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Original Research

Dyslipidemia in Lichen Planus: A Case-control Study

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Abstract

Objectives: Lichen planus (LP) is a chronic inflammatory disease that affects the skin, mucous membranes, scalp and nails. It has been reported that diabetes mellitus and dyslipidemia prevalence were higher in patients with LP. However, most of these reports were retrospective, database search, which included patients who were on lipid-lowering drugs. This study aims to conduct a prospective case-control study to investigate the association between LP and dyslipidemia.

Methods: This study was conducted on 49 patients with LP (mucosal or cutaneous) and 99 healthy controls. All patients were subjected to clinical and histological examination, whereas controls were subjected to clinical examination. The variables analyzed were age, sex, tobacco consumption, hypertension, lipid profiles and fasting blood glucose.

Results: Serum levels of triglycerides, total cholesterol and LDL cholesterol were higher in patients with LP. However, there was no significant difference between patients with LP and controls. No significant differences between LP patients and controls were observed with the average age, sex, tobacco consumption and hypertension.

Conclusion: This prospective case-control study demonstrated that dyslipidemia was more common among patients with LP. Physicians should be aware of this association and consider screening them for dyslipidemia.

Keywords: Case-control; lichen planus; dyslipidemia.

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Lichen planus (LP) is an inflammatory dermatosis that is common in the society, involving skin, skin appendages and mucous membranes. LP usually leads to a subacute or chronic course. It was first described by Erasmus Wilson in 1869.[1] The Greek lichen originates from the words "wood moss" and Latin planus "flat/flat". Typical skin lesion of LP is purple-colored flat polygonal papules that are specific to the disease.

LP is a chronic inflammatory skin disease and occurs in the middle age group in both sexes. The average age of onset of the disease is 50-60 years in mucosal and 40-45 years in cutaneous LP forms.[1] There is no significant difference between genders, but studies have reported that oral LP is seen more frequently in women.[2–4]

Epidemiological studies are inadequate due to the lack of definite diagnostic criteria of LP disease, especially because oral LP disease may progress asymptomatically.[5] McCartan and Healy examined 45 studies with available incidence and prevalence data related to oral lichen planus and found age-adjusted standardized prevalence as 1.27% (1.57% in women and 0.96% in men).[6] Currently, increased cardiovascular mortality and morbidity has been proven in psoriatic patients.[7] Long-term release of cytokines due to chronic inflammation which leads to deterioration of lipid metabolism resulting in a decrease in HDL and an increase in triglycerides is considered to be one of the etiologic factors of this increased risk.[8] It has also been reported that lipid/carbohydrate metabolism and adipogenesis are af-

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fected in many skin diseases, such as psoriasis, rosacea and seborrheic dermatiti.[6] Although the exact pathogenesis of LP is not yet known, similar to psoriasis, T cell-mediated autoimmune mechanisms are thought to cause keratinocyte necrosis by initiating the chronic inflammatory process.

The similarity between their pathogenetic factors and the presence of a chronic inflammatory process raises the question of the risk of metabolic syndrome and dyslipidemia in LP. In previous studies, a relationship was found between LP and dyslipidemia[7] and diabetes mellitus.[8,9] However, these studies retrospectively scanned dyslipidemia codes or investigated patients using fibrate and/or statins. We planned a prospective case-control study to examine and shed light on the relationship between LP and dyslipidemia.

Methods

The patient group was composed of patients between the ages of 18-70 with mucosal or cutaneous lesions clinically compatible with histopathologically confirmed LP. The control group was selected from age-, and gender-matched healthy volunteers. Exclusion criteria were determined as using drugs that are known to affect lipid metabolism (fibrate, statins, glucocorticoids, retinoids, immunosuppressive drugs) and having known diagnoses of diabetes mellitus and/or metabolic syndrome.

Histopathologically, the diagnosis of LP was made by the pathologist, with damage and lymphocytic lichenoid interphase reaction in epidermal basal keratinocytes, which are two main pathological findings. Fasting blood glucose, triglyceride (TG), total cholesterol, HDL and LDL levels were measured in venous blood taken from the patient and control groups after 12 hours of fasting. Demographic data, disease duration, smoking and laboratory data were recorded. Dyslipidemia criteria were accepted as TG >150 mg/dL, total cholesterol >200 mg/dL, LDL -C >130 mg/dL, and HDL-C <40 mg/dL "According to the Third Report of the National Cholesterol Education Program Expert Panel on the Detection, Evaluation and Treatment of High Blood Cholesterol in Adults (NCEP ATP III) criteria.[9] Approval of the ethics committee for this study was also obtained.

SPSS 15.0 for Windows program was used for statistical analysis. Descriptive statistics and categorical variables were given as number and percentage, mean, standard deviation, minimum, maximum and median for numerical variables. Since numerical variables did not meet the criteria of the normal distribution, two groups were compared using the Mann-Whitney U test. The rates in the groups were compared with Chi-square tests. Results were expressed with their OR and 95% confidence Interval. Statistical alpha significance level was accepted as $p<0.05$.

Results

The patient group consisted of 49 (28 female and 21 male patients), and the control group comprised of 99 (43 female and 54 male patients) patients. There was no statistically significant difference in the mean age, gender, smoking and hypertension rates of the patient and control groups ($p=0.386$, $p=0.232$, $p=0.116$, and $p=0.775$, respectively). The mean blood glucose level of the patient group was statistically significantly lower than the control group ($p<0.001$ $p=0.022$) (Table 1).

Only three patients (6%) had mucosal involvement, 46 pa-

Table 1. Comparisons between patient and control groups concerning demographic characteristics and blood fasting glucose levels

	Patient Group (n=49)	Control Group (n=99)	p
Age			
Mean±SD (Min-Max)	47.5±13.5 (19-71)	45.5±14.6 (18-79)	0.386
Disease duration (mo) n (%)	8.4±8.3 (0.5-36)		
Gender, n (%)			
Female	28 (57.1)	43 (43.4)	0.116
Male	21 (42.9)	56 (56.6)	
Smoking n (%)			
Nonsmoker	28 (57.1)	59 (59.6)	0.775
Smoker	21 (42.9)	40 (40.4)	
Hypertension n (%)			
No	43 (87.8)	93 (93.9)	0.212
Yes	6 (12.2)	6 (60.1)	
Fasting blood glucose level			
Mean±SD (Min-Max	92.3±12.6 (72-122)	109.7±37.9 (69-339)	<0.001
Fasting blood glucose level n (%)			
<110	43 (87.8)	70 (70.7)	0.022
≥110	6 (12.2)	29 (29.3)	

tients had only cutaneous LP lesions. Considering the subtypes of the disease, 42 patients were identified as classical, four patients as pigmented, three patients as hypertrophic and one patient as actinic LP. When the distribution of the lesions was examined, lesions involved face in 4, upper extremities in 36, lower extremities in 30, and trunk in 18 patients. The mean±SD body surface area involvement of the patients was 2.75±3.54.

In the patient group, HbsAg positivity was detected in three patients and anti-HCV positivity in one patient, while HbsAg was positive in only one patient in the control group. However, this difference was not statistically significant (p=0.75). When concomitant diseases of LP patients were examined, hypertension was detected in 43, allergic asthma in three patients and COPD in one patient. There was no statistically significant difference in the frequency of hypertension compared to the control group (p=0.212).

Hyperglycemia (FBG, ≥110 mg/dL) was detected in six (12.2%) patients with LP, while in 29 (29.3%) patients in the control group. The mean (± SD) values of the blood lipids in the patient group were higher than the healthy group, TG: 136.6±95.8 mg/dL, total cholesterol: 202.9±47.2 mg/dL and LDL: 127.8±36.7 mg/dL. However, this difference was not statistically significant (Table 2). According to the NCEP ATP III criteria, 67.3% (n=33) of the patient and 64.6% (n=64) of the control group had dyslipidemia, the risk rate of dyslipidemia was calculated as 1.128 (95% confidence interval 0.546-2.330).

Discussion

Dyslipidemia and metabolic syndrome have been reported to be more common in patients with LP.[10] In a meta-analysis published in 2016, in which 4733 patients with LP were examined, increases in total cholesterol and LDL values, especially in TG, compared to the control group, but this difference was not statistically significant.[11] However, most of these studies are retrospective trials and LP disease has not been histopathologically proven. In the study conducted by Saleh et al.[12] with 40 patients and 40 controls, the frequency of dyslipidemia was found to be statistically significantly higher in patients with LP. However, since the control group was selected from healthy volunteers without diabetes mellitus or metabolic syndrome, and these patients were not excluded from the LP group, relatively higher results may be obtained from these patients. However, Baykal et al.[10] detected dyslipidemia in 90% of the patients with LP with mucosal involvement and thought that mucosal involvement is a risk factor for dyslipidemia. In our study, lipid levels may have been lower because only concomitant mucosal involvement was seen in three patients. In their retrospective study, Baykal et al. reported that diabetes mellitus was more common in patients diagnosed with LP. Interestingly, in our study, we found higher blood sugar levels in the control group, which may be related to the exclusion of metabolic syndrome patients in the study.

Many factors, such as genetic factors, drugs (NSAIDs, beta-blockers), dental procedures, hepatitis C, autoimmunity and stress, have been implicated, although their etiology is not certain. Antigen-specific and nonspecific mechanisms play a role in the pathogenesis of LP.[13] We did not find any difference between the patient and control groups concerning hepatitis serology. In the antigen-specific mechanism, the immune process is thought to be initiated by the LP-specific endogenous antigen.

The properties of the LP specific endogenous antigen are unknown. It is theoretically thought to be an autoreactive peptide and endogenously stimulates the specific antigen response. Apart from this, drugs, contact allergens, viral or infectious agents may also exhibit exogenous antigen characteristics and cause the stimulation of natural immune response in genetically susceptible individuals.[14] In the development of the disease, both CD4 + helper T cells and CD8 + cytotoxic T cells are activated. Activated CD8 + cytotoxic T lymphocytes make up the majority of T cells in the LP infiltrate.[14] T cell-mediated chronic inflammation is thought to impair adipogenesis. However, it has a shorter duration than chronic skin diseases, which have

Table 2. Comparison between patient and control groups concerning lipid levels

	Patient Group			Control Group			
	Mean±SD	Min-Max	Median	Mean±SD	Min-Max	Median	p
TG (mg/dL).	136.6±95.8	33-518	107	124.3±58.1	37.9-305	115	0.867
Total Cholesterol (mg/dL.)	202.9±47.2	109-363	201	193.5±48.8	93.2-368.7	189	0.199
LDL (mg/dL.)	127.8±36.7	54-259	121.78	119.4±41.0	15.1-253.9	117	0.175
HDL (mg/dL.)	51.2±14.4	30-91.9	48	47.9±14.4	25.9-90.4	45.6	0.145

TG: triglyceride; LDL: low-density lipoprotein cholesterol; HDL: high-density lipoprotein cholesterol.

been found to be associated with dyslipidemia, such as LP, psoriasis, and hidradenitis suppurativa. The disease mostly limits itself within 1-2 years, and rarely, it may progress with chronic recurrences over the years.[15] Therefore, it is less likely to be associated with dyslipidemia.

Four hypotheses have been proposed that predict that autoimmune reaction may take place in LP pathogenesis. These hypotheses include the deficiency of TGF-β 1, which has an immunosuppressive effect, absence of keratinocyte-mediated T cell apoptosis, the maturation of Langerhans cells and the increased expression of keratinocytes and increased expression of heat shock proteins.[13] Regarding humoral immunity, autoantibodies circulating against desmoglein 1 and 3 have been shown in a study and case reports concerning oral erosive LP patients.[16,17] Further studies are needed to prove this relationship. LP is also seen with an increased frequency in people with autoimmune disease (autoimmune chronic active hepatitis, primary biliary cirrhosis). Apart from these, there are studies in which malignancies, diabetes mellitus, ulcerative colitis and other autoimmune diseases (alopecia areata, Hashimoto thyroiditis, Sjögren's syndrome) are associated with LP.[18-21] However, in a prospective case-control study published in 2014 with 130 oral LP and 130 control patients, it was found that there was no increase in the incidence of autoimmune diseases in LP patients.[22] We did not encounter autoimmune disease that was found in our patient group.

The limitations of our study are as follows. Since the rate of dyslipidemia in LP patients may be underestimated, and establishment of a histopathologically confirmed definitive diagnosis of the patients was planned in addition to the difficulty of localization of oral LP based on histopathological examination of biopsy materials, we selected only cutaneous LP patients for our study.

In our study, we found higher mean lipid levels of LP patients than the control patients, but we did not find a statistically significant intergroup difference. Further cohort studies are required to investigate this relationship.

Disclosures

Ethics Committee Approval: The Ethics Committee of Şişli Hamidiye Etfal Training and Research Hospital provided the ethics committee approval for this study (06.03.2018-955).

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References

1. Le Cleach L, Chosidow O. Clinical practice. Lichen planus. N Engl J Med 2012;366:723–32. [CrossRef]
2. Brown RS, Bottomley WK, Puente E, Lavigne GJ. A retrospective evaluation of 193 patients with oral lichen planus. J Oral Pathol Med 1993;22:69–72. [CrossRef]
3. Silverman S Jr, Gorsky M, Lozada-Nur F. A prospective follow-up study of 570 patients with oral lichen planus: persistence, remission, and malignant association. Oral Surg Oral Med Oral Pathol 1985;60:30–4. [CrossRef]
4. Thorn JJ, Holmstrup P, Rindum J, Pindborg JJ. Course of various clinical forms of oral lichen planus. A prospective follow-up study of 611 patients. J Oral Pathol 1988;17:213–8. [CrossRef]
5. Gorouhi F, Davari P, Fazel N. Cutaneous and mucosal lichen planus: a comprehensive review of clinical subtypes, risk factors, diagnosis, and prognosis. ScientificWorldJournal 2014;2014:742826.
6. McCartan BE, Healy CM. The reported prevalence of oral lichen planus: a review and critique. J Oral Pathol Med 2008;37:447–53.
7. Rocha-Pereira P, Santos-Silva A, Rebelo I, Figueiredo A, Quintanilha A, Teixeira F. Dislipidemia and oxidative stress in mild and in severe psoriasis as a risk for cardiovascular disease. Clin Chim Acta 2001;303:33–9. [CrossRef]
8. Wakkee M, Thio HB, Prens EP, Sijbrands EJ, Neumann HA. Unfavorable cardiovascular risk profiles in untreated and treated psoriasis patients. Atherosclerosis 2007;190:1–9. [CrossRef]
9. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III). JAMA 2001;285:2486–97. [CrossRef]
10. Baykal L, Arıca DA, Yaylı S, Örem A, Bahadır S, Altun E, et al. Prevalence of Metabolic Syndrome in Patients with Mucosal Lichen Planus: A Case-Control Study. Am J Clin Dermatol 2015;16:439–45. [CrossRef]
11. Lai YC, Yew YW, Schwartz RA. Lichen planus and dyslipidemia: a systematic review and meta-analysis of observational studies. Int J Dermatol 2016;55:e295–e304. [CrossRef]
12. Saleh N, Samir N, Megahed H, Farid E. Homocysteine and other cardiovascular risk factors in patients with lichen planus. J Eur Acad Dermatol Venereol 2014;28:1507–13. [CrossRef]
13. Roopashree MR, Gondhalekar RV, Shashikanth MC, George J, Thippeswamy SH, Shukla A. Pathogenesis of oral lichen planus-a review. J Oral Pathol Med 2010;39:729–34. [CrossRef]
14. Zhou XJ, Sugerman PB, Savage NW, Walsh LJ, Seymour GJ. Intraepithelial CD8+ T cells and basement membrane disruption in oral lichen planus. J Oral Pathol Med 2002;31:23–7. [CrossRef]
15. Carbone M, Arduino PG, Carrozzo M, Gandolfo S, Argiolas MR, Bertolusso G, et al. Course of oral lichen planus: a retrospective study of 808 northern Italian patients. Oral Dis 2009;15:235–43.

16. Lukac J, Brozović S, Vucicević-Boras V, Mravak-Stipetić M, Malenica B, Kusić Z. Serum autoantibodies to desmogleins 1 and 3 in patients with oral lichen planus. Croat Med J 2006;47:53–8.
17. Kinjyo C, Kaneko T, Korekawa A, Rokunohe A, Aizu T, Matsuzaki Y, et al. Oral lichen planus with antibodies to desmogleins 1 and 3. J Dermatol 2015;42:40–1. [CrossRef]
18. Epidemiological evidence of the association between lichen planus and two immune-related diseases. Alopecia areata and ulcerative colitis. Gruppo Italiano Studi Epidemiologici in Dermatologia. Arch Dermatol 1991;127:688–91. [CrossRef]
19. Bermejo Fenoll A, López Jornet MP. Oral lichen planus and Sjogren's syndrome. 2 cases of association. Av Odontoestomatol 1991;7:29–38.
20. Zaraa I, Mahfoudh A, Sellami MK, Chelly I, El Euch D, Zitouna M, et al. Lichen planus pemphigoides: four new cases and a review of the literature. Int J Dermatol 2013;52:406–12. [CrossRef]
21. Compilato D, Paderni C, Di Fede O, Gulotta G, Campisi G. Association of oral lichen planus with thyroid disease in a Finnish population: a retrospective case-control study: "A different finding from a Mediterranean area". Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2011;111:12–4. [CrossRef]
22. López-Jornet P, Parra-Perez F, Pons-Fuster A. Association of autoimmune diseases with oral lichen planus: a cross-sectional, clinical study. J Eur Acad Dermatol Venereol 2014;28:895–9. [CrossRef]