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ORAL LESIONS IN PATIENTS WITH LICHEN PLANUS

Sanja Peršić[1], Liborija Lugović Mihić[2], Jozo Budimir[1], Mirna Šitum[2], Vedrana Bulat[2] and Iva Krolo[2]

[1]School of Dental Medicine, University of Zagreb; [2]University Department of Dermatology and Venereology, Sestre milosrdnice University Hospital, Zagreb, Croatia

SUMMARY – Forty patients with lichen planus admitted to University Department of Dermatology and Venereology, Sestre milosrdnice University Hospital in Zagreb during the 2004-2006 period were assigned to this retrospective study. In these 40 patients (27 female and 13 male), lichen planus was diagnosed on the basis of clinical presentation, laboratory findings and histopathologic analysis. The results obtained indicated an increased prevalence of lichen planus in middle-aged patients (40% of patients were aged 40-60), with a significant female predominance (67.5% *vs.* 32.5%). The majority of patients with lichen planus presented with both cutaneous and oral lesions (62.5%), one third of cases had only cutaneous lesions (35%), and only one patient had isolated oral lesions (2.5%). The initial symptoms in patients with lichen planus usually manifested on the skin (82.5%), in oral cavity (5%), or both simultaneously. Oral lesions usually developed on buccal mucosa (88.5%) in the form of Wickham's striae. All patients were administered topical therapy (corticosteroids, keratolytics), while 55% of patients were given both systemic and topical therapy (corticosteroids, retinoids). Phototherapy was used in 27.5% of patients. The management of patients with oral lichen planus lesions requires multidisciplinary approach including dermatologists and oral pathologists, general practitioners, as well as ENT specialists, internal medicine specialists, and others.

Key words: *Lichen Planus; Mouth Mucosa – pathology; Lichen Planus, Oral – diagnosis; Lichen Planus, Oral – pathology; Lichen Planus, Oral – complications*

Introduction

Lichen planus (lichen ruber planus, lichen), is a non-infectious, pruritic, distinctive papular skin disease of unknown etiology, commonly affecting mucous membranes[1]. This relatively common dermatosis is usually seen in middle-aged patients, with mean age at onset of 40 years, and predominantly affecting women[1-3]. Lichen planus can manifest on the skin, mucous membranes or both. The prevalence of solitary skin lesions is 0.9%-1.2%, and of oral lesions 0.1%-2.2%. According to literature data, oral lesions as the only clinical manifestation occur in 30%-70% of patients with lichen planus[2].

Correspondence to: *Liborija Lugović Mihić, MD, PhD*, University Department of Dermatology and Venereology, Sestre milosrdnice University Hospital, Vinogradska c. 29, HR-10000 Zagreb, Croatia
E-mail: liborija@yahoo.com
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The etiopathogenesis of lichen planus is largely unknown, with several potential etiologic factors[2,4]. Lichen planus has been associated with chronic liver disease, primary biliary cirrhosis, hepatitis B and C, diabetes mellitus, ulcerative colitis, Crohn's disease, a wide variety of medications (thiazides, diuretics, β-blockers, penicillamine, salicylic acid, lithium, ketoconazole, streptomycin)[1,2-7]. Some dental materials have also been reported as potential etiologic factors in oral lichen (allergic or toxic reaction to particular components of dental reconstructive materials)[2].

The characteristic skin lesion is a smooth, flat, reddish-blue, polygonal papule on cutaneous tension lines. The surface of lichen papules shows a network of white lines (Wickham's striae) due to histologic focal thickening of the stratum granulosum[1-3]. Papules may coalesce resulting in lichen skin plaques.

According to clinical features and histopathologic analysis, there are several variants including exanthe-

Table 1. Clinical variants of lichen planus (according to Braun-Falco, 2000)[3]

Lichen planus exanthematicus	multiple skin lesions, potential progression into erythroderma
Lichen planus localisatus	solitary lesions on the neck, penis and lower trunk
Lichen planus linearis	linear streaks of fused papules, potentially resembling nevus verrucosus
Lichen planus hypertrophicus	localized on dorsa of the feet and lower extremities, severe itching
Lichen planus bullosus	very rare, vesicles and bullae that rupture rapidly
Lichen planus erosivus	erosions can evolve into painful ulcerations, slow healing
Lichen planus palmoplantaris	localized on hands and feet, painful keratotic plaques, resistant to therapy
Lichen planus actinicus	photoexposed areas, brown plaques
Lichen planus nodularis	hyperkeratotic papules coalesce into larger nodules
Lichen planus annularis	papules form hyperkeratotic rings with central clearing
Lichen planus atrophicans	localized on lower extremities, well-defined lesions without hair or follicles
"Lichen planus – lupus erythematosus" overlap	variant of these two diseases
Lichen planus follicularis	localized on flexural side of the extremities, hyperkeratotic, follicular papules
Lichen planopilaris	skin lichen lesions on the scalp, more often in females, may evolve into cicatri-
Lichen planus unguium	cial alopecia longitudinal ridges and thickening on the nails, pterygium or "twenty nail dystrophy"

matous, localized, linear, hypertrophic, bullous, erosive, palmoplantar, nodular and many other as well as mucosal forms (oral, genital and perianal), which are often therapy-resistant[9-13] (Tables 1 and 2).

The estimated prevalence of oral lichen planus is about 50% in patients with lichen planus. It commonly presents as slightly raised whitish linear lines (Wickham's striae) on buccal mucosa, lips and occasionally tongue. Squamous cell carcinoma has been reported in patients with non-healing erosive oral lichen lesions. Such lesions are rather therapy-resistant.

Oral lichen planus is usually recognized on time, and can appear in several clinical forms including lichen ruber planus (at the mucosal level), bullous type of oral lichen planus (above the level of oral mucosa), and erosive type of oral lichen planus (below the level of oral mucosa)[2]. Although with heterogeneous clinical presentation, lichen planus has identical characteristic histopathologic features. Papular form of oral lichen planus is characterized by slightly raised papules on buccal mucosa, which may coalesce into Wickham's striae. A lace-like pattern on the buccal mucosa and the tongue is referred to as the reticular form of lichen planus. The plaque form of oral lichen planus is characterized by plaque-like lesions, most frequently on the dorsum of the tongue and gingiva, clinically resembling oral leukoplakia. Annular form arises from expansion of the middle portion of the reticular net, and is characterized by erosive base with elevated hyperkeratotic edges[2].

Atrophic form is characterized by atrophic, inflammatory mucosa, most commonly on the dorsum of the tongue, which eventually becomes smooth, without papillae (post-inflammatory absence of lingual papillae). The bullous form is a very rare variant of oral lichen (2% of patients), characterized by the formation of bullae of oral mucosa, which rupture rapidly, thus forming residual erosive and ulcerative lesions[2].

According to the World Health Organization criteria from 1978, oral lichen planus is considered to be a premalignant lesion which may evolve into squamous cell

Table 2. Clinical forms of lichen planus according to mucosal lesions

Lichen planus mucosae oris	Hyperkeratotic papules, striae, plaques, bullae and erosions on buccal mucosa, lips, gingiva and tongue, precancerous lesions
Lichen planus genitalis	Annular lesions on glans in male patients, hyperkeratotic lesions on labia minora in female patients
Lichen planus perianalis	Wickham's striae, common cause of pruritus, biopsy needed

carcinoma[1-3,14,15]. The prevalence of malignant transformation in longstanding, non-healing oral lichen planus varies from 1.3% to 2.2%[2]. Malignant transformation is more common in atrophic, erosive and ulcerative forms of oral lichen planus, in lesions situated on the ventral side of the tongue or sublingual regions[2,15].

The characteristic histopathologic features of lichen planus include hyperkeratosis, orthokeratosis with focal thickening of the granular layer, acanthosis with intercellular edema, epidermal sawtoothing with keratinization of the basal layer, and liquefactive degeneration of epidermal basal cells associated with a dense band of lymphocytes in the papillary dermis[1-3].

The management of the disease involves topical and systemic therapy[16-19]. Vitamin A derivatives are largely used, e.g., acitretin (25-50 mg/day), with efficient morbistatic effect, or isotretinoin (0.3-0.5 mg/kg/day)[3,18]. Treatment can include systemic corticosteroids, e.g., prednisolone, 20-40 mg/day for several weeks (with gradual dose reduction) or parenteral application of triamcinolone-acetonide[1-3]. Phototherapy is applicable for widespread skin lesions and PUVA bath for largely expanded pruritic forms[1,3].

The majority of our patients were administered topical corticosteroid therapy, frequently under occlusion. Topical corticosteroid therapy is beneficial for oral lichen planus lesions; intralesional corticosteroid therapy can also be very effective (triamcinolone acetonide diluted with topical anesthetic or saline solution at 1:5 ratio)[1]. Oral lesions can also be treated with topical antiseptics, antibiotics, antimycotics, vitamin A, retinoic acid derivatives or keratolytics[2]. Topical corticosteroid lotions and solutions are used for scalp lesions.

Exanthematous lichen planus lesions may relapse in two years, but typically resolve within the same period of time[3,19]. Some lichen planus variants are more therapy-resistant and tend to be more persistent, such as hypertrophic lichen planus, oral lichen, lichen planopilaris and nail lichen planus[1].

The aim of the study was to obtain information regarding oral lesion prevalence in patients with lichen planus, with comparison to other studies. The study included data on age and sex, habits, lesion localization, onset of symptoms and therapy. The results obtained in this study were compared with the results reported by other authors in order to achieve better treatment outcome for patients with lichen planus in the future.

Material and Methods

This retrospective study included patients admitted to University Department of Dermatology and Venereology, Sestre milosrdnice University Hospital in Zagreb for lichen planus during the 2004-2006 period. Medical data kept at Department were used for research purposes. Preliminary evaluation was made for each patient, including medical history, clinical picture and biopsy with histopathologic findings, in order to confirm the diagnosis of lichen planus. Data on patient age and sex, habits, lesion localization, onset of symptoms and therapy were analyzed.

Results

Our study included 40 patients, 27 female and 13 male, diagnosed with lichen planus according to clinical, laboratory and histopathologic findings. According to the results obtained, lichen planus predominantly manifested between the age of 40 and 60 (45%) (Table 3). Lichen planus was more prevalent in female (67.5%) than in male patients (32.5%).

Table 3. Characteristic features in patients with lichen planus

Age (yrs)	20-40	7/40 (17.5%)
	40-60	18/40 (45%)
	60-80	15/40 (37.5%)
Sex	M	13/40 (32.5%)
	F	27/40 (67.5%)
Habits	Smoking	11/40 (27.5%)
	Alcohol	4/40 (10%)
Underlying diseases	Diabetes mellitus	5/40 (12.5%)
	Hypertension	5/40 (12.5%)
	Chronic liver disease	2/40 (5%)
Primary localization	Oral mucosa	2/40 (5%)
	Skin	33/40 (82.5%)
	Both	5/40 (12.5%)

We noticed that skin lesions preceded the onset of oral lesions in 82.5% patients with lichen planus, while oral lesions preceded cutaneous lesions in only 5% of cases; a simultaneous onset of oral and skin lesions was recorded in 12.5% of patients.

Skin lesions were associated with oral lesions in the majority of patients with lichen planus (62.5%) (Table

Table 4. Localization of skin and mucosal lesions in patients with lichen planus

Involvement	Skin	14/40 (35%)
	Oral mucosa	1/40 (2.5%)
	Skin + oral mucosa	25/40 (62.5%)
Most common localization of skin lesions	Trunk	19/39 (48.7%)
	Limbs	32/39 (82%)
	Scalp	3/39 (7.7%)
Time from diagnosis to therapy	<1 month	5/40 (12.5%)
	1 month – 6 months	22/40 (55%)
	6 months – 1 year	5/40 (12.5%)
	>1 year	3/40 (7.5%)

4). One third of our patients had isolated cutaneous lesions (35%), and only one patient had oral lesions alone (2.5%). Oral lesions were most often localized on buccal mucosa (88.5%) and most commonly presented as Wickham's striae (65.4%) (Table 5). All patients were treated by topical therapy (corticosteroids, keratolytics), while approximately one half also received systemic therapy (corticosteroids, retinoids) along with topical agents (Table 6). Phototherapy was used in 27.5% of patients.

Discussion

Lichen planus is a noninfectious, pruritic, papular skin disease, commonly affecting mucous membranes, characterized by the appearance of characteristic smooth, flat, reddish-blue polygonal papules, often with whitish freckles (Wickham's striae). The papules may coalesce, resulting in lichen skin plaques with various clinical features[1-3]. We acquired important clinical experience from the study through monitoring patients with lichen planus during the aforementioned period of time.

Table 5. Mucosal lesions in patients with lichen planus

Mucosal lesions	Oral mucosa	26/40 (65%)
	Genital mucosa	6/40 (15%)
Oral lesions	Localization	
	gingiva	2/26 (7.7%)
	buccal mucosa	23/26 (88.5%)
	tongue	3/26 (7.7%)
	Form	
	plaque	5/26 (19.2%)
	papular	4/26 (15.4%)
	reticular (Wickham's striae)	17/26 (65.4%)
	erosive	3/26 (11.5%)
	bullous	1/26 (3.8%)

Lichen planus predominantly affects middle-aged and elderly people; mean age at onset is 40 years, and shows a female predominance, which is consistent with literature data[1,2]. Our study results indicated that lichen planus primarily affected middle-aged, 40- to 60-year-old individuals (45%). With respect to sex predilection, lichen planus predominantly affected women (67.5% *vs.* 32.5%), which is also consistent with literature reports.

Table 6. Treatment of patients with lichen planus

Therapy	Corticosteroids	34/40 (85%)
Topical	Keratolytics	5/40 (12.5%)
	Antimycotics	4/40 (10%)
	Intralesional corticosteroids	1/40 (2.5%)
Systemic	Corticosteroids	3/40 (7.5%)
	Antihistaminics	15/40 (37.5%)
	Retinoids	5/40 (12.5%)
Other	Phototherapy	11/40 (27.5%)

Lichen planus has been associated with chronic liver disease, primary biliary cirrhosis, hepatitis B and C, diabetes mellitus and other diseases[1-3]. Results obtained from our study revealed lichen planus association with other diseases in several patients, most often in those with diabetes (12.5%), hypertension (12.5%) and chronic liver disease (5%).

There were patients with isolated cutaneous lesions, sole oral lesions or both. According to the literature, the incidence of lichen planus varies. There are data on the incidence of lichen planus on the skin ranging from 0.9% to 1.2%, and of oral lichen planus from 0.1% to 2.2%[2]. According to other sources, solitary oral lesions (without skin manifestations) are common and appear in 30%

to 70% of cases[2]. According to dermatological practice reports, solitary oral lesions are rare. Results obtained in our study showed the majority of patients with lichen planus to have cutaneous and oral lesions (62.5%), while 35% of patients presented with isolated skin lesions, and only one patient had solitary oral lesion (2.5%).

While literature reports describe the occurrence of oral manifestations without skin lesions in 30% to 70% of patients with lichen planus, our results yielded a lower incidence of oral lichen planus (2.5% of patients). The lower incidence of oral lesions in our dermatological practice could probably be attributed to the fact that the majority of patients with oral lesions had been diagnosed and treated exclusively by oral pathologists, whereas those with skin lesions were managed by dermatologists.

With respect to the disease onset, we found oral lesions to have preceded the onset of skin lesions in 5% of our patients, while simultaneous appearance of oral and skin lesions occurred in 12.5% of our patients. According to literature reports, oral lesions appear in 50% of patients with lichen planus, whereas our study showed oral lesions in 65% of patients, predominantly localized on buccal mucosa (88.5%), usually in the form of Wickham's striae.

In some patients, it took several months to up to one year to reach the accurate diagnosis, pointing to the necessity of timely recognition as an imperative for appropriate treatment and prognosis. Several diagnostic procedures such as thorough medical history, clinical picture and histopathologic analysis may frequently be needed to make an accurate diagnosis[2]. On taking medical history we pay due attention to personal habits, systemic diseases or medications in order to identify the etiology of the disease. Treatment of underlying disorders improves the course and prognosis of lichen planus. It is important to specify clinical findings, such as inflammation, hyperkeratosis, size of lesions, and type of lesions (bullae, erosions) in order to establish an accurate clinical diagnosis[2].

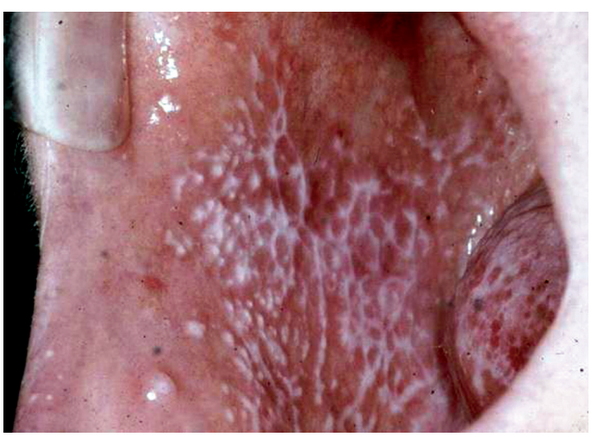

Fig. 1. Oral lesions in lichen planus (www.lindeberg.suite.dk).

There are various therapeutic modalities available for the treatment of lichen planus. All our patients were treated with topical therapy, and about one half received systemic therapy in adjunction to the respective topical management. Phototherapy was used in 27.5% of our patients. Topical corticosteroids and keratolytics under occlusion were often applied. Systemic retinoids were used in 12.5% and systemic corticosteroids in 7.5% of our patients.

Oral lichen planus is a chronic disease characterized by remissions and relapses. The prognosis of oral lichen planus is unpredictable and depends upon the adequacy of care provided to these patients[1-3]. It is of vital importance to treat underlying diseases through specialist care. Various agents can be used to enhance keratinization of the oral epithelium, in order to prolong the time of remission[2]. Malignant transformation of longstanding, non-healing oral lichen planus is possible[2]. Prevention and timely recognition of premalignant oral lesions is mandatory, with follow up, repeat oral lesion biopsies (every 5-12 months) and retinoic acid derivative therapy[2].

In the management of patients with oral lichen planus lesions, multidisciplinary care including a dermatologist, oral pathologist, general practitioner, ENT specialist, internal medicine specialist and other specialized care, is of utmost importance and contributes greatly to the improved prognosis of the disease.

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Sažetak

PROMJENE NA SLUZNICI USNE ŠUPLJINE KOD BOLESNIKA S LIHEN PLANUSOM

S. Peršić, L. Lugović Mihić, J. Budimir, M. Šitum, V. Bulat i *I. Krolo*

Ovo retrospektivno istraživanje obuhvatilo je bolesnike hospitalizirane zbog lihen planusa u Klinici za dermatovenerologiju KB „Sestre milosrdnice“ u Zagrebu u razdoblju od siječnja 2004. do kraja 2006. godine. Obuhvaćeno je 40 bolesnika (27 žena i 13 muškaraca) koji su bolovali od lihen planusa, a dijagnoza je postavljena na temelju kliničko-laboratorijskih pretraga te patohistološkog nalaza. Prema našim rezultatima lihen se najčešće javljao u dobi od 40. do 60. godine (45%), češće kod žena (67,5%) nego kod muškaraca (32,5%). Većina bolesnika je istodobno imala promjene na koži i sluznici (62,5%), kod oko trećine bolesnika promjene su bile isključivo na koži (35%), dok je samo jedan bolesnik imao promjene isključivo na sluznici usne šupljine (2,5%). Bolest je najčešće započinjala na koži (82,5%), zatim na sluznici usne šupljine (5%), dok je istodobni početak pojave promjena na sluznici usne šupljine i koži zabilježen u 12,5% bolesnika. Promjene usne šupljine najčešće su bile lokalizirane na bukalnoj sluznici (88,5%), uglavnom u obliku Wickhamovih strija (65,4%). Kod svih bolesnika se primijenila lokalna terapija (kortikosteroidi, keratolitici), dok je 55% bolesnika uz lokalnu primilo i sistemsku terapiju (kortikosteroidi, retinoidi). Kod 27,5% bolesnika je provedena fototerapija. S obzirom na to da se promjene kod lihen planusa često javljaju na sluznici usne šupljine potreban je multidisciplinski pristup koji uključuje suradnju specijalista dermatovenerologa, oralnog patologa, liječnika obiteljske medicine, ORL, internista i drugih.

Ključne riječi: *Lichen planus; Sluznica usne šupljine – patologija; Lichen planus oralni – dijagnostika; Lichen planus oralni – patologija; Lichen planus oralni – komplikacije*