RESEARCH ARTICLE

Inter- and Intra-Observer Variability in Diagnosis of Oral Dysplasia

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Abstract

Background: Oral potentially malignant disorders (OPMDs) are lesions from which malignancy is more likely to develop that from other tissues. The potential for malignant transformation of OPMDs is estimated by determining the degree of dysplastic changes in the epithelium. Dysplasia grading has been criticized for lack of reproducibility and poor predictive value but is still considered the gold standard for diagnosing OPMDs. Since grading of dysplasia is based on architectural and cytological changes, there can be considerable inter- and intra-observer variability due to subjective impressions. This aim in this study was to assess the degree of agreement between two pathologists grading dysplasia in the same patients and review the existing grading system. **Materials and Methods:** In this hospital-based cross-sectional study, 100 patients with clinically diagnosed OPMDs were subjected to biopsy followed by histopathological examination. The slides were examined by two pathologists using WHO and binary systems of classification and both were blinded to the clinical and each other's histological diagnosis. For statistical analysis the Chi square test was applied. **Results:** Statistical analysis showed poor inter-observer variability with P values of 0.8 using the WHO classification and 0.3 using the binary classification. **Conclusion:** Our study provides evidence that the existing systems for grading dysplasia are not competent to rule out subjectivity. There is a need for a classification system that can overcome this drawback.

Keywords: Oral potentially malignant disorders- epithelial dysplasia- inter observer agreeability- grading dysplasia

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Introduction

Many oral squamous cell carcinomas are preceded by clinically evident OPMDs. The hazard ratios of various OPMDs are not well known (Ho et al., 2009). It is difficult to predict which lesions will undergo malignant transformation. At present, the gold standard in the diagnosis of OPMDs is histopathological investigation. Lesions with a higher grade of dysplasia are considered to be at a higher risk of transformation. Determination of dysplasia is subjective and not reproducible. Grading of dysplasia is based on architectural and cytological changes, and there can be considerable inter and intra observer variability due to its subjective impression (Rastogi et al., 2010).

This study was planned to assess the variability in pathological diagnosis of dysplasia by pathologists.

Materials and Methods

100 patients with OPMDs were included in the study. Written informed consent was obtained, detailed habit history along with clinical images of the lesion were obtained. A provisional clinical diagnosis was determined and biopsy site was selected based on clinical judgment of severity.

Incisional biopsy was performed and tissue was stored in 10% formalin, coded and stained with hematoxylin and eosin. Each slide was examined by two oral pathologists who were blinded to the clinical diagnosis and each other's diagnosis. Grading of dysplasia was made using the WHO classification and binary classification. Their diagnoses were tabulated and compared.

Of these 100 slides, one pathologist screened 20 randomly-selected slides twice at an interval of six months.

Results

100 patients with clinically diagnosed potentially malignant disorders were included in the study. 92 were males and 8 were females. Their ages ranged from 20 to 75 years. 13 of them did not give an adverse habit history, 21 had a smoking habit, and 47 had tobacco chewing

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Table 1. Comparison of Histopathological Diagnosis Using WHO Classification

	Diagnosis by second pathologist								Total
Diagnosis by first pathologist	Hyperkeratosis	Micro invasive carcinoma	Mild dysplasia	Moderate dysplasia	Severe Dysplasia	Lichenoid Lesion	Normal epithelium	OSMF	
Hyperkeratosis	1	0	0	0	0	0	0	0	1
Micro invasive carcinoma	2	0	1	0	0	0	0	0	3
Mild dysplasia	13	0	7	0	0	3	2	2	27
Moderate dysplasia	21	0	13	0	0	12	1	0	47
Severe dysplasia	11	1	5	0	0	4	0	1	22
Lichenoid lesions	0	0	0	0	0	0	0	0	0
Normal epithelium	0	0	0	0	0	0	0	0	0
OSMF	0	0	0	0	0	0	0	0	0
Total	48	1	26	0	0	19	3	3	100

Table 2. Comparison of Histopathological Diagnosis Using Binary Classification

First pathologist	Second pathologist		Total
	Low Risk	High Risk	
Low Risk	29 (100.0%)	0 (0%)	29 (100.0%)
High Risk	69 (97.2%)	2 (2.8%)	71 (100.0%)
Total	98 (98.0%)	2 (2.0%)	100 (100.0%)

habit. Clinical diagnosis included 48 cases of homogenous leukoplakia, 32 cases of tobacco pouch keratosis, 7 cases of lichen planus, 6 cases of speckled leukoplakia, 4 erythroplakia, 2 cases of oral sub mucous fibrosis and 1, verrucous leukoplakia.

Histopathologic diagnosis based on WHO criteria is given in Table 1. Chi-square value of 13.724 with a P value of 0.844 were obtained, indicating poor agreement. Both

Table 3. Histopathological Diagnosis by Single Pathologist at Different Intervals

Reading 1	Reading 2					Total
	Hyperkeratosis	Mild dysplasia	Lichenoid Lesion	HyperPlastic Hyperkeratotic Epithelium	Lichenoid Dysplasia	
Hyperkeratosis	6	0	0	0	0	6
Mild dysplasia	0	9	0	0	1	10
Lichenoid Lesion	0	0	3	0	0	3
HyperPlastic Hyperkeratotic Epithelium	0	0	0	1	0	1
Lichenoid dysplasia	0	0	0	0	0	0
Total	6	9	3	1	1	20

Table 4. Comparison of Histopathological Diagnosis with Clinical Diagnosis

Diagnosis by pathologists		Clinical Diagnosis							Total
		Erythroplakia	Homogenous Leukoplakia	Lichen Planus	Speckled Leukoplakia	Tobacco pouch keratosis	Verrucous leukoplakia	OSMF	
Hyperkeratosis	1*	0	1	0	0	0	0	0	1
	2*	2	25	3	1	16	0	1	48
Micro invasive carcinoma	1	0	3	0	0	0	0	0	3
	2	0	0	0	0	0	1	0	1
Mild dysplasia	1	1	15	3	2	4	0	2	27
	2	1	14	1	3	7	0	0	26
Moderate dysplasia	1	3	23	3	0	18	0	0	47
	2	0	0	0	0	0	0	0	0
Severe dysplasia	1	0	6	1	4	10	1	0	22
	2	0	0	0	0	0	0	0	0
Lichenoid Lesion	1	0	0	0	0	0	0	0	0
	2	1	5	3	1	9	0	0	19
Normal epithelium	1	0	0	0	0	0	0	0	0
	2	0	2	0	1	0	0	0	3
OSMF	1	0	0	0	0	0	0	0	0
	2	0	2	0	0	0	0	1	3
Total No. of cases		4	48	7	6	32	1	2	100

1*, First pathologist; 2*, second pathologist

pathologists also provided the Binary Classification for the same slides. (Table 2) Chi square value of 0.834 and P value of 0.361 were obtained showing no statistically significant agreement. Histopathologic diagnosis of the same slides given by one pathologist at six month interval is shown in Table 3. There was almost perfect intraobserver agreement. A comparison of histopathologic diagnosis by two pathologists with clinical diagnosis is given in Table 4.

Discussion

OPMDs are disorders of varying etiologies, usually tobacco; characterized by mutagen-associated, spontaneous or hereditary alterations or mutations in the genetic material of oral epithelial cells with or without clinical and histomorphological alterations that may lead to oral squamous cell carcinoma (Sarode et al., 2010). Lesions having potential for malignant transformation include: leukoplakia, erythroplakia, palatal lesions in reverse smokers, oral submucous fibrosis, actinic keratosis, lichen planus, discoid lupus erythematosus, dyskeratosis congenita and epidermolysis bullosa. (Warnakulasuriya et al., 2007)

Clinically, OPMDs have a varied clinical manifestation ranging from harmless appearing keratotic white patch to an aggressive red and white lesion with ulceration. While it is not possible to predict the probability of malignant transformation based on clinical appearance, a non-homogenous appearance suggests a higher potential. (Warnakulasuriya et al., 2007).

Biopsy is considered mandatory for a definitive diagnosis and further management. Histopathological assessment provides information on the degree of dysplasia. The sequential changes occuring in the oral epithelium transforming it from normal through dysplastic and finally to carcinoma is adopted from the changes observed in the cervical mucosa. It is believed that genetic alterations begin from the basal cell layer and progressively inviolve the higher layers. (Izumo, 2011)

In general, the severity of epithelial dysplasia is proportional to the risk of subsequent cancer development. (Tabor et al., 2003) Surgical excision appears to decrease, although not eliminate this risk. Thus surgical excision is generally carried out for high-grade lesions (Mehanna et al., 2009). At the same time, mild dysplasias rarely transform to malignancy and hence, excision is usually not recommended (Bouquot et al., 2006). Accurate histopathological assessment is crucial to develop an effective treatment plan.

Hence, this study was conducted to assess the agreeability in the histopathological diagnosis by two different experienced pathologists. However, there was poor agreement between them on using either WHO or binary system of classification. Intraobserver agreeability was also examined, which showed good agreement.

Histopathologic changes in OPMDs have been classified using multiple systems. The cervical pathological classification was modified for the oral mucosa as Squamous intraepithelial neoplasia (Richart, 1967), however this was not adopted by the WHO. The Ljubljana system was proposed by laryngeal pathologists in 1971, but as it was extensive and complicated, it was not adopted for oral lesions (Kambic and Lenart, 1971). Pindborg et al., (1985) suggested the need for an internationally accepted set of criteria for oral epithelial dysplasia. In 1997, WHO proposed a grading system based on thirds, consisting of allocating to categories based on architectural features and cytological alterations.

Abbey et al., (1995) studied consistency in diagnosing epithelial dysplasia and found that exact agreement between pathologists was only 50.5%, but agrrement on differentiating dysplasia from no dysplasia was 81.5%. Karabulut et al., (1995) concluded that interobserver variability was due to individual differences, rather than educational background. Brothwell et al., (2003) suggested that interobserver agreement was substantial to perfect in diagnosing epithelial dysplasia based on a 5-point scale and using quadratic Kw statistic. Fischer et al., (2004) found that presence or absence of inflammation, lesion site, and biopsy technique modifies the reliability of histopathologic grading of dysplasia. Kujan et al., (2006) proposed a new scheme of grading dysplasia into 'low risk' or 'high risk' based on the same morpological criteria used by WHO classification. They evaluated this system in 68 oral dysplastic lesions and found moderate agreement when compared to WHO system which showed fair agreement.

In a subsequent study, Kujan et al., (2007) found poor to moderate agreement on grading individual characteristics of architectural and cytological changes, but good to substantial agreement was seen on using 2005 WHO criteria or Binary system.

Speight et al., (2015) reported that the incorporation of an adjudicator to review the histopathological slides improved the inter-observer full agreement from 69.9% of cases to 92.7%.

Till date there are no definitive criteria for the grading of dysplasia. Thus, a clinician needs to combine clinical features such as a larger size of lesion, non-homogenous appearance, and occurrence in high-risk sites to guide further investigations and follow-up. Meanwhile studies exploring the use molecular biomarkers along with histopathological analysis are neeeded. Also, long term prospective studies are required to understand factors which can predict malignant transformation.

Grading system for oral epithelial dysplasia is vital for treatment planning. It is desirable to have a simple grading system which brings about a greater agreement among pathlogists. The WHO classification though widely used, is subjective and more specific. Hence, from a clinical standpoint, we recommend the binary classification which is likely to have a better concordance among pathologists. However, it is desirable to utilize information obtained from identification of biomarkers for epithelial dysplasia to predict malignant transformation.

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