Original Article

IMPACT OF CLINICAL HISTORY ON HISTOPATHOLOGIC GRADING IN ORAL EPITHELIAL DYSPLASIA

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Abstract:
Objective: To compare the grade of oral epithelial dysplasia (sign out diagnosis) with the clinical history of the patient and subjects habit duration if any. Study design: 45 histologic sections of oral epithelial dysplasia, 15 each of mild, moderate and severe dysplasia (sign out diagnosis) based on WHO classification system were selected. The sections were of acceptable diagnostic quality, were from an intra-oral site and included referral information on age, sex and site of the lesion and habit history if any as clinical details for a sign out diagnosis. Result: Of the 45 histologic sections, a male predilection was noticed in all the grades of dysplasia; but it could not be taken as a clinical parameter to decide the grade of dysplasia as no statistical significance was found. An insignificant relation was seen between site and grade of dysplasia (P= 0.077). The age of individual and his/her habit duration of smoking; chewing tobacco and alcohol respectively were correlated and found to be important with a significant P value of 0.000, 0.099, 0.033 and 0.024 respectively. Conclusion: Grading of lesions of oral epithelial dysplasia, keeping in view the clinical features needs to be precise and accurate with respect to the overall prediction of disease progression.
Key words: Clinical features, Leukoplakia, Oral epithelial dysplasia.

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INTRODUCTION

Of all the disciplines in clinical medicine, histopathology is often credited with being the most scientific. There is no doubt that pathological examination has led to many of the currently used disease classifications and that morphological observation and correlation of the observations with clinical parameters has provided a sound basis for clinical medicine as it is today. It is also true, however, that not all of histopathology is evidence based; with the increasing demands for 'evidence based medicine', notoriously subjective histopathological approaches do need to be redefined and concepts, as well as diagnostic criteria, scientifically validated.[1]

The process by which a pathologist makes a diagnosis is inherently subjective. Factors as diverse as clinical features of the lesion, clinical impression offered by the surgeon, and the training and experience of the pathologist all play a part in determining the final "sign out" diagnosis. The diagnosis of oral epithelial dysplasia (OED) has caused considerable distress for pathologists because of ambiguous diagnostic criteria and differences of opinion among pathologists about what constitutes "epithelial dysplasia".[2,3] Oral epithelial dysplastic lesions may be morphological phenotypes of the different steps in the progression from normal to malignant tissue.[4] While the histological connotation is epithelial dysplasia, clnically the term used is Leukoplakia.

Leukoplakia represents 80% of potentially malignant oral lesions and is defined as a 'white patch or plaque that cannot be characterized clinically or pathologically as any other disease and is not associated with any physical or chemical causative agent

except the use of tobacco.'[5] This is a diagnosis by exclusion for a lesion that cannot be given another specific diagnostic name and does not typically disappear with removal of known aetiological factors, excepting smoked tobacco.[5,6] It occurs most frequently on the lip vermilion, buccal mucosa, lateral border of tongue, floor of mouth and gingival mucosa.[6,7] It should be emphasized that it is a diagnosis of exclusion that requires the clinician to be so well acquainted with all other white oral lesions as to be able to rule them out prior to using the term leukoplakia for a particular keratosis in a particular patient. It must also be emphasized that leukoplakia is a clinical term. The presence or absence of dysplastic cells does not alter the clinical diagnosis, although a recent World Health Organization (WHO) Workshop on Potentially Malignant Oral Mucosal Lesions and Conditions has suggested that the term leukoplakia be redefined to become a combined clinical/histological term.[8] Krutchkoff and his colleagues[9] suggested that relevant clinical factors should play a key role in the diagnostic evaluation of lesions suspected of being epithelial dysplasia. If dysplasia is identified, then appropriate interventions can be used, including excision, habit discontinuation which may prevent the progression of these precancerous lesions to squamous cell carcinoma. A necessary prerequisite to such preventive effects is the accurate diagnosis of oral epithelial dysplasia.

The present study was designed to compare the grade of dysplasia (sign out diagnosis) with the clinical history of the patient and subjects habit duration if any. It was done to assess whether the inclusion of such demographic data can further improve examiner accuracy in the diagnosis of oral epithelial dysplasia.

MATERIAL AND METHODS

Forty five histologic sections of OED were selected from departmental archives from the department of Oral Pathology, ITS-CDSR. The tissues given were previously reported for mild, moderate and severe dysplasia (sign out diagnosis) based on WHO classification system.[10] The sign out diagnosis was given by a collaborative agreement of three certified oral pathologists when the slide was viewed collectively. WHO System[10] defines and lists out 12 histologic characteristics that characterize epithelial dysplasia into grades of mild, moderate and severe.

Mild dysplasia: slight nuclear abnormalities, most marked in the basal third of the epithelial thickness and minimal in the upper layers, where the cells show maturation and stratification. A few, but no abnormal mitoses may be present, usually accompanied by keratosis and chronic inflammation.

Moderate dysplasia: More marked nuclear abnormalities and nucleoli tend to be present, with changes most marked in the basal 2/3rd of the epithelium, nuclear abnormalities may persist up to the surface, but cell maturation and stratification are evident in the upper layers. Mitoses are present in the parabasal and intermediate layers, but none is abnormal.

Severe dysplasia: Marked nuclear abnormalities and loss of maturation involving more than 2/3rd of the epithelium, with some stratification of the most superficial layers. Mitoses some of which are abnormal may be present in the upper layers.

To be selected for the current study, sections had to meet the following criteria: acceptable diagnostic quality, intra-oral site and included referral information on age, sex and site of the lesion and habit history if any as clinical details for a sign out diagnosis. The final 45 cases were signed out as follows: 15 with mild dysplasia, 15 with moderate dysplasia and 15 with severe dysplasia.

The data collected was first visualized to confirm their normal distribution. The resulting data was analyzed using SPSS

version 10 and Epi-Info 6.04 d software. Following this, descriptive statistics including the mean values and standard deviations, 95% confidence intervals, interquartile ranges (25^{th} and 75^{th} percentiles) were calculated for each variable. Pearson chi square test was carried out to determine the level of correlation or association between the groups under study. Differences between the different variables were analyzed using Anova test and Post Hoc test. Beside this Kruskal-Wallis one way test was also applied to compare skewed data among the groups followed by Mann-Whitney U test adjusted for probabilities. P value <0.05 was considered as significant.

RESULTS

The grade of dysplasia (sign out diagnosis) was compared with the clinical features and its effect on histopathological diagnosis was analyzed.

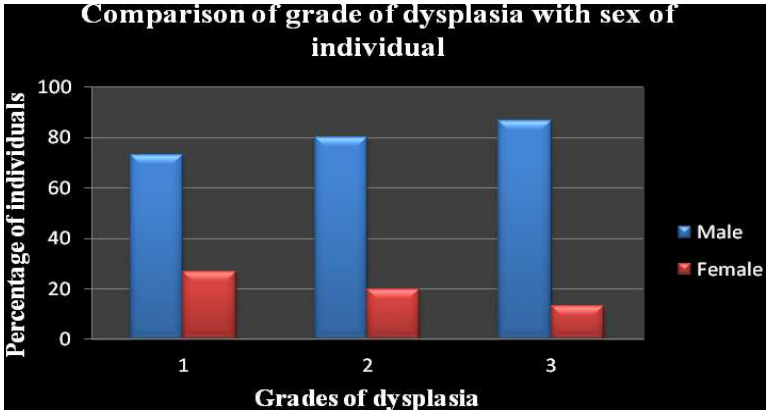
Graph 1 (bar diagram) shows the comparison of grade of dysplasia with the sex of individual. A male predilection was noticed in all the grades of dysplasia. It was seen that with the increasing grade of dysplasia male predilection was increasing and the female predilection was decreasing. Of the 15 sign out diagnosis of mild dysplasia 73.3% were males and 26.7% were females. 15 sign out diagnosis of moderate dysplasia comprised of 80% males and 20% females. 15 sign out diagnosis of severe dysplasia comprised of 86.7% males and 13.3% females. Pearson chi square test was applied to test the level of significance which was found to be statistically insignificant. (P>0.05)

Graph 2 (bar diagram) shows the comparison of grade of dysplasia with site of lesion. Of the total 45 cases, it was seen that in the 15 sign out diagnosis of mild dysplasia, 80% (n= 12) of the lesions were present on buccal mucosa and 20% (n= 3) were present on floor of mouth. In 15 sign out diagnosis of moderate dysplasia, 66.7% (n= 10) of the lesions were present on buccal mucosa, 13.3% (n= 2) were present on palate, 6.7% (n=1) were present on tongue and 13.3% (n= 2) were present on floor of mouth. In 15 sign out diagnosis of severe dysplasia, 33.3% (n= 5) of the lesions were present on buccal mucosa, 13.3% (n= 2) on palate, 33.3% (n=5) on tongue, 6.7% (n= 1) on lips and 13.3% (n= 2) were present on floor of mouth. Buccal mucosa was the most prominent site for dysplasia in all the grades. Tongue was a prominent site in severe dysplasia. . Pearson chi square test was applied to test the level of significance which was found to be statistically insignificant. (p>0.05).

Grade of dysplasia was compared with age of individual and his/ her habit duration (in years) **(**Table 1). Analysis of Variance and statistically non parametric Kruskal- Wallis test was applied to test the level of significance which was found to be statistically significant. (P<0.05).

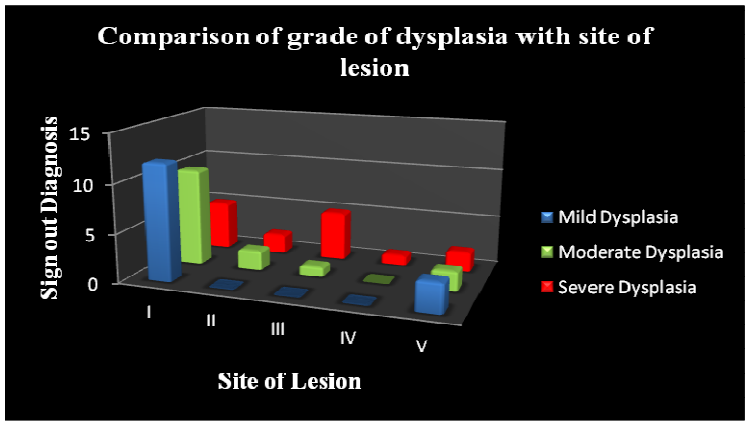
Grade of dysplasia was compared with age of individual with respect to their reliability among various grades of dysplasia (Table 2). Analysis of Variance and Post - Hoc test was applied to test the level of significance. Age was significant in differentiating mild from severe dysplasia and moderate from severe dysplasia with a P value of 0.000 and 0.004 and not significant in differentiating mild from moderate dysplasia (P= 0.094).

Grade of dysplasia was compared with his/ her habit duration with respect to their reliability among various grades of dysplasia (Table 3). Mann-Whitney U test was applied to test the level of significance. Smoking duration was not significant in differentiating mild from moderate dysplasia (P=.166). Tobacco chewing duration was not significant in differentiating mild from moderate dysplasia (P=.476) and moderate from severe dysplasia (p=.082). Alcohol duration was not significant in differentiating mild from moderate dysplasia (p=.413) and moderate from severe dysplasia (p=.065).



1: Mild dysplasia 2: Moderate dysplasia 3: Severe dysplasia

Graph 1: Comparison of grade of dysplasia with the sex of individual.



I Buccal mucosa II Palate III Tongue IV Lips V Floor of mouth

Graph 2: Comparison of grade of dysplasia with site of lesion.

Table 1: Comparison of grade of dysplasia with age of individual and his/ her habit duration (in years)

Clinical feature	Grades of dysplasia						p value
	Mild dysplasia		Moderate dysplasia		Severe dysplasia		
	Mean	Standard deviation	Mean	Standard deviation	Mean	Standard deviation	
Age of individual	30.47	5.592	36.20	6.516	45.13	8.667	.000
Smoking duration	5.27	5.418	8.87	7.150	16..53	11.186	.009
Tobacco chewing duration	4.60	4.188	7.60	7.679	13.07	9.277	.033
Alcohol duration	0.67	1.291	3.67	6.321	10.53	10.875	.024

Table 2: Comparison of grade of dysplasia with age of individual with respect to their reliability among various grades of dysplasia

Clinical feature	Comparison in Grades of dysplasia								
	Mild & Moderate dysplasia			Mild & Severe dysplasia			Moderate & Severe dysplasia		
	Mean diff	Std. Error	Sig.	Mean diff	Std. Error	Sig.	Mean diff	Std. Error	Sig.
Age	-5.73	2.572	.094	-14.7	2.572	.000	-8.93	2.572	.004

Table 3: Comparison of grade of dysplasia with his/ her habit duration with respect to their reliability among various grades of dysplasia

S No.	Clinical feature	Comparison in Grades of dysplasia					
		Mild & Moderate dysplasia		Mild & Severe dysplasia		Moderate & Severe dysplasia	
		Mann-Whitney U	Sig.	Mann-Whitney U	Sig.	Mann-Whitney U	Sig.
1.	**Smoking duration**	79.500	.166	44.500	.005	64.500	.046
2.	**Tobacco chewing duration**	95.500	.476	51.000	.010	71.000	.082
3.	**Alcohol duration**	96.500	.413	57.000	.011	71.500	.065

DISCUSSION

Oral carcinomas frequently arise from a spectrum of abnormalities ranging from hyperplasia to intraepithelial neoplasia termed histopathologically oral epithelial dysplasia (OED).[11] In head and neck pathology, the term dysplasia is increasingly used. In standard medical terminology, dysplasia means an abnormality of deve-lopment, while in histomorphology it expresses cellular and structural changes of the epithelium. Considering these abnormalities as typical of the progression from normal epithelium to cancer, the lesions are graded into different risk groups .[12,13]

In the diagnosis of oral epithelial dysplasia it is customary to distinguish between various grades. However, the histopathologic diagnosis is often biased by incorporation of the clinical facts and the description from the clinician. The clinician often uses terms such as "histologic verification" of the clinical diagnosis and the histopathologists diagnosis and grading of dysplasia are often used as a "gold standard". When the clinician interprets the vhistopathologic diagnosis, he or she should be aware that the histopathologist may be influenced by the clinical findings and thereby avoid a double weighting.[12,14]

In the present study the clinical findings were compared with the sign out diagnosis. Of the 15 sign out diagnosis of mild dysplasia 73.3% were males and 26.7% were females with a male: female ratio of 2.8:1. 15 sign out diagnosis of moderate dysplasia comprised of 80% males and 20% females with a male: female ratio of 4:1, while 15 sign out diagnosis of severe dysplasia comprised of 86.7% males and 13.3% females with a male: female ratio of 6.5: 1. A male predilection was noticed in all the grades of dysplasia; but it could not be taken as a clinical parameter to decide the grade of dysplasia as no statistical significance was found. Male predilection

could be because of the ease of habit forming products being available to them and its usage by them without any social stigma. On comparing site of lesion with grade of dysplasia, an insignificant relation was seen between site and grade of dysplasia (P= 0.077).

The age of individual and his/her habit duration of smoking; chewing tobacco and alcohol respectively were correlated and found to be important with a significant P value of 0.000, 0.099, 0.033 and 0.024 respectively. On comparing the age of individual and his/her habit duration with its reliability among various grades of dysplasia it was found that age and smoking duration were not significant in differentiating mild from moderate dysplasia with a P value of 0.094 and 0.166 respectively. The other parameters such as tobacco chewing duration and alcohol duration were not significant in differentiating mild from moderate dysplasia (P= 0.476 and P= 0.413 respectively) and moderate from severe dysplasia (P= 0.082 and P=0.065 respectively.

Abbey et al[15] had assumed that the availability of clinical information was directly proportional to the ability to make an accurate diagnosis, but this was not the case. With respect to clinical details, the results of their group with the availability of clinical information when compared to those from a previous study in which the same examiners had evaluated the same slides but without clinical histories, represented a 2.5% to 20% decrease for exact agreement among the six pathologists, a 0% to 8.5% decrease for agreement within one histologic grade, and a 0% to 23.4% decrease for agreement regarding the presence or absence of epithelial dysplasia.

An appreciation of the various clinical forms and presentations of this condition has led to finer levels of prognostication depending upon site, appearance, and clinical qualities. Habit histories like tobacco chewing, smoking and alcohol consumption are strong risk factors in the development of leukoplakia. Clinical management modalities include removal of exposures, chemoprevention, and ablative therapies.[16]

The site of involvement may also have a marked influence on the risk of malignant change. Of all leukoplakias, those of the floor of the mouth and the ventral surface of the tongue, and especially leukoplakia confined to those areas, seem to carry a very high risk of malignant change. In the current study a high number of cases of severe dysplasia were seen on the tongue which is in accordance with the study of Kramer in a US population.[17]

The results of the current study highlights the probability that clinical information on a patient is pushed through demographic and epidemiologic filters; and perhaps it allows accumulated data from previous cases to influence in particular cases more than they should. Also the kind of clinical history and demographic information that is provided and the means by which any given pathologist applies that information to the histomorphologic picture are more complexly involved in diagnosis than has previously been thought.

CONCLUSION

Probability is the state of knowledge greater than ignorance but lesser than certainty. Although not all premalignant lesions have shown to be transforming to squamous cell carcinoma, the probability of these progressing to frank invasion is quite high for them to be ignored. Thus, the grading of lesions of OED, keeping in view the clinical features needs to be precise and accurate with respect to the overall prediction of disease progression.

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