RESEARCH ARTICLE

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

Shubhasini A R¹, Praveen B N¹*, Usha Hegde², Uma K³, Shubha G¹, Keerthi G¹, Shiladitya Sil¹

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

Asian Pac J Cancer Prev, 18 (12), 3251-3254

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.

¹Department of Oral Medicine and Radiology, ¹Department of Oral Pathology and Microbiology, K.L.E.Society’s Institute of Dental Sciences, Bangalore, ²Department of Oral Pathology and Microbiology, JSS Dental College, Mysore, India. *For Correspondence: subhashiniar@gmail.com
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

| Diagnosis by first pathologist | Hyperkeratosis | Micro invasive carcinoma | Mild dysplasia | Moderate dysplasia | Severe Dysplasia | Lichenoid Lesion | Normal epithelium | OSMF | Total |
|------------------------------|----------------|-------------------------|---------------|-------------------|-----------------|-----------------|------------------|------|-------|
| Hyperkeratosis               | 1              | 0                       | 0             | 0                 | 0               | 0               | 0                | 1    | 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

| Diagnosis by 2nd pathologist | Low Risk | High Risk | Total |
|------------------------------|----------|-----------|-------|
| Hyperkeratosis               | 29 (100.0%) | 0 (0%) | 29 (100.0%) |
| Mild dysplasia               | 97.2% | 2.8% | 100.0% |
| Lichenoid Lesion             | 0      | 0        | 0     |
| HyperPlastic Hyperkeratotic Epithelium | 0 | 0 | 0 |
| Lichenoid dysplasia          | 0      | 0        | 0     |
| Total                        | 98 (98.0%) | 2 (2.0%) | 100 (100.0%) |

Table 3. Histopathological Diagnosis by Single Pathologist at Different Intervals

| Diagnosis by pathologists | Clinical Diagnosis | Total |
|---------------------------|--------------------|-------|
| Erythroplakia             | 1*                 | 1     |
| Homogenous Leukoplakia    | 2*                 | 48    |
| Lichen Planus             | 1                  | 1     |
| Speckled Leukoplakia      | 2                  | 27    |
| Tobacco pouch keratosis   | 2                  | 47    |
| Verrucous leukoplakia     | 2                  | 19    |
| OSMF                      | 4                  | 100   |

Table 4. Comparison of Histopathological Diagnosis with Clinical Diagnosis

| Diagnosis by pathologists | Clinical Diagnosis | Total |
|---------------------------|--------------------|-------|
| 1*, 2*                    |                    |       |

1*, First pathologist; 2*, second pathologist
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 agreement 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 of 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 morphological 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 needed. 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 pathologists. 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.

References

Abbey LM, Kaugars GE, Gunsolley JC, et al (1995). Intraexaminer and interexaminer reliability in the diagnosis of oral epithelial dysplasia. Oral Surg Oral Med Oral
Patghol Oral Radiol Endod, 80, 188-91.
Bouquot JE, Speight PM, Farthing PM (2006). Epithelial dysplasia of the oral mucosa: diagnostic problems and prognostic features. 
Curr Diag Pathol, 12, 11-21.
Brotherwell DJ, Bradley G, Leong I (2003). Observer agreement in the grading of oral epithelial dysplasia. 
Community Dent Oral Epidemiol, 31, 300-5.
Fischer J, Epstein J, Morton TH, Schwartz S (2004). Interobserver reliability in the histologic diagnosis of oral premalignant and malignant lesions. 
J Oral Pathol Med, 33, 65-70.
Ho PS, Chen PL, Warnakulasuriya S, et al (2009). Malignant transformation of oral potentially malignant disorders in males: a retrospective cohort study. 
BMC Cancer, 9, 260 doi: 10.1186/1471-2407-9-260.
Izumo T (2011). Oral premalignant lesions: from the pathological viewpoint. 
Int J Clin Oncol, 16, 15-26.
Kambic V, Lenart I (1971). Notre classification des hyperplasies de l’epithelium du larynx au point de vue prognostic. 
J Fr Otorhinolaryngol Audiophonol Chir Maxillofac, 20 (2011), 1145-50.
Karabulut A, Reibel J, Therkildsen MH, et al (1995). Observer variability in the histologic assessment of oral premalignant lesions. 
J Oral Pathol Med, 24, 198-200.
Kujan O, Oliver RJ, Khattab A, et al (2006). Evaluation of a new binary system of grading oral epithelial dysplasia for prediction of malignant transformation. 
Oral Oncol, 42, 987-93.
Kujan O, Khattab A, Oliver R, et al (2007). Why oral histopathology suffers interobserver variability on grading oral epithelial dysplasia: An attempt to understand the source of variation. 
Oral Oncol, 43, 224-31.
Mehanna HM, Rattay T, Smith J, McConkey CC (2009). Treatment and follow-up of oral dysplasia- a systematic review and meta analysis. 
Head Neck Oncol, 31, 1600-9.
Pindborg JJ, Reibel J, Holmstrup P (1985). Subjectivity in evaluating oral epithelial dysplasia, carcinoma in situ and initial carcinoma. 
J Oral Pathol, 14, 698-708.
Rastogi V, Puri N, Mishra S, et al (2012). An insight to oral epithelial dysplasia. 
Int J Head Neck Surg, 4, 74-82.
Richart RM (1967). Natural history of cervical intraepithelial neoplasia. 
Clin Obstet Gynec, 10, 748-84.
Sarode SC, Sarode GS, Patil A (2010). Criteria to define true second primary oral squamous cell carcinoma. 
Oral Oncol, 46, 834.
Speight PM, Abram TJ, Floriano PN, et al (2015). Interobserver agreement in dysplasia grading: toward an enhanced gold standard for clinical pathology trials. 
Oral Surg Oral Med Oral Pathol Oral Radiol, 120, 474-82.
Tabor MP, Braakhuis BJM, van der Wal JE, et al (2003). Comparative molecular and histological grading of epithelial dysplasia of the oral cavity and the oropharynx. 
J Pathol, 199, 354-60.
Warnakulasuriya S, Johnson NW, van der Waal I (2007). Nomenclature and classification of potentially malignant disorders of the oral mucosa. 
J Oral Pathol Med, 36, 575-80.