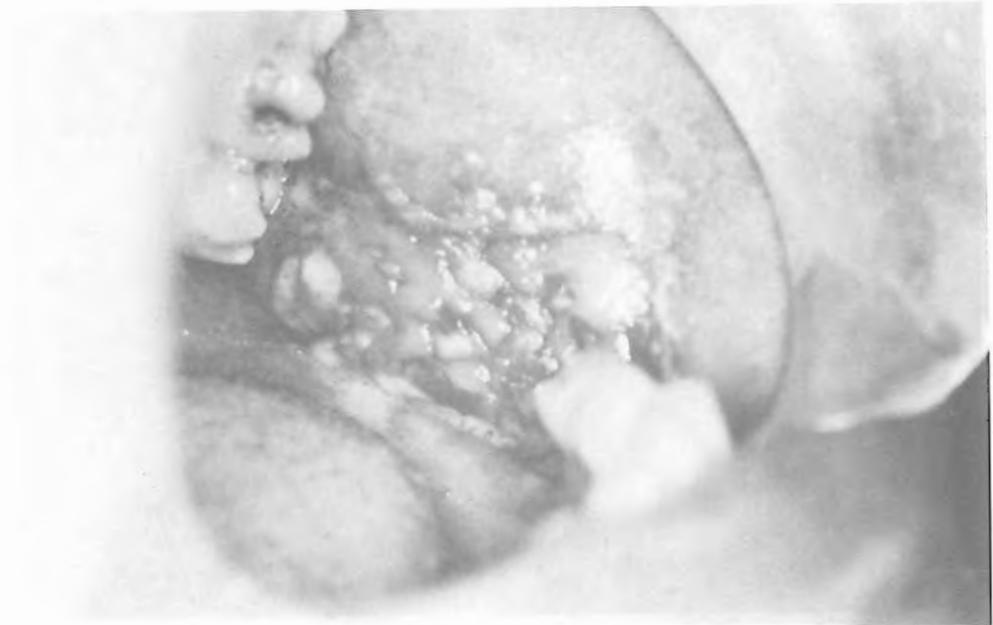


A.



B.

Fig. 2 Right (A) and left (B) buccal mucosa showed improvement of the lesion after treatment with fluocinolone acetonide 0.1 % in solution.



**Fig. 3** Severe flared up lesion on the left buccal mucosa after administration of chlorpropamide.



**Fig. 4** Skin lesions on the buttocks with white scale on top of the lesions.



Fig. 5 Generalized dusky pink papules on the back.

### DISCUSSION

Various drugs have been found to be able to induce lichen planus or lichenoid reactions. They may act as exogeneous agents in upregulated expression of heat shock protein (HSP) by stressed oral keratinocytes followed by tissue damage and then induce OLP lesions.<sup>(8)</sup> So

methyldopa and chlorpropamide play a potential role of the initial onset and exacerbations of this case. Drug such as methyldopa which is commonly used in the treatment of hypertension has been reported to have relationships with lichenoid reaction.<sup>(9-12)</sup> This drug, therefore, should be considered its side effect of lichenoid eruption before use. Medico-dental relationship is found to be very important for the best result of treatment. The physician reported a clear medical history of this patient and changed methyldopa to atenolol. Topical steroid-fluocinolone acetonide 0.1% solution was found to yield a good result for the treatment of oral lichenoid lesions at the period of withdrawal methyldopa. Chlorpropamide was also a medication related to lichenoid lesions.<sup>(5,13)</sup> So both oral and skin lesions were severely flared up possibly as a result of the induction of chlorpropamide. Although the nature of lichen planus or lichenoid lesion was found difficult to be treated successfully,<sup>(14-18)</sup> various forms of steroids have been widely used to reduce

pain and inflammation.<sup>(19-24)</sup> Moreover, it is important and reasonable to advise the physician that there may be some clinical benefit in changing medication from methyl dopa and chlorprolamide to the others if possible. Patients with skin lesions eruption should consult the dermatologist and should be advised to return to clinic for periodic reevaluation. In our knowledge, there are no previous reports about lichenoid eruption on the oral mucosa due to methyl dopa and chlorpropamide in Thai patients.

#### ACKNOWLEDGMENTS

We would like to express our sincere thanks to the staff of the Dermatology Unit, Faculty of Medicine, Chulalongkorn Hospital.

#### REFERENCES

1. Jones JH, Mason DK. Oral manifestations of systemic disease. 1st ed. London:W.B. Saunders Co, 1980 : 459.
2. Scully C, Elkom M., Lichen planus : review and update on pathogenesis. *J Oral Pathol* 1985 ; 14 : 431-458.
3. Holt PJ, Navaratnam A. Lichenoid eruption due to methyl dopa. *Br Med J* 1974 ; 3 : 234.
4. Stevenson CJ. Lichenoid eruptions due to methyl dopa. *Br J Dermatol* 1981 ; 85 : 600.
5. Dinsdale RCW, Ormerod TP, Walker AE. Lichenoid eruption due to chlorpropamide. *Br Med J* 1968 ; 1 : 100.
6. Hamburger J, Potts AJC. Non-steroidal anti-inflammatory drugs and oral lichenoid reactions. *Br Med J* 1983 ; 287 : 1248.
7. Walsh LJ, Savage NW, Ishii T, Seymour GJ. Immunopathogenesis of oral lichen planus. *J Oral Pathol Med* 1990 ; 19 : 389-96.
8. Sugerman PB, Savage NW, Xu LJ, Walsh LJ Seymour GJ. Heat shock

- protein expression in oral lichen planus. *J Oral Pathol Med* 1995 ; 24 : 1-8.
9. Burry JN. Ulcerative lichenoid eruption from methyldopa. *Arch Dermatol* 1976 ; 112 : 880.
  10. Hay KD, Read PC. Methyldopa as a cause of oral mucosa membrane reactions. *Br Dent J* 1978 ; 145 : 195-203.
  11. Brook SL. Lichenoid reaction of oral mucosa and skin to methyldopa. *J Oral Med* 1982 ; 37 : 42-44.
  12. William BG, Brook S. Oral drug reaction to methyldopa. *Oral Surg* 1983 ; 56 : 375-377.
  13. Barnett III, Barnett SM. Lichenoid drug reactions to chlorpropamide and tolazamide. *Cutis* 1984 ; 34 : 542-544.
  14. Sloberg K, Hersle K, Mobacken H, Thilander H. Topical tretinoin therapy and oral lichen planus. *Arch Dermatol* 1979 ; 115 : 716-718.
  15. Bagan JV, Sifverstre FJ, Mestre S, Gisbert C, Bermejo A, Agramunt J. Treatment of lichen planus with griseofulvin-report of seven cases. *Oral Surg Oral Med Oral Pathol* 1985 ; 60 : 608-610.
  16. Urata M, Yosida H, Yanagawa T, et al. Interferon activity and its characterization in the sera of patients with premalignant lesions arising in oral mucosa. *Int J Oral Maxillofac Surg* 1986 ; 15 : 134-147.
  17. Horch HH, Gerlach KL, Schaefer HE. CO<sub>2</sub> laser surgery of oral premalignant lesions. *Int J Oral Maxillofac Surg* 1986 ; 15 : 19-24.
  18. Camisa C, Allen CM. Treatment of erosive lichen planus with systemic isotretinoin. *Oral Surg Oral Med Oral Pathol* 1986 ; 62 : 393-396.
  19. Tyldesly WR and Harding S. Betametasone valerate aerosol in the treatment of oral lichen planus. *Br J Dermatol* 1977 ; 96 : 659-662.
  20. Zegarelli DJ. Multimodality steroid therapy of erosive and ulcerative oral lichen planus. *J Oral Med* 1983 ; 38 : 127-130.
  21. Pedersen A, Klausen B. Glucocorticosteroids and oral medicine *J Oral Pathol* 1984 ; 13 : 1-15.
  22. Vincent SD, Fotos PG, Baker KA Williams TP. Oral lichen planus The

- clinical, historical, and therapeutic features of 100 cases. *Oral Surg Oral Med Oral Pathol* 1990; 70 : 165-171.
23. Thongprasom K, Luangjarmekorn L, Sererat T, Taweessap W. Relative efficacy of fluocinolone acetonide compared with triamcinolone acetonide in treatment of oral lichen planus. *J Oral Pathol Med* 1992 ; 21 : 456-458.
24. Lozada - Nur F, Miranda C, Maliksi R. Double - blind clinical trial of 0.05% clobetasol propionate ointment in orabase and 0.05% fluocinonide ointment in orabase the treatment of patients with oral vesiculoerosive diseases. *Oral Surg Oral Med Oral Pathol* 1994 ; 77 : 598-604.