

LETTER TO THE EDITOR

Patient with oral lichen planus successfully treated with irsogladine maleate

Dear Editor,

We herein describe a patient with oral lichen planus (OLP) treated successfully with irsogladine maleate (IM), a mucosal protective agent for gastritis and peptic ulcers.

An 86-year-old Japanese woman visited our hospital for the evaluation of erosions of the oral mucosa that had lasted for 2 months. She complained of difficulties eating due to intense oral cavity pain. Physical examination revealed multiple painful erosions on her lower lip, tongue and buccal mucosa. Atrophic erythematous lesions with fine white radiating striae at the periphery were also noted (Fig. 1a). A biopsy specimen from the lower lip revealed mild hyperkeratosis with a focal ulcer, sawtooth-like epithelial ridges, vacuolar degeneration of the basal layer and band-like lymphocytic infiltration in the upper layer of the lamina propria (Fig. 1b). Our diagnosis was OLP. Because her mucosal lesions showed only limited response to 3-week application of topical triamcinolone acetonide and her pain persisted, we

added IM. Her oral lesions and pain improved remarkably in 5 weeks (Fig. 1c).

Oral lichen planus is a chronic oral mucosal disease with a higher prevalence in women. It is a localized autoimmune disease induced by T-cell dysfunction. Corticosteroids are the first treatment choice; although they ameliorate the symptoms of OLP, the relapse rate is high. The repeated or long-term use of corticosteroids can have adverse effects. While calcineurin inhibitors and retinoids have also been used, they fail to treat OLP reliably and satisfactorily.

Irsogladine maleate is used in patients with gastritis and peptic ulcers. The loss of gap junctional intracellular communication is responsible for these gastric disorders.¹ A major mode of IM action is to enhance the function of intercellular communications through the gap junctions between gastric epithelial cells.² *In vitro*, IM enhances the function of gap junctions through a rise in intercellular pH mediated by Na^+/H^+ exchangers and through the phosphorylation of connexin by

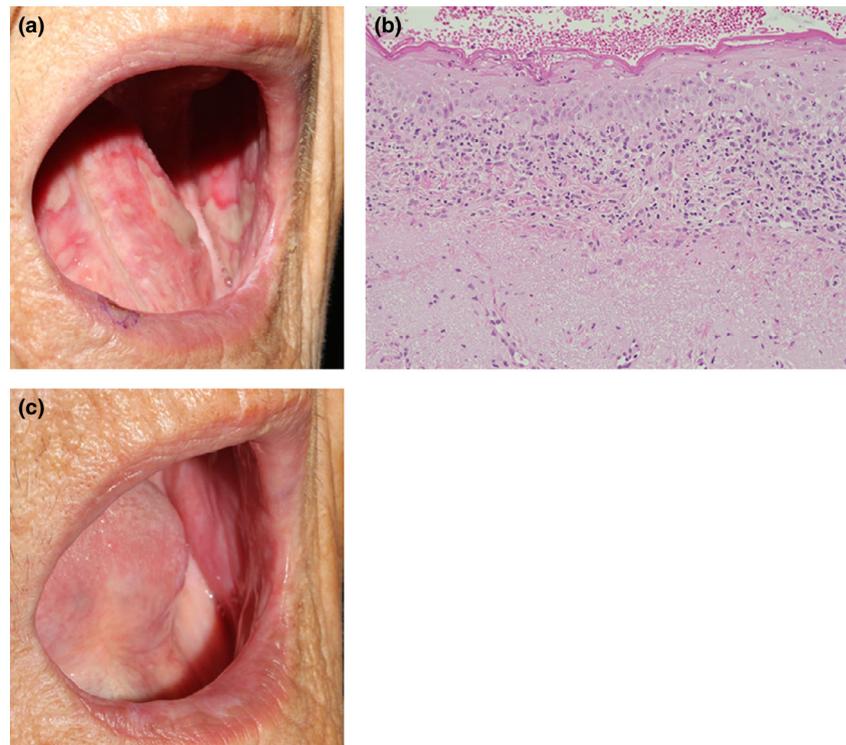


Figure 1. (a) Initial clinical presentation. Note extensive erosions on the tongue and oral mucosa. (b) Histopathological examination of the lower lip revealed mild hyperkeratosis, saw-tooth epithelial ridges, vacuolar degeneration of the basal layer in the epidermis, band-like lymphocytic infiltration and leukostasis (hematoxylin–eosin, original magnification $\times 200$). (c) Clinical presentation after 5 weeks of treatment with irsogladine maleate.

cyclic adenosine monophosphate. These cellular mechanisms may underlie the potent clinical effect of IM.

Irsogladine maleate is also useful for aphthous stomatitis (AS). Hara *et al.*³ demonstrated the presence of connexins 26 and 32, components of the gap junction, in the oral mucosa and showed the therapeutic effectiveness of IM on AS; it also lowered the expression of connexin 26 in patients with OLP. Taken together, it is suggested that IM may restore the function of gap junctions and lead to clinical improvement of OLP as well as gastritis, peptic ulcers and AS.

Other studies detected abnormal expression patterns of inflammatory cytokines such as interleukin (IL)-1, IL-8, γ -interferon and tumor necrosis factor (TNF)- α in lesions, saliva, serum and peripheral blood mononuclear cells from patients with OLP.⁴ Zang *et al.*⁵ reported that IM exerts its protective effect on indomethacin-induced gastric injury by suppressing mucosal TNF- α , IL-1 β and IL-8 production. Thus, IM may improve OLP by inhibiting the production of mucosal pro-inflammatory cytokines.

We attribute the successful IM treatment of our OLP patient to the drug-induced improvement of gap junctional function and the inhibition of pro-inflammatory cytokine production in the oral mucosa.

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REFERENCES

- 1 Maes M, Crespo YS, Willebrords J, Cogliati B, Vinken M. Connexin and pannexin signaling in gastrointestinal and liver disease. *Transl Res* 2015; **166**: 332–343.
- 2 Akagi M, Amagase K, Murakami T. Takeuchi Irsogladine: overview of the mechanisms of mucosal protective and healing-promoting actions in the gastrointestinal tract. *Curr Pharm Des* 2013; **19**: 106–114.
- 3 Hara A, Murata T, Uemura R *et al.* Identification of connexins in human oral mucosa and therapeutic effect of irsogladine maleate on aphthous stomatitis. *J Gastroenterol* 1999; **34**: 1–6.
- 4 Lu R, Zhang J, Sun W, Du G, Zhou G. Inflammation-related cytokines in oral lichen planus: an overview. *J Oral Pathol Med* 2015; **44**: 1–14.
- 5 Zhang X, Tajima K, Kageyama K, Kyoji T. Irsogladine maleate suppresses indomethacin-induced elevation of proinflammatory cytokines and gastric injury in rats. *World J Gastroenterol* 2008; **14**: 4784–4790.