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Original Research Article

Prevalence of Human Papilloma Virus in Oral lichen planus

Sami Khalaf Jabar
College of Medicine, University of Maysan, Al-Amara, IRAQ

E-mail Sami_ Khalaf2006@yhoo.com

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Abstract

Oral lichen planus (OLP) is a common chronic inflammatory and immune mediated disease. The diagnosis require clinical and histopathological examination to rule out other possible diseases. Viral infection has been hypothesized as a predisposing factor in the development of this disease. It is possible that oral mucosal viral infections including HPV infection may enroll as a causative agent in OLP pathogenesis. The study aimed to investigate the prevalence of human papilloma virus in oral lichen planus. The samples were obtained from the archives of the department of Oral & Maxillofacial Pathology/ College of Dentistry/University of Baghdad during the period 1990-2015. The study was composed of (30) paraffinized samples of previously diagnosed oral lichen planus and (30) paraffinized samples of nonpathogenic mucosa were studied. In situ hybridization was used for detection of DNA HPV. The data were analyzed with SPSS software and chi square test was used to find the possible relation between HPV infection and oral lichen planus. Four out of 30 (13.3%) lichen planus samples and three out of 30 (10%) controls were HPV positive. No significant correlation (*P>0.05*) was observed between HPV infection and oral lichen planus. The study revealed that might be not relationship between human papillomavirus and incidence of oral lichen planus.

Key Words: Oral Lichen Planus Human papillomavirus, in situ Hybridization.

الخلاصة

مرض الحزاز المسطح الفموي مرض التهابي ومناعي بصوره عامه. تشخيص المرض يتطلب فحص النسيج المرضي والفحص السريري لاستبعاد الأمراض الأخرى المحتملة. تم افتراض العدوى الفايروسية كعامل مؤهب في تطور هذا المرض، لذلك فمن الممكن أن الالتهابات الفايروسية الفموية بما في ذلك الفايروس الحليمي البشري قد يسجل كعامل مسبب للمرض. تهدف الدراسة إلى التحري في انتشار فايروس الورم الحليمي البشري في الحزاز المسطح الفموي. تتكون الدراسة من(٣٠)عينة من الحزاز المسطح الفموي الذي تم تشخيصه مسبقآ، وكذلك تم تدراسة(٣٠) عينة من الغشاء الفموي السليم كمجموعة سيطره. تم استخدام التهجين الموقعي للكشف عن فايروس الورم الحليمي البشري للحامض النووي. تم تحليل البيانات لإيجاد العلاقة المحتملة بين الاصابه بفايروس الورم الحليمي البشري والحزاز المسطح الفموي. وكانت النتائج وجود(٤) عينات مصابه من أصل ٣٠ عينه (١٣,٣٪) حزاز مسطح فموي و(٣) منأصل ٣٠ عينه (١٠٪) للأنسجة السليمة (مجموعة السيطرة). كشفت الدراسة انه قد لا تكون هناك علاقة بين فايروس الورم الحليمي البشري وحدوث الحزاز المسطح الفموي.

الكلمات المفتاحية: التهجين الموضعي، الفايروس الحليمي البشري، الحزاز الفموي.

Introduction

Oral lichen planus (OLP) is a chronic immunological mucosal disease [1]. The etiology of OLP not well understood involves the degeneration of the basal cell epithelial layer, induced by cell-mediated immunological reactions. The causative factors such as stress, trauma, hepatitis C, and diabetes have different degrees of support. Lichen planus affects about two percent of the population [2]. In spite of the disorder may occur in all age groups,

the women are most commonly affected twice as often as men [3].

In contrast to cutaneous lichen planus, oral lichen planus lesions may persist for several years and tend to be difficult to treat. Atrophic and erosive lichen planus is associated with a risk of potential malignant transformation [3].

Human papillomaviruses are epithelia-tropic viruses. The erosive and atrophied variants of OLP recorded the highest prevalence of HPV DNA than normal oral mucosa [4]. The HPV viral protein increases the degradation of p53 [3]. This leads to cell cycle dysregulation and eventually may lead to malignant transformation. Many studies, which included meta-analysis and review studies, suggest an important association between HPV and OLP [5].

In situ hybridization (ISH) is a type of hybridization has shown the higher sensitivity that uses complementary DNA with different labels to localize a specific DNA or RNA sequence in a portion or section of tissue. In situ hybridization (ISH), considered as a direct signal detection assay, it has the advantage of preserving the morphologic context of viral DNA signals; its application mainly in viral infectious diseases such as the typing of human papillomavirus (HPV) [6].

The present study aimed to investigate the prevalence of HPV in tissue biopsies of patients with oral Lichen planus.

Materials and Methods

A total of 30 Iraqi patients with OLP will be enrolled in this case control study. The samples were obtained from the archives of the department of Oral & Maxillofacial Pathology/ College of Dentistry/ University of Baghdad during the period 1990-2015. Demographic and clinical data were collected, including patient's information concerning age, sex, site of the tumor, as well as other information of occupation. Control group will be consisted of 30 healthy individuals their age, gender matched with patients group.

Paraffin-embedded tissue blocks of both; study and control groups were collected. New sections were made from each of the paraffin embedded blocks which include, four μm thick cross sections were made and fixed on ordinary slides to be stained by hematoxyline and eosin stain to confirm the diagnosis. For the purpose of conducting in-situ hybridization procedure to detect the HPV other 4 μm thick sections were made on positively charged slides.

In situ hybridization is a method for localizing and detecting specific DNA or RNA sequences in morphologically preserved tissue sections. Briefly, the method involved deproteinization of fixed tissue sections mounted on slides; hybridization of a biotinylated probe to the target sequence, the hybridized probe is then detected by addition of a streptavidin – alkaline phosphatase (streptavidin-AP) conjugate (DNA probe hybridization/ Detection system).

Upon addition of the single component BCIP/NBT solution (substrate) which is 5-brom-4 chloro-3 indolyl phosphate/Nitro blue tetrazolium, an intense blue signal appears at the specific site of the hybridized probe. This streptavidin-AP conjugate directly linked to the biotiny lated probe provides a rapid and highly sensitive detection method. Positive control was included for each run of in situ hybridization. The positive control was obtained by replacing the probe with housekeeping gene probe. To assess the statistical significance association of HPV and existence OLP, the Chi square test will apply. P values were considered statistically significant if $P<0.05$.

Results

The study groups consisted of 60 specimens 30 from patients with OLP and 30 from healthy individuals were control group. 60% of these patients were males and 40% were females in affected group. The mean age and HPV infection were 43y, 13.3% of affected (Table 1). Of thirty volunteers of control group 50% of each males and females mean age 45y only 10% was with HPV infection. There was no significant difference between males and

females regarding HPV signals (P>0.05) as well, although males were 4 cases (13.3%) higher than females who were (10%) (Table 1).

Table 1 : Distribution of HPV positive cases according to the sex of patients

	Lichen planus		Control group	
Gender	**Males**	**Females**	**Males**	**Females**
	18 (60%)	**12 (40%)**	**15 (50%)**	**15 (50%)**
HPV infection	**2 (6.7 %)**	**2 (6.7%)**	**2 (6.7 %)**	**1 (3.3%)**
Mean age	**43 Y**		**45 Y**	

Chi-square=1.623 P=0.084 P>0.05 Non significant

The site of involvement showed the buccal mucosa was predominant site of disease (23 case) while the gingiva and tongue showed (5, 2 cases) respectively (Figure 1). OLP showed positive ISH signals for HPV in (4) cases all were detected in non-keratinized buccal mucosa. There was no significant correlation between the site & HPV positivity with P-value 0.43 (Table 2).

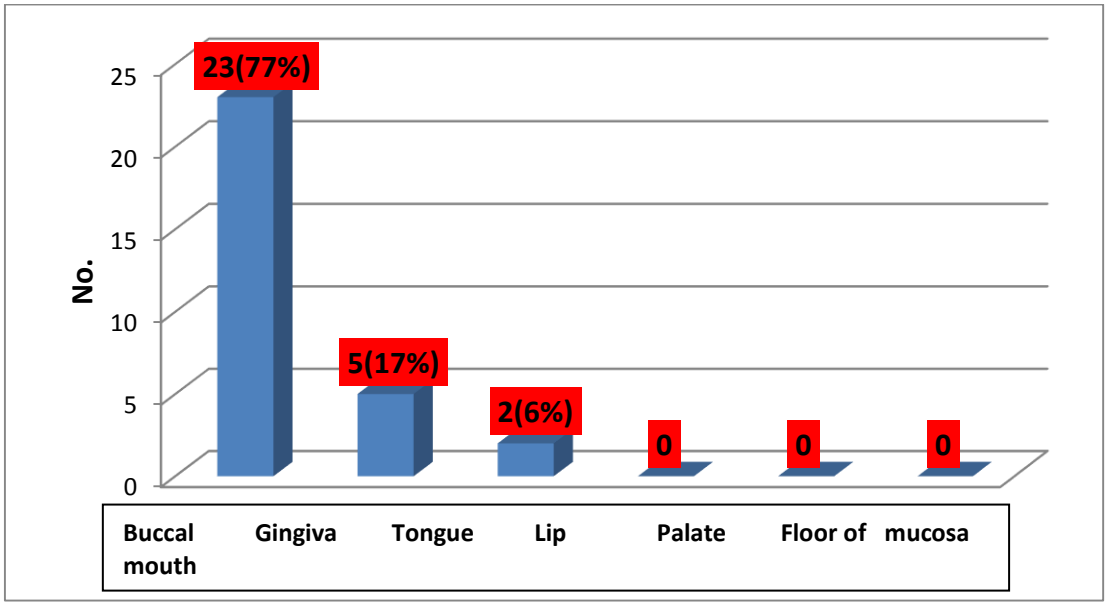

Figure 1: Distribution of the patients according to the localization of the OLP.

Table 2: Site distribution of HPV-16 positive cases.

Site	No.	%	HPV+Ve No. %
Buccal mucosa	23	77%	4
Gingiva	5	17%	0
Tongue	2	6%	0
Lip	0	0%	0
Palate	0	0%	0
Floor of mouth	0	0%	0
Total	30	100%	4(13.3%)

P-value =0.43

Discussion

In this study most sensitive molecular method for in situ viral detection was applied. Ming *et al*. evaluated (ISH) for detection of HPVs compared to PCR assay showed that both methods detected HPV (DNA) without significant difference [7].

The buccal mucosa being the most commonly involved site. The finding consistent with our study the reticular form with bilateral posterior buccal mucosa was predominant site and account(47%), (77%) respectively [8]. The results of the study were conflicted others previous studies in Egyptian samples of patients [9].Similar results also observed by Campisi *et al*., [10].

Great efforts in exploring the relation between OLP and HPV have mainly focused on many epidemiological studies of different populations. It is noticeable that there have been wide variations in the results found among different geographical distribution of populations [11].

In the present study, HPV DNA was found in four cases of oral lesions (13.4%) and three cases in control group (10%) without significant difference in both groups; Syrjänen *et al*, done systematic review shows a statistically significant difference (11% versus 23%) between HPV associated with OLP lesions and HPV found in normal tissue. This difference might explain the regional differences in the distribution of risk factors other than HPV infection; The risk of oral HPV infection such as history of sexually transmitted disease, sexual behavior, HIV infection, and severity of immune-suppression and difference in the accuracy and sensitivity methods of detection, sampling methodologies, the characteristic of patient and the types of studied specimens (e.g., biopsy tissue, saliva, oral mucosal scrapings) [11]. Many Studies in the USA used in situ hybridization on paraffin embedded tissues did not find any relationship between HPV and OLP and these results coincided with our results. In contrast, patients with OLP in European countries have been reported to have high HPV prevalence; in study from Italy the HPV found in 12 of 49 (25%). High risk-HPV was found in (7/16) (43.7%) cases of OLP in Germany [12].

In addition it has been found that HPVs infect the basal cell epithelial layer and in order for HPVs to reach and infect epithelial basal cells [13]; viral particles must enter through the epithelium that was broken mucosal injury, and subsequently reach the basal cell layer. In present study the four cases with HPV infection (13.3%) were seen in buccal mucosa the reason may be the region lined by non-keratinizing epithelium and these region of oral cavity more liable for injury and viral infection than keratinizing epithelium. Nishimura *et al*. also reported that HPV infection was frequently observed in the oral mucosa of patients wearing dentures, suggesting that chronic stimulation of the mucosa by the denture and subsequent erosion of the mucosa are the reason for the frequent infection [15]. Many studies found high percentage of HPV cases in

non-keratinizing oral mucosa, Giovannelli found that HPV infection can be affected by keratinization, so that the keratinized mucosa is more resistant to HPV infection. The proliferation rate of virus increase in non-keratinized tissue can make it more susceptible to HPV infection.

Based on the above data, it is necessary to further investigate the association between HPV and OLP by using other screening methods.

Conclusion

OLP is autoimmune disease. Infectious agents might be proposed as one of the causes of OLP. Our study showed a low prevalence of HPV infection in OLP lesions. The study concludes that HPV may be not act an actual role in patients with OLP.

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