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Oral Lichen Planus and Celiac Disease: is there any Relationship?

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Abstract

Background: Lichen planus is an autoimmune disorder and is associated with other autoimmune diseases. There is, however, little evidence of the association of oral lichen planus with celiac disease. The aim of this work was to investigate, for the first time, such an association in patients in the city of Mashhad, Iran.

Methods: This case-control study was performed during October 2017 to March 2018 in the department of Oral and Maxillofacial Medicine, Faculty of Dentistry, Mashhad University of Medical Sciences, in Iran. All participants were evaluated for Anti-TTG (IgA) and Total IgA, and in some cases for Anti-TTG IgG. Data were analyzed using SPSS software v.20.

Results: A total of 96 subjects were considered in the study; 32 in the case group, and the rest in the control group. The mean value of Anti-TTG IgA was 0.12 ± 1.51 Au/ml in the oral lichen planus group, while it was 0.57 ± 1.20 Au/ml in the control group with no significant difference (P=0.167). The mean value of the Total IgA was 134.96 ± 42.86 mg/dl in the lichen planus group, and it was 129.85 ± 55.28 mg/dl in the control group, as they differ negligibly either (P=0.639). Moreover, celiac disease was not present in the population.

Conclusions: We showed that there was no celiac disease present in the oral lichen planus patients as well as healthy subjects. Further studies are required to imply or to rule out the association of oral lichen planus and celiac disease.

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Introduction

Oral lichen planus (OLP) is a chronic inflammatory disorder affecting oral mucosa with a variety of clinical conditions, including keratotic, atrophic, erosive, and ulcerative lesions (1). Despite abundant research in the past, the pathophysiology of T-cells and their role in OLP is still not clear (2). OLP is driven by autoreactive T-cells, which are

presumably targeted to the oral epithelium. They stimulate the apoptosis of basal keratinocytes, leading to chronic inflammation (3). OLP is also linked with several diseases, drugs, and infectious agents (4). The etiology of OLP has not been thoroughly recognized so far (4), and the incidence of OLP ranges between 1 and 2% of the population (5).

OLP is associated with various systemic disorders such as diabetes mellitus, hypertension, thyroid diseases, cardiac diseases, and squamous cell carcinoma. It is also associated with autoimmune disorders like primary biliary cirrhosis, chronic active hepatitis, ulcerative colitis, and thymoma. OLP is observed predominantly in individuals above 50 years old, and it increases chances for coincidental systemic diseases such as celiac disease (6).

Oral stigmata might be a good indicator of systemic diseases like celiac, e.g., during a simple oral examination. OLP is probably a presentation of celiac disease (7). In some rare cases, association of OLP and celiac disease have been reported (8, 9). The first reported case of association of OLP and celiac is in a 70- year old male with a biopsy-proven erosive OLP (10). Celiac disease is a lifelong abnormal immune system sensitivity disorder provoked by the use of gluten, a protein in wheat, rye and barley, in genetically susceptible people (11, 12). Remarkable progression in distinguishing celiac disease during the last decade has demonstrated. Celiac disease possess a heterogeneous, wide, and often unsuspected range of clinical presentations (13).

Diagnostic serological tests for celiac disease include IgA anti-transglutaminase antibodies (Anti-TTG IgA) and IgA endomysial autoantibodies (EMA) and total IgA, with a sensitivity and specificity greater than 90%. The TTG antibody test is currently the test of choice and is widely available. IgA deficiency is common in celiac disease and, hence, total serum IgA level is recommended to be measured to avoid a false-negative result. Patients with a positive TTG antibody test should be referred for an endoscopic biopsy of small intestine for confirmation of the diagnosis (14).

Celiac disease subjects are more affected by other immune-mediated disorders like OLP compared to the general population (15). There are many cases, who have not been aware of having celiac disease until their middle age (16). In a review, the prevalence of celiac disease in Iran has been estimated to be 1% (17). To our knowledge, there is only one study that evaluates the association of celiac disease with OLP in a case control investigation (14). There is, however, little evidence regarding such an association until yet. Due to the high prevalence of OLP in the city of Mashhad, Iran (18), as well as the association of OLP and autoimmune disorders, we decided to investigate the association of oral lichen planus with celiac disease in Mashhad, Iran.

Material and Methods

Patients

This case-control study was accomplished during October 2017 to March 2018 in the Department of Oral and Maxillofacial Medicine, Faculty of Dentistry, Mashhad University of Medical Sciences, in Iran. Patients with OLP lesions who referred to the clinic were included in the study, and they admitted the written consent for participation. Inclusion criteria in the case group were to be above 18 years old, and to be diagnosed with OLP upon histopathological confirmation. We excluded patients diagnosed with disorders accompanied by lichen planus, like hepatitis C and lichenoid reactions. In the control group, we included healthy volunteers

referred to our department for dental procedures. We calculated the sample size according to Cigic *et al.* (14), and considered at least 32 subjects for each group in order to improve the study. For more reliable results, the number of subjects in the control group was chosen to be twice that of the case group. Ethical committee of Mashhad University of Medical Sciences approved this work under the code IR.MUMS.sd.REC.1394.272.

We completed for each patient a checklist containing demographic, as well as histological data including severity of pain by visual analogue scale, severity of lesions based on the Thongprasom *et al.* criteria (19), OLP type (keratotic and atrophic), and gastrointestinal symptoms. Such gastrointestinal symptoms included history of chronic or recurrent diarrhea, malabsorption, malnutrition, weight loss and constipation, severe lactose intolerance, Irritable bowel syndrome (IBS), bloating, and dyspepsia.

The clinical examination was performed by an oral and maxillofacial medicine specialist, and was confirmed through histopathological diagnosis. Biopsies of oral lesions were also collected and OLP was confirmed by direct immunofluorescence (DIF) hematoxylin-eosin staining.

Antibody analysis

Blood samples were collected for the serologic evaluation of anti-transglutaminase IgA (Anti-TTG IgA), Total IgA, CBC, FBS, Iron serum, and ferritin. As Anti-TTG IgA is the screen test in diagnosing celiac, we called all patients for this test. They also underwent Total IgA serum test in order to diagnose patients with IgA deficiency. Total IgA test was performed using Human IgA Kappa Kit (Binding Site, England). Moreover, Anti-TTG IgA test was performed by (Liaison, Italy) with the following laboratory indicators; negative, borderline, and positive corresponding to <7, 7-9, and >9 Au/ml respectively. A Gastroenterologist examined 16 patients with IgA deficiency (<86 mg/dl) to confirm celiac disease through complementary assessment with Anti-TTG IgG. The cutoff level of Anti-TTG IgG recommended by the manufacturer was 20 U/ml. After laboratory evaluation, all OLP patients underwent standard treatment and followed up.

Specifying statistical procedures

Data were analyzed using SPSS software v.20. For descriptive variables, data were presented by frequency, mean, and standard deviation or, median and interquartile range (IQR). In order to compare quantitative variables in the two groups, T-Test was used for normal distribution, and Mann-Whitney test for the case of non-normality. The significant level was set to 0.05 in all tests.

Results

Description of subjects

A total of 96 subjects were considered in the study, where 32 of them were in the case group, and the rest in the control group. The mean age of all participants was 43.27 ± 14.29 years old, and the male/female ratio was 0.5. Demographic data related to the control and case groups are given in Table 1.

According to table 1, age, gender and literacy were significantly different between the two groups. Six patients in the case group had keratotic lichen planus (18.8%) and 26 of them had atrophic lichen planus (78.1%).

None of participants in this study had any gastrointestinal symptoms.

Table 1. Demographic data of the case and control groups

Characteristic	Group		p value
	Case (n = 32)	Control (n = 64)	
Age (years)	51.22± 13.88	38.97± 12.66	<0.001 [a]
Gender n (%)			
Male	6 (18.8)	26 (40.6)	0.048 [b]
Female	26 (81.3)	38 (59.4)	
Marital Status n (%)			
Married	29 (90.6)	54 (84.3)	0.424 [b]
Single	3 (9.4)	10 (15.6)	
Literacy n (%)			
Illiterate	4 (12.5)	3 (4.7)	
Elementary	13 (40.6)	7 (10.9)	0.001 [b]
Diploma	9 (28.1)	18 (28.1)	
Higher	6 (18.8)	36 (56.2)	
Occupation n (%)			
None	0 (0)	2 (3.1)	
Student	1 (3.1)	6 (9.4)	
Employed	5 (15.6)	10 (15.6)	0.080 [b]
Self-employed	26 (81.3)	35 (54.7)	
Healthcare worker	0 (0)	11 (17.1)	
Smoking n (%)			
Yes	1 (3.1)	3 (4.7)	0.573 [b]
No	31 (96.9)	61 (95.3)	

[a]: Independent Sample T-Test, [b]: Chi-Square Test

Data are presented as mean±S.D. and n (%).

Laboratory Findings

Baseline laboratory data in the two groups have been listed in Table 2 and as it is seen, there were no significant difference between the two groups in the laboratory findings (P>0.05), except for the serum iron level (P=0.032) and the platelet count (P=0.022). Twelve cases in the case group (33.3%) and 17 cases in the control group (26.5%) had ferritin levels less than 25 ng/mL. Thus, there was no significant difference in the two groups with respect to the ferritin levels (P> 0.05). Ferritin levels less than 25 ng/mL indicate anemia. Therefore, anemia was also present in both groups, although the difference of ferritin levels between them was not significant.

Table 2. Baseline laboratory data in the case and control groups

Characteristic	Case Group (n= 32)	Control Group (n= 64)	p value
Serum Iron (µg/dL)	76.64 ± 31.22	94.89 ± 39.6	0.032 [a]
RBC (Mil/µL)	4.69 ± 0.4	4.85 ± 0.51	0.137 [a]
Hb (g/dL)	13.79 ± 0.99	14.28 ± 1.6	0.089 [a]
HCT (%)	41.66 ± 2.86	42.91 ± 4.38	0.117 [a]
MCV (fL)	88.58 ± 5.44	88.65 ± 6.12	0.963 [a]
MCH (pg)	29.51 ± 1.9	29.4 ± 2.23	0.83 [a]
MCHC (g/dL)	33.09 ± 0.74	33.21 ± 0.79	0.483 [a]
Platelet (Tho/µL)	260.06 ± 61.75	230.93 ± 51.59	0.022 [a]
FBS (mg/dL)	96 (10)	97 (19.25)	0.642 [b]
Ferritin (ng/mL)	36.15(63.75)	53.65(85.15)	0.257 [b]
WBC (Tho/µL)	6.05(2.13)	6.25(2.3)	0.770 [b]
RDW-CV (%)	13.75(1.65)	14.1(1.45)	0.138 [b]

[a] Independent Sample T-Test; [b] Mann-Whitney Test. Data are presented as mean±S.D. and median (IQR)

The mean values of IgA Anti-TTG and the Total IgA were not significantly different in the OLP group and the control group (P>0.05). In both groups, the level of total IgA was normal. Other results have been shown in Table 3.

Table 3. Comparison of antibody levels in the control and lichen planus groups

Variable	Groups	N	Mean	±	Std. Deviation	p Value*
Anti-TTG(IgA) (Au/ml)	case	32	0.12	±	1.51	0.167
	control	64	0.57	±	1.20	
Total IgA (mg/dL)	case	32	134.96	±	42.86	0.639
	control	64	129.85	±	55.28	

* All tests were done by Independent Sample T-Test.

Our results showed that in patients with IgA deficiency (n=16), the level of Anti-TTG IgG was normal, and no patient had celiac disease in both of the case and control groups.

In the subgroup analysis, there was no significant difference between levels of Anti-TTG IgA, Total IgA and Anti-TTG IgG in patients with keratotic or atrophic OLP (P>0.05). We showed by the Pearson correlation test that there was no significant correlation between severity of oral lichen planus by Thongprasom criteria, Anti-TTG IgG (r=−0.544, P=0.456), Total IgA (r=0.064, P=0.756), and Anti-TTG IgA (r=−0.076, P=0.699).

As age, sex, and serum iron levels differed significantly between the two groups, logistic regression was applied to assess interacting variables, and no association was found

between Anti-TTG IgA and OLP (P=0.482). Therefore, differences in age, sex, and serum iron levels in the two groups did not effectively alter the main results. Results have been presented in Table 4.

Table 4. Results for the logistic regression in associating OLP and Anti-TTG IgA

	B	S.E.	Sig.	OR(odds ratio)	95% C.I for OR	
					Lower	Upper
Anti-TTG(IgA) *	-.272	.386	.482	.762	.357	1.624
Age	.068	.022	.002	1.070	1.025	1.117
Gender	-1.208	.668	.070	.299	.081	1.106
Serum Iron	-.011	.008	.147	.989	.974	1.004
Constant	-5.162	2.117	.015	.006		

*Comparison of antibody levels was also made after adjusting for age, gender, and serum iron levels. Again, no significant difference was found between the two groups.

Discussion

In this study, we investigated the association of oral lichen planus with celiac disease. The main findings were the absence of celiac disease in OLP patients and low level of Anti-TTG IgA in both healthy subjects and patients.

The immune responses in celiac disease are varied. An implication could be the increase in patients' intestinal permeability, related to the direct toxic effect of gliadin on the surface of the intestinal epithelium (20, 21). This enables the passage of gluten peptides and other related peptides into the bloodstream, which in turn causes the appearance of different inflammatory or autoimmune processes that might affect organs or tissues. It can be the result of aberrant immune responses (22). In the submucosa of the small intestine, upon the action of tissue transglutaminase type 2 which unfolds gluten, a cascade of events occurs. They cause a Th1 response that stimulates B lymphocytes, while they release IgE and other immunoglobulins (23). It plays an important role in the appearance of urticaria and atopic dermatitis, and the stimulation of Th2 mediated by T-lymphocytes, which in turn releases pro-inflammatory cytokines, such as TNF and interferon gamma (IFN) among others (24). In addition, these immunological responses can also cause production of circulating immune-complexes due to antigen–antibody interactions, which predominates in vasculitis lesions (15).

The risk of enteropathy-associated T-cell lymphoma is greatly due to T-cell stimulation during the pathogenesis of the disease (16), and it increases in celiac disease. The wide range of celiac disease clinical manifestations should prompt specialists to consider it when a patient presents extra intestinal signs and symptoms that might be related to the celiac disease (25). Some oral ailments have been also reported as possible atypical aspects of celiac disease, mainly dental enamel defects (DEDs) as well as recurrent aphthous stomatitis (RAS) (26).

An unusual association of OLP and celiac disease was reported in 1993 in a case with a biopsy-proven erosive OLP, iron, folate and vitamin B12 deficiencies, and demonstrated celiac disease. Surprisingly, gluten-free diet (GFD) resulted in the relief of OLP within 6 months (10). However, the hypothesis of the association of celiac disease and OLP was

promptly refuted by Scully *et al.* referring one month later that they had investigated 103 patients with OLP, while none of them had celiac disease. Therefore, they concluded that OLP would seem only rarely associated with celiac disease (27). In 1998, 39 patients with OLP were screened for celiac disease; 22 patients were positive for IgA gliadin antibody test and 4 for endomysium antibody test, but only one had small intestinal signs of celiac disease (28). In another case, the association of erosive mucosal lichen planus was reported with hyper IgE syndrome and celiac disease (8). However, there is little evidence for the association of celiac disease and OLP disorder.

Compilato *et al.* assessed the frequency of undiagnosed celiac disease among OLP patients and the possible effects of a gluten-free diet (GFD) on OLP lesions in celiac disease patients. They considered 23 patients with clinically and histologically confirmed OLP receiving topical corticosteroid treatment, and underwent blood sampling to assess full blood count, serum folate, vitamin B12, iron and celiac disease antibodies levels. Two female patients without any further systemic signs and symptoms were found to have positive celiac disease antibodies associated with hematinic deficiencies, and diagnosed with celiac disease after small intestinal biopsy, and were reevaluated after six months of GFD. They presented atrophic/erosive OLP localized on the buccal mucosa (associated with a burning sensation despite topical corticosteroid therapy). Six months after GFD, a normalization of serum levels of folate, vitamin B12 and iron, accompanied by an improvement of the oral soreness and of the atrophic/erosive areas, were observed in both patients (29). Cigic *et al.* assessed whether the incidence of celiac disease was higher in OLP patients than in patients with healthy oral mucosa. They came upon eight new celiac disease cases in OLP patients (four with erosive lichen planus and four with reticular lichen planus), and confirmed the increased prevalence of celiac disease in the OLP patients compared to the control group (14).

To the best of our knowledge, our study is the second case-control study that investigates the association of oral lichen planus with celiac disease. Our findings revealed no explicitly diagnosed celiac disease in OLP patients, which was compliant with Scully *et al.* (27), and contrary to Cigic *et al* findings (14).

It seems that such contradictory evidences for association of OLP and celiac disease could be due to ethnical (or racial) differences, various HLA (human leukocyte antigen) as well as the prevalence of the risk factors of both diseases in different areas and populations.

In our study, there was no celiac disease present in OLP patients and healthy subjects. Although celiac was not observed in the population under our study, the association of celiac disease and OLP cannot still be dismissed due to ethnic or genetic differences, as well as various criteria used in diagnosing OLP. OLP has unknown etiology and its risk factors are varying in different communities. Some of its risk factors are stress, deficiency or marginally low levels of vitamins B1, B6, B12, iron and folate (30). Therefore, further studies are necessary in order to appropriately distinguish such an association.

Study limitations

Our study had the limitation of ethnical variations. Therefore, large-scale multi-centric prospective studies have to be considered. Further meta-analyses or systematic investigations are suggested in order to find out the association of celiac disease and OLP.

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Conflict of interest

The authors declare no conflict of interests.

References

1. Lodi G, Scully C, Carrozzo M, Griffiths M, Sugerman PB, Thongprasom K. Current controversies in oral lichen planus: report of an international consensus meeting. Part 2. Clinical management and malignant transformation. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2005; 100(2):164-78.
2. Erickson BA, Elliott SP, Myers JB, Voelzke BB, Smith 3rd TG, McClung CD, et al. Understanding the relationship between chronic systemic disease and lichen sclerosus urethral strictures. J Urol 2016; 195(2):363-8.
3. Kurago ZB. Etiology and pathogenesis of oral lichen planus: an overview. Oral Surg Oral Med Oral Pathol Oral Radiol 2016; 122(1):72-80.
4. Robledo-Sierra J, Landin-Wilhelmsen K, Nyström HF, Mattsson U, Jontell M. Clinical characteristics of patients with concomitant oral lichen planus and thyroid disease. Oral Surg Oral Med Oral Pathol Oral Radiol 2015; 120(5):602-8.
5. Carrozzo M. How common is oral lichen planus? Evid Based Dent 2008; 9(4):112-3.
6. Gupta S, Jawanda MK. Oral lichen planus: an update on etiology, pathogenesis, clinical presentation, diagnosis and management. Indian J Dermatol 2015; 60(3):222-9.
7. Rashid M, Zarkadas M, Anca A, Limeback H. Oral manifestations of celiac disease: a clinical guide for dentists. J Can Dent Assoc 2011; 77(b39).
8. Ruiz Villaverde R, Blasco Melguizo J, Menéndez García Estrada A, Díez García F. Erosive mucosal lichen associated to hyper IgE syndrome and coeliac disease. An Pediatr (Barc) 2004; 60(3):281-2. [In Spanish].
9. Compilato D, Carroccio A, Campisi G. Hidden coeliac disease in patients suffering from oral lichen planus. J Eur Acad Dermatol Venereol 2012; 26(26):390-1.
10. Fortune F, Buchanan J. Oral lichen planus and coeliac disease. Lancet 1993; 341(8853):1154-5.
11. Acar S, Yetkıner AA, Ersın N, Oncag O, Aydogdu S, Arıkan C. Oral findings and salivary parameters in children with celiac disease: a preliminary study. Med Princ Pract 2012; 21(2):129-33.
12. Muñoz F, Del Río N, Sóñora C, Tiscornia I, Marco A, Hernández A. Enamel defects associated with coeliac disease: putative role of antibodies against gliadin in pathogenesis. Eur J Oral Sci 2012; 120(2):104-12.
13. Green PH, Rostami K, Marsh MN. Diagnosis of coeliac disease. Best Practice & Research Clinical Gastroenterology 2005; 19(3):389-400.

14. Cigic L, Gavic L, Simunic M, Ardalic Z, Biocina-Lukenda D. Increased prevalence of celiac disease in patients with oral lichen planus. Clin Oral Investig 2015; 19(3):627-35.

15. Rodrigo L, Beteta-Gorriti V, Alvarez N, Gómez de Castro C, de Dios A, Palacios L, et al. Cutaneous and Mucosal Manifestations Associated with Celiac Disease. Nutrients 2018; 10(7):800.

16. Goddard CJ, Gillett HR. Complications of coeliac disease: are all patients at risk? Postgrad Med J 2006; 82(973):705-12.

17. Nejad MR, Rostami K, Emami MH, Zali MR, Malekzadeh R. Epidemiology of celiac disease in Iran: a review. Middle East J Dig Dis 2011; 3(1):5-12.

18. Pakfetrat A, Javadzadeh-Bolouri A, Basir-Shabestari S, Falaki F. Oral lichen planus: a retrospective study of 420 Iranian patients. Med Oral Patol Oral Cir Bucal 2009; 14(7):E315-8.

19. Thongprasom K, Carrozzo M, Furness S, Lodi G. Interventions for treating oral lichen planus. Cochrane Database Syst Rev 2011; 7:CD001168.

20. Losurdo G, Principi M, Iannone A, Amoruso A, Ierardi E, Di Leo A, et al. Extra-intestinal manifestations of non-celiac gluten sensitivity: an expanding paradigm. World J Gastroenterol 2018; 24(14):1521-30.

21. Catassi C, Bai JC, Bonaz B, Bouma G, Calabrò A, Carroccio A, et al. Non-celiac gluten sensitivity: the new frontier of gluten related disorders. Nutrients 2013; 5(10):3839-53.

22. Catassi C, Elli L, Bonaz B, Bouma G, Carroccio A, Castillejo G, et al. Diagnosis of non-celiac gluten sensitivity (NCGS): the Salerno experts' criteria. Nutrients 2015; 7(6):4966-77.

23. Spencer J, Sollid LM. The human intestinal B-cell response. Mucosal Immunol 2016; 9(5):1113-24.

24. Jabri B, Sollid LM. Mechanisms of disease: immunopathogenesis of celiac disease. Nat Clin Pract Gastroenterol Hepatol 2006; 3(9):516-25.

25. Green PH, Jabri B. Celiac Disease. Annu Rev Med 2003; 57:207-21.

26. Pastore L, Carroccio A, Compilato D, Panzarella V, Serpico R, Muzio LL. Oral manifestations of celiac disease. J Clin Gastroenterol 2008; 42(3):224-32.

27. Scully C, Porter SR, Eveson JW. Oral lichen planus and coeliac disease. Lancet 1993; 341(8861):1660.

28. Jokinen J, Peters U, Mäki M, Miettinen A, Collin P. Celiac sprue in patients with chronic oral mucosal symptoms. J Clin Gastroenterol 1998; 26(1):23-6.

29. Compilato D, Carroccio A, Campisi G. Hidden coeliac disease in patients suffering from oral lichen planus. J Eur Acad Dermatol Venereol 2012; 26(3):390-1.

30. Nosratzehi T. Oral lichen planus: an overview of potential risk factors, biomarkers and treatments. Asian Pac J Cancer Prev 2018; 19(5):1161-7.