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Steroid Therapy in Oral Lichen Planus

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Abstract

Oral lichen planus (OLP) is a chronic inflammatory disease characterized by cellular-mediated inflammatory reactions which render apoptotic epithelial cells and degeneration of the basal epithelial layer. Eighteen volunteering cases of OLP were scheduled, after getting their informed consents, to be reported in this study. All of them were diagnosed histologically. The diagnosis was confirmed via immunofluorescence. Another incisional sample was scheduled after finishing the recruited treatment. The patient histological findings were contrasted, before and after treatment, to ten cases of non-lesional archival cases of oral mucosa as a control group. Results revealed no difference in the response to the pharmaceutical form of steroids used in treating OLP. Although steroid therapy is the mainstay treatment of OLP, adjuvant treatment modalities should be recruited for improving the healing process.

Keywords: Oral lichen planus; Steroid therapy; Injectable intralesional steroids; Triamcinolone acetonide; Betamethasone

Introduction

Oral lichen planus (OLP) is a mucocutaneous disease characterized by a cellular inflammatory infiltrate enriched in CD4+ cells, by the presence of acidophilic bodies that may represent apoptotic epithelial cells, and by vacuolating degeneration of the basal epithelial layer [1].

Clinically, OLP is most commonly encountered in the buccal mucosa of middle-aged females more frequently than of males. OLP can also be noted on the tongue, the gingiva and lips. Of the configuration of such a white lesions, the reticular form, which is characterized by numerous interlacing white keratotic lines or striae (so-called Wickham's striae) that produce an annular or lacy pattern, is the most frequent pattern. The plaque form of lichen planus tends to resemble leukoplakia clinically but has a multifocal distribution with a predilection to the dorsum of the tongue and the buccal mucosa. The erythematous or atrophic form of lichen planus appears as red patches with fine white striae. It may be seen in conjunction with reticular or erosive variants. In the erosive form of lichen planus, the central area of the lesion is ulcerated. A fibrinous plaque or pseudomembrane covers the ulcer. The bullous variant is generally short lived and, on rupturing, leaves a painful ulcer. Lesions are usually seen on the buccal mucosa, especially in the posterior and inferior regions adjacent to the second and third molars. Cutaneous representation of lichen planus, if evident, is characterized by the presence of small, violaceous, polygonal, flat-topped, pruritic papules on the flexor surfaces of the forearm and anterior tibial surfaces [2].

Although several cases were reported to be refractory to steroids, tacrolimus, pimecrolimus, thalidomide, low-level laser therapy, photodynamic therapy, and surgical excision were suggested. Notwithstanding, these treatment options are not approved in randomized controlled trials and do not have a long-term safety profile. Surgical excision, cryotherapy, CO_2 laser and Nd:YAG laser have all been used for treatment of OLP. In general, surgery is reserved for removal of dysplastic areas in patients at high risk. The well recognized Koebner phenomenon would be a contraindication to more frequent use of these techniques [3]. There is a *bona fide* risk that oral squamous cell carcinoma will develop in oral lichen planus, but this risk is very low [2]. This study contrasts three routes of applying steroid therapy in treating OLP: topical, systemic and interalesional steroid administration.

Patient and Methods

Eighteen volunteering cases of OLP were scheduled, after getting their informed consents, to be reported in this study. All of them were diagnosed histologically. The diagnosis was confirmed via immunofluorescence. Another incisional sample was scheduled after finishing the recruited treatment. The patient histological findings were contrasted, before and after treatment, to TEN non-lesional archival cases of oral mucosa as a control group. The submitted cases were subcategorized into three groups. **Group 1** included six cases which were treated via interalesional triamcinolone acetonide (ITA) injection, 5-10 mg/mL weekly or for 4 weeks (Cases 1-6). **Group 2** included another six cases which were treated via topical application of betamethasone (Cases 7-12) while the last six cases, **Group 3**, were treated via systematic glucocorticosteroid (daily 30 mg Hostacortin-H® for two weeks). One-way ANOVA, chi-square, Mann Whitney U tests were applied when indicated. Statistical significance was coined when p-value was less than 0.05.

Results

The average age of the studied case was 43.38 (SD=10.78). Of these, 9 cases showed a bilateral reticular pattern (50%). Seven cases revealed atrophic (n=4) and plaque patterns (n=3) [(22%), (17%)]. Single cases demonstrated bullous (6%) and ulcerative (erosive: 6%) patterns as shown in Table 1.

The different lines of treatment rendered a dramatic healing effect clinically and histologically. However, the improvement was not statistically significant as regards the used treatment line. The histological changes are represented in Table 2. Histologically, all cases showed a remarkable decrease in the accruement of the inflammatory

infiltrates. However, the subepithelial lymphocytic population remained, in a significant configuration, persistent.

	Age	Gender	Site	Pattern	Association with Diseases	Treatment
Case # 1	23	M	BM	Ulcerative	None	ITA
Case # 2	45	F	PM, ARM	Atrophic	HCV	ITA
Case # 3	21	F	BM, LL	Reticular	LE	ITA
Case # 4	54	F	PM, T	Plaque	HCV	ITA
Case # 5	42	F	BM	Reticular	HCV	ITA
Case # 6	38	F	BM	Bullous	None	ITA
Case # 7	44	F	BM	Reticular	None	TPM
Case # 8	39	F	PM, T	Plaque	None	TPM
Case # 9	33	F	BM	Reticular	None	TPM
Case # 10	51	F	T	Atrophic	DM (II), HCV	TPM
Case # 11	29	M	BM	Reticular	None	TPM
Case # 12	59	M	BM	Atrophic	HCV	TPM
Case # 13	63	M	BM	Reticular	None	HCH
Case # 14	47	M	BM, OC	Reticular	None	HCH
Case # 15	39	F	BM	Reticular	None	HCH
Case # 16	55	F	PM, T	Plaque	DM (II)*	HCH
Case # 17	36	F	BM	Reticular	None	HCH
Case # 18	45	F	BM	Atrophic	None	HCH

ARM: Alveolar Ridge Mucosa; BM: Buccal Mucosa; DM-II: Diabetes Mellitus type II ; F: female; HCH: Hostacortin- H®; HCV: Hepatitis C Virus; ITA: Interalesional Triamcinolone Acetonide; LL: Lower Lip; M: Male; OC: Oral Commissure; PM: Palatal Mucosa; T: Tongue; TBM: Topical Betamethasone; (*): the patient was treated via insulin injection.

Table 1: Clinical data of the submitted cases

Histological Feature	Sample 1		Sample 2
	No. of cases	Degree	Change
Subepithelial lymphoid infiltrate	18/18	Abundant (extending into the CT)	Fewer (epithelial-CT interface)
Hydropic degeneration	4/18	Focal	Less remarkable
Erosion	4/18	Multi-focal	Absent
Atrophy	4/18	remarkable	Less remarkable
Acanthosis	14/18	Variable amounts	Less remarkable
Hyperorthokeratosis	2/18	Thick	Thinner
Hyperparakeratosis	12/18	Abundant	Less remarkable
Aggregate of civatte bodies	2/18	At the BM	Less remarkable
Germinal-like foci	3/18	Deep in the CT	Absent

Table 2: Histological features in the submitted cases

Discussion

Oral lichen planus is a cell-mediated autoimmune reaction against keratinocytes, extrinsic antigens or metabolites, bound to or expressed by keratinocytes. Keratinocytes, along with T cells, ascertains to mediate basal cell death through triggering of apoptosis [2,3]. Moreover, Langerhans cells, CD1a+ dendritic cells, and macrophages appear to contribute to the virulence of OLP via maintaining a higher level of cytokines. The pharmaceutical forms aside, topical triamcinolone, betamethasone and fluocinolone acetonide have been shown to be effective in small studies, but there have been few placebo controlled trials. Although intralesional triamcinolone acetonide injection, 5-10 mg/mL weekly for 4 weeks, is always preferred in treating ulcerative OLP, hydrocortisone, dexamethasone and methyl prednisolone have been used either [3,4].

Oral lichen planus demonstrates multiple reactions, sometimes resistant, to the treatment lines. Such responses are expected to be multifactorial. Cytological abnormalities, clinical forms of OLP, histological variations, general health condition and association with other diseases are considered exacerbating factors which may complicate the pathological course of OLP [5]. Cytologically, DNA Ploidy analysis, via automated image cytometry, has been suggested to be effective in predicting the malignant changes in non-dysplastic oral lichen planus [6]. Clinically, erosive and erythematous OLP have the greatest malignant potential [7]. Histologically, the dysplastic OLP is natively considered a premalignant condition. Epithelial atrophy and inflammatory cytokine-rich microenvironment associated with OLP or lichenoid reactions, particularly tertiary lymphoid follicles and subepithelial lymphocystic populations, were blamed for tumor promotion. Proinflammatory cytokine production of interleukin 1 (IL-1) leads to activation of several prostaglandin-mediated events, principally prostaglandin E2 level, via the action of the enzyme cyclooxygenase-2 (COX-2) on arachidonic acid [8]. Khan et al indicated that both pro-inflammatory (IFN-g and TNF-a) and immunosuppressive (TGF-b1) cytokines are present in OLP [9].

Concerning the association with other diseases, OLP was associated with a plethora of hepatic and connective tissue diseases. Hepatitis C is most commonly blamed for co-existing with OLP [10-12], especially resistant cases, so that some countries, Italy and Japan, recommended running routine screening to patients with OLP for hepatitis C and other liver abnormalities. However, this was not the case in the American patients [8]. This association was anticipated to result from a direct immune aggression of epithelial cells expressing HCV antigens or may be sustained by a cytokine environment favorable to trigger and maintain autoimmune reactions [10-12].

Gels and creams appear to be well accepted by patients, more so than ointments, although they often taste bad and sometimes cause burning or stinging. Elixir forms of corticosteroids, such as dexamethasone or triamcinolone, can be used as an oral rinse for patients with diffuse oral involvement or for elderly patients who may find it technically difficult to apply medication to various active locations of the oral cavity. Unfortunately there is potentially greater risk for systemic absorption and candidal infection with corticosteroid rinses. Commonly corticosteroids are extemporaneously compounded with an occlusive dressing such as Orabase, even though a controlled study suggests that such adhesive bases do not increase efficacy [2,3,13] .

Rödström et al. [14] found no statistically significant correlation between cortisol concentration and stress level. A meta-analysis and a current Cochrane review of the literature provide only little evidence for the superiority of the assessed interventions over placebo for palliation of symptomatic OLP [15]. Supporting these findings, this study could not find any statistical significance of applying steroid therapy in any forms: ITA, topical betamethasone or Hostacortin-H® tablets. Also, this study suggests that subepithelial lymphocytic populations, probably memory cells, are responsible for the recurrence and exacerbation in OLP. Steroid therapy, per se, is not effective in obviating them.

Conclusion

Steroid therapy is the mainstay treatment of OLP. However, adjuvant treatment modalities should be recruited for improving the healing process and decreasing the confluence of inflammatory cytokine-rich populations in the microenvironment of OLP. The epithelial-CT interface may be the genuine complex which is responsible for feeding recurrence.

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