

Thorough Clinical Evaluation of Skin, as well as Oral, Genital and Anal Mucosa is Beneficial in Lichen Planus Patients

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ABSTRACT

Lichen planus (LP) is a common mucocutaneous disease of unknown aetiology with various geographical prevalence, may be related to some serious disorders such as squamous cell carcinoma and often remains underdiagnosed. The aim of this retrospective study was to thoroughly determine localization and clinical characteristics of LP lesions in a cohort of 173 Slovenian patients in association to the presence of accompanying symptoms and history of potential stressful events. Isolated cutaneous lesions of LP were found in 56.6% and isolated oral LP in 3.5% of patients. Thirty-four percent presented orocutaneous LP, whereas genitocutaneous LP was noted in 1.2%, orogenito-cutaneous LP in 4% and orogenital LP in 0.5% of patients. Underlying stressful events were noted in 36 out of 137 (26.3%) patients. Despite obviously visible localization of the lesions various medical specialists should be familiar with LP and thoroughly examine the complete skin, as well as oral, genital and anal mucosa in each LP patient to avoid a delay in diagnosing this disease and possibly disclose a much serious underlying condition. Psychological support should be offered, if needed.

Key words: lichen planus, localization, stressful events, pruritus

Introduction

Lichen planus (LP) is a common skin disease, affecting 1 to 2% of the population¹. Its incidence is equal to or even greater compared to diseases such as psoriasis². It is a chronic inflammatory dermatosis. Infectious (e.g. hepatitis C virus), autoimmune, metabolic, genetic or psychosomatic factors have been proposed to be involved in its aetiology^{3–5}. Herpes simplex virus 1 DNA was occasionally found in erosive form of OLP⁶. Stressful events are closely related with this disease^{7,8}. The role of dental materials in development of oral LP (OLP) is unclear, but interactions of different dental alloys (polymetalism) as amalgam and various prosthetic alloys could have a negative effect on oral mucosa, resulting as OLP⁹.

Lichen planus is clinically and histologically typical, usually pruritic papular disease which can affect skin and mucosa on various body regions (oral cavity, anogenital region, oesophagus, etc.) (Figures 1 and 2). Lesions

of LP may be described using the six »P«: pruritic, poly-oral, plane, purple papules and plaques. Predominant locations of skin involvement are flexure surfaces of wrists, anterior surface of the lower limbs and lumbar region. While some patients may be asymptomatic, most experience intense pruritus. Lichen planus may also involve the nails, which produces thinning and ridging of nail plate and splitting of distant free edge of nail. Healing with a scar may produce a pterygium. Scalp LP presents with areas of hair loss with keratotic follicular papules and, if left untreated, these areas progress to scarring alopecia and re-growth of hair will not occur. Two types of OLP have been described: reticular and erosive with buccal, tongue and gingival mucosa being predominantly affected. Skin lesions may be disfiguring and involvement of the oral, genital or anal mucosa may be debilitating in severe cases. Erosive oral or anogenital



Fig. 1. Cutaneous lichen planus of a 54-year old female patient. a) Forearm b) Hand.

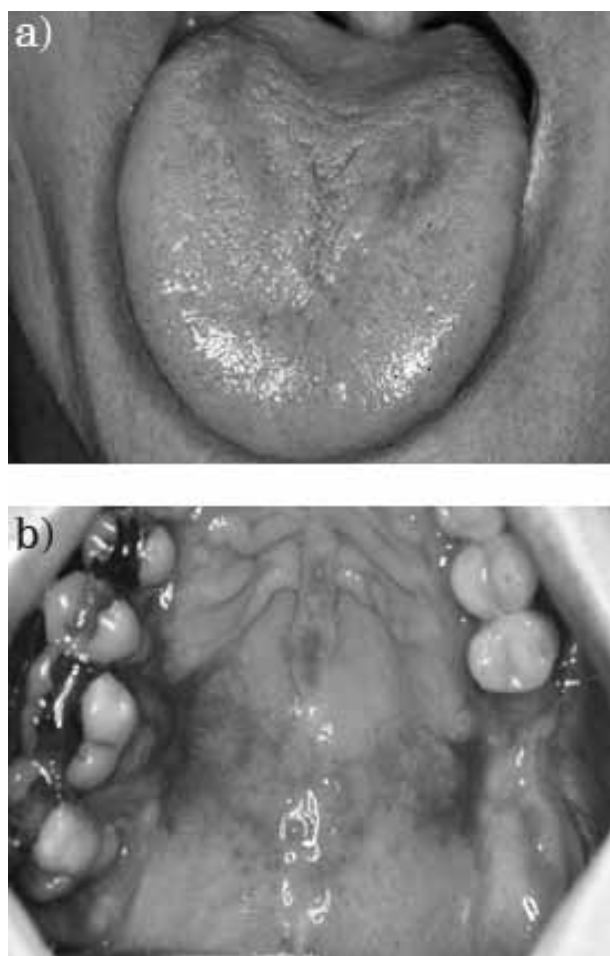


Fig. 2. Oral lichen planus in a 46-year old male patient. a) Tongue b) Hard palate.

LP may be very painful. Long-standing cases may lead to alterations of the genital architecture¹⁰ and squamous cell carcinoma (SCC) has been reported in patients with genital and anal LP^{11–13}. Neoplastic transformation of hypertrophic LP on extremities has also been reported¹⁴, as well as SCC developing within oral cavity⁶. Therefore, follow-up and biopsy of any suspicious lesions are necessary. Moreover, the diagnosis of LP may disclose some other life threatening underlying diseases like chronic hepatitis C.

The only differential diagnosis to be considered in a typical case of LP is that of lichenoid eruptions induced by drugs (antihypertensives, nonsteroidal anti-inflammatory drugs, etc.) or colour developer, both based on the history of triggering agents¹⁵. Less typical cases of LP may be mistaken for plane warts, eczematous eruptions with lichenification from scratching, pityriasis rosea or lichen simplex chronicus¹⁶. The occasional cases of LP without itching must be distinguished from secondary syphilis as well. Some cases of LP may clear spontaneously in a few weeks, but most acute and subacute attacks may last from six to nine months unless treated with potent topical or systemic corticosteroids¹⁵.

The aim of our study was to determine the localization and clinical characteristics of LP lesions in a cohort of Slovenian patients and find out a possible association to some chosen variables including stressful events assuming that the thorough evaluation of the skin and all the reachable mucosa is obligatory.

Methods

We retrospectively studied medical records of all the patients treated for LP at the Department of Dermatovenereology, University Medical Centre, Ljubljana, Slovenia in the period from January 2001 to January 2006. Data from patients' medical records used for analysis were retrieved by one research dermatologist at a single point in time. They comprised basic clinical evaluation of LP patients which was performed by the personal dermatologist of each patient; occasionally patients with mucosal LP were examined by either proctologist, gynecologist or dentist, as well. The analyzed medical records were evaluated for localization of the lesions, the presence of accompanying symptoms and history of possible stressful events prior to LP appearance. Stressful events

TABLE 1
CLINICAL CHARACTERISTIC OF THE LICHEN PLANUS PATIENTS

	Total (N=173)	Males (N=65)	Females (N=108)	p
Age (mean±SE)	50±14	45.8±1.7	52.0±1.3	0.005
Clinical groups of LP				
Mucosal	7 (4.1%)	2 (3.1%)	5 (4.6%)	NS
Cutaneous	98 (56.6%)	37 (56.9%)	61 (56.5%)	
Mucocutaneous	68 (39.3%)	26 (40.0%)	42 (38.9%)	
Pruritus	153 (88.4%)	55 (84.6%)	98 (90.7%)	NS
Hospitalization	48 (27.7%)	22 (33.8%)	26 (24.1%)	NS

p – statistically significant comparison between males and females, NS – not statistically significant, SE – standard error, LP – lichen planus

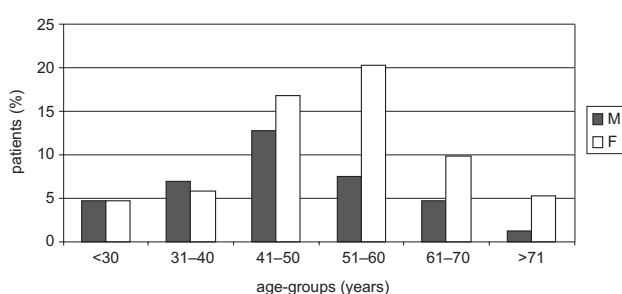


Fig. 3. Distribution of lichen planus in 173 patients according to age groups and sex. F – females, M – males.

were categorized into three groups: underlying disease, job related problems and family matters. The patients suspected of drug-induced lichenoid eruptions were not included. The diagnosis of LP was primarily made clinically by a typical skin and/or mucosal manifestation and, in case of severe, long-lasting, neoplastic suspicious lesions histopathologic confirmation was performed. Lichen planus was classified clinically as mucosal (oral, genital, anal), cutaneous and mucocutaneous. In case of missing data the patients were re-invited to the Department for completion of the records (thorough dermatological examination, history of possible stressful events).

The χ^2 -test and independent samples t-test were used for group comparison, calculated with the Systat 5.0 statistical package. Statistical significance was set at the $p < 0.05$.

The study was approved by the Ethics Committee of the Ministry of Health of Republic of Slovenia.

Results

There were all together 173 patients included, 108 females (62.4%) and 65 males (37.6%), mean age was 50 ± 14.1 years (Table 1). Male to female ratio was 1:1.6. The female patients with LP were significantly older than the male patients ($p = 0.005$). Ninety-seven patients (56.1%) fell in the age group of 41 to 60 years (Figure 3). The youngest patient was a boy of 12 years, and the oldest patient was a 86-year-old female. As shown in Table 1

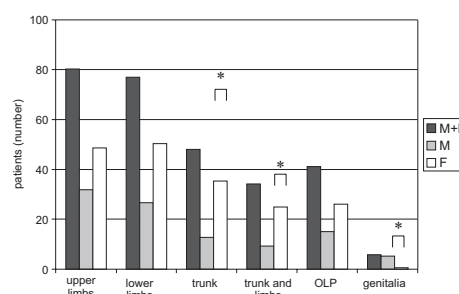


Fig. 4. Body site involvement of lichen planus in 173 patients according to sex. F – females, M – males, * $p < 0.005$.

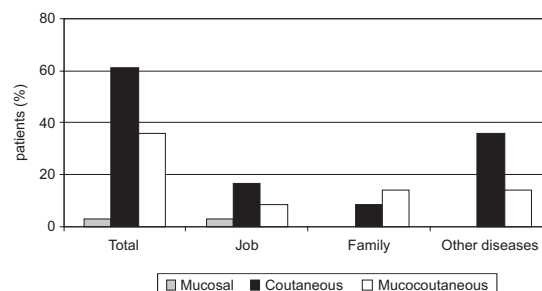


Fig. 5. Stressful events prior to lichen planus appearance according to the three clinical groups of lichen planus patients, N=36.

isolated cutaneous manifestations were present in 98 patients (56.6%), isolated mucosal lesions in 7 patients (4.1%) and a combination of mucosal and cutaneous lesions were observed in 68 (39.3%). Upper limbs were most commonly involved (80.3%), followed by lower limbs (76.9%) and trunk (48.0%) as seen in Figure 4. None of the patients had a face or scalp involvement. Fifty-nine patients (34.1%) presented orocutaneous lesions, two patients (1.2%) had genitocutaneous involvement and 7 patients (4.0%) presented orogenito-cutaneous lesions. Six patients (3.5%) had an isolated OLP, one (0.5%) suffered from orogenital (vulvovaginal-gingival syndrom) mucosal involvement and none had anal lesions. Considering location only, OLP was present in 71 patients (41.0%) and genital appearance in 10 patients (5.8%) (Figure 4). Nail involvement was noted in 11 patients (6.4%).

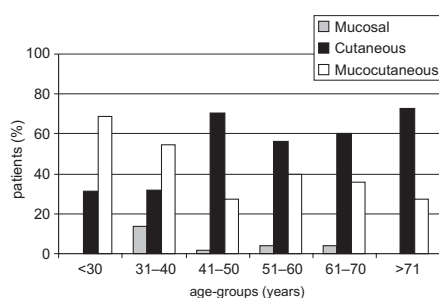


Fig. 6. The three clinical groups of lichen planus patients according to age groups, $N=173$.

In males, genital lesions were significantly more common than in females ($p=0.005$), while the latter presented significantly more generalized lesions ($p=0.042$) (Figure 4).

No statistical differences between the sexes were found comparing the appearance of cutaneous LP and OLP.

Squamous cell carcinoma was not found in any patient.

Forty-eight patients (27.7%) had been hospitalized because of generalized eruption. The hospitalized patients were significantly younger than the outpatient ones ($p=0.043$) and had a significantly larger skin involvement of trunk ($p=0.005$), lower extremities ($p=0.014$) or the whole body ($p=0.005$). There was no significant difference concerning clinical classification (mucous, mucocutaneous, cutaneous group), pruritus, stressful event, OLP and age groups between hospitalized and non hospitalized patients.

Pruritus was the main complaint reported in 153 patients (88.4%), 55 of whom (35.9%) were male and 98 (64.1%) were female. Other sporadic accompanying symptoms (pain, burning) were detected in only a small number of patients.

None of the patients reported dysphagia.

Data on possible stressful events prior to LP appearance were found in 36 out of 137 (26.3%) patients interviewed. Unfortunately, these answers were unavailable for the remaining 36 patients. They were categorized according to stress precursors into three groups. In 18 cases (50.0%) the underlying disease (breast cancer, prostatic disease, depression, ulcerative colitis, respiratory infection, measles, etc.) was the possible stress precursor, in 10 patients (27.7%) job-related problems (retirement, reorganisation at work, conflicted personal relationships etc.) were noted and in eight patients (22.3%) stress events within family (death, childbirth, wedding, divorce, etc.) preceded the eruption of LP. Patients with stress precursors more frequently suffered from cutaneous LP (Figure 5), especially patients with LP on the trunk, compared to patients with no stress predisposition. No such difference was found for OLP. For genital LP the numbers were too small for further evaluation.

No significant difference was found among the three LP clinical groups regarding their age (Figure 6), sex, hospitalization and pruritus.

Familial LP was not observed.

Discussion

Several studies have shown geographical variations in the prevalence of LP from 0.4% in the USA to 6.2% in some African countries^{17,18}. To the best of our knowledge, this is the first study to evaluate a thorough localization of LP in a cohort of patients in the Central Europe with LP prevalence around 1% or less (the prevalence in Slovenia is estimated below 1%) and associate it to some chosen variables^{19–24}. Previously some studies on OLP patients and extraoral localization of LP from the USA and China had been published^{25,26}. However, our group of patients involved dermatologic patients and the comparison with OLP patients remains to be discussed.

Among 173 patients included in the present study, more females (62.4%) than males (37.6%) were involved contrary to the previous studies from Egypt and India where males were predominant^{27,28}. However, our results are in accordance with the study from Greece²⁹ where women with LP were affected in 58.4%. These data from different geographic regions may indicate that some geographical factors like environmental, immunological and/or epidemiological may play an important role in sex distribution of the disease although LP appears to affect females preferentially³⁰.

The median age of female patients with LP was statistically higher compared to the median age of male patients. These results are in accordance with the results of previous studies, where the average age of female patients with LP was higher in comparison to the average age of males with LP²², too. Our study revealed that the average age of the majority of male patients was as much as a decade lower than the average age of the majority of female patients which is comparable to findings of other European studies of LP patients^{31,32}. However, the study from India showed just the opposite result with the average age of all patients being lower and the maximum age range frequency for males being even two decades lower than that of females²⁸.

The portion of isolated skin lesions in our patients (56.7%) was the same as in Bhattacharya et al.²⁸ trial (58.2%, $N=232$). Interestingly enough, in Indian patients the isolated mucosal involvement (25%) and involvement of the nails (15.1%) was much higher compared to the Slovenian ones (4.1% for mucosa, 6.4% for nails). The variations in assessment of LP mucosal involvement might be due to personal dermatologist's opinion during clinical examination of the patient. In the literature³³ the reported average nail involvement was 10% showing that nail changes are most probably not specific or pathognomonic for LP. However, the Greeks report 0.6% whereas the Egyptians showed even 18.0% of nail involvement in their LP patients^{27,29}.

In the study presented from the Department of Dermatology significantly fewer women had genital involvement compared to men which is completely opposite to the results of Eisen et al. reporting genital involvement in 20–25% of women with OLP compared to 3.7% of men²⁵. However, some of our results are comparable to the Indian and Egyptian studies which were focused on

dermatologic patients^{27,28}. In the Indian study similar results concerning OLP (41.8%) and genital (5.2%) involvement with male predominance in the latter were stated²⁸. A much higher genital involvement (24%) was reported by Anbar et al. in the Egyptian LP patients²⁷. Vulvovaginal-gingival and peno-gingival syndromes³⁴ represent typical LP variants that include lesions on two completely separate body regions. Among the studied population one patient with orogenital localization (vulvovaginal-gingival syndrome), two patients with cutaneous and genital lesions and seven with genital, oral and cutaneous LP were found. These cases would have probably not been recognized unless a thorough uniform clinical evaluation had been undertaken in all patients. We agree with Moyal-Barracco et al.³⁵ that the incidence of genital LP is still underestimated because physicians do not routinely examine the anogenitalia of their patients with LP and, secondly, because genital lesions may be asymptomatic or subclinical. However, a long-term follow-up and biopsy of all non-healing ulcerative and papular lesions are recommended as the risk for developing SCC may be increased³⁶. Using strict diagnostic criteria several studies have shown a significant risk of malignant transformation of LP to SCC varying between 0.4 to 5.0%, most probably being independent of clinical type or treatment used³⁷.

Fortunately, none of our patients suffered from SCC. Patients with oral LP should be examined for other mucosal (genital and anal) lesions and in patients with anogenital LP their oral cavity should be inspected^{38–40}. A multidisciplinary approach is often necessary to evaluate the extent of the disease, since the cutaneous manifestation of LP may represent only the top of the iceberg. Studies have demonstrated that one to two thirds^{30,34,41} of patients with cutaneous LP concomitantly present oral lesions, one third of them being asymptomatic³⁰. Similar results were found in our study as 68 patients (39.3%) had orocutaneous or orogenito-cutaneous lesions. Since atrophic and erosive OLP could have a malignant potential, a thorough oral examination, evaluation of the disease and follow up are mandatory to detect carcinomas in the early stages or even prevent them⁴². Such preventive strategy is reliable only if clinical evaluation of oral and anogenital region is routinely performed in all patients with cutaneous LP, since mucosal manifestations usually persist further on despite spontaneous cutaneous remission.

Pruritus was a noteworthy symptom present in 88% of our patients which is comparable to Bhattacharya et al. results (79.3%) and much higher than reported by Egyptians (50%)^{27,28}.

Dickens et al. reported oesophageal LP in nearly one third of patients with oral LP who had performed endoscopy during the screening programme⁴³. Since most of the oesophageal LP appears to be asymptomatic this condition remains unrecognized and underreported, which was most probably the case in our study where no such complaints were found in the group of studied patients. However, one should be aware that chronic oesophageal

pain and oesophageal strictures had been previously mentioned due to untreated oesophageal LP⁴⁴. Therefore, all patients with OLP should be questioned about dysphagia and evaluated by endoscopy, if symptomatic³⁰.

Since LP and OLP in particular are suggested to be one of the psychosomatic diseases, the evaluation of the psychological status should always be involved as a part of a careful history examination⁴⁵. Depression, anxiety and increased stress level (divorce or spouse death) are common in these patients^{46,47} and stress is known to be one of the most frequent causes of acute exacerbations of LP⁴⁸. Various stress precursors of LP were found in 26.3% (36/137) of our studied patients. However, no control group was included in our study to evaluate the data on stressful events. A much smaller portion of patients (5.2%) was aware of a precipitant stressful incident before the onset of disease in the Indian study²⁸. However, in the same study chronic anxiety had been reported as an aggravating factor of LP in 20.3% of Indian patients. The involvement of a psychologist has been suggested in order to optimize the investigation and treatment in a severe disease with symptoms and complications affecting the patient's quality of life⁴⁷.

Since patients with LP vary greatly in severity of symptoms, extent of lesion involvement, their location, as well as psychological vulnerability and exposure to stressful events beside individualized therapy, the patient education on LP should represent an important part of a treatment process. We should reassure patients that LP is not contagious and that the natural course of the disease may last on the average for as long as one to two years, yet symptomatic treatment often relieves itching and improves the appearance. Avoiding skin injuries (scratching, accidents, sunlight) should be encouraged since new lesions may form in damaged skin. As stress and mental disturbance could contribute to LP appearance and reappearance, patients should avoid conflicting situations as much as possible and psychologist counselling may be beneficial along with the conventional therapy⁴⁹. We believe that patient education, treatment, as well as emotional support could provide improvement in patients' quality of life.

Although thorough examination and treatment of skin and mucous LP lesions are expected to be the competence of dermatologists, other medical specialists such as family physicians, dentists, gynaecologists, proctologists, paediatricians, etc. are more or less faced with LP patients at their routine work. It is highly advisable that they should all be involved in complete management of the latter. Our study clearly suggests that they should perform or assure a thorough examination of the skin including oral, genital and anal mucosa in each patient with LP to avoid a delay in diagnosis and proper treatment and even to possibly disclose a much more serious underlying condition such as disorders of autoimmune origin (myasthenia gravis, ulcerative colitis, coeliac disease) and eventual HCV infection^{6,50,51}. Besides, psychological support should be offered, in case the patient's thorough history implicates the need for it.

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KORISNOST TEMELJITE KLINIČKE EVALUACIJE KOŽE TE ORALNE, GENITALNE I ANALNE SLUZNICE KOD PACIJENATA S DIJAGNOZOM LICHEN PLANUSA

SAŽETAK

Lichen planus (LP) uobičajena je sluzokožna bolest nepoznate etiologije s različitom geografskom prevalencijom, a može biti povezana s nekim ozbiljnim poremećajima poput skvamoznog karcinoma stanice i obično ostaje nedijagnostificirana. Cilj ove studije bio je temeljito determinirati lokalizaciju i kliničke karakteristike LP lezija na 173 slovenska pacijenta u asocijaciji s prisutnošću pratećih simptoma i povijesti potencijalno stresnih događaja. Izolirane kožne lezije LP-a pronađene su u 56,6%, a izolirani oralni LP u 3,5% pacijenata. Prisutnos LP na usnoj sluznici je 34%, dok je prisutnost LP na sluznici genitalija zabilježena u 1,2%, na orogenitalnoj koži u 4% i orogenitalni LP u 1,5% pacijenata. Inherentni stresni događaj zabilježen je kod 36 od 137 (26,3%) pacijenata. Unatoč očitij vidljivosti lezija doktori medicine trebali bi biti upoznati s LP-om te temeljito pregledati kožu, jednako kao i oralnu, genitalnu i analnu sluznicu kod svakog LP pacijenta kako bi se izbjegla zakašnjela dijagnoza bolesti i moguće priopćavanje o teškom temeljnom stanju. Psihološka podrška trebala bi također biti ponuđena ako je potrebna.