Leukoplakia and erythroplakia: A clinicians perspective and histopathologist verdict - A retrospective study

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Abstract

Background: Precancerous lesions and conditions which are replaced by the term potentially malignant disorders (PMDs) may precede oral cancer. The PMDs present as visible clinical changes may belie the true nature of the lesion. Histopathologic diagnosis is the gold standard in evaluating these lesions for dysplasia and malignant potential. The aim of the present study is to evaluate the clinicopathological findings of oral leukoplakia and erythroplakia.

Materials and Methods: Pathological report of cases, which were clinically diagnosed as leukoplakia and erythroplakia, were studied retrospectively from 2013 to 2015.

Results: Of the 20 cases reviewed, 12 were homogenous leukoplakia, 3 speckled leukoplakia, and 5 erythroplakia cases. Age ranged from 27 to 77 years. Males 14 and females 6. The buccal mucosa was the common site. Histopathology study revealed out of 12 cases of homogenous leukoplakia, 9 showed hyperkeratosis and mild epithelial dysplasia was seen in 3 cases. In 3 cases of speckled leukoplakia, mild epithelial dysplasia was seen in 2 cases (2/3) and severe epithelial dysplasia was seen in 1 case (1/3). In 5 cases of erythroplakia, 2 showed mild dysplasia, 1 showed severe dysplasia, and 1 squamous cell carcinoma (SCC).

Conclusion: Oral leukoplakia and erythroplakia can demonstrate a wide spectrum of histopathological features ranging from hyperkeratosis, dysplasia to SCC.

Keywords
Epithelial dysplasia, erythroplakia, leukoplakia

Introduction

Leukoplakia and erythroplakia are the two prevalent oral potentially malignant disorders (OPMDs). OPMDs include both premalignant lesions and conditions, which shows higher risk of transformation to malignancy, especially in the form of oral squamous cell carcinoma (OSCC).¹,²

OPMDs may indicate an increased risk for malignancy not only at the site of the lesion but also in normal appearing oral mucosa. The World Health Organization (WHO) working group on oral cancer have included the following lesions under OPMDs, which includes leukoplakia, erythroplakia, oral submucous fibrosis, palatal changes associated with reverse smoking, oral lichen planus, and discoid lupus erythematosus.³

The histopathologic evidence in the form of presence and the degree of epithelial dysplasia are the important and best predictors for indicating the risk of malignancy. The clinical presentation of OPMDs may present with varying microscopic evidence ranging from hyperkeratosis to epithelial dysplasia, to SCC. Epithelial dysplasia has susceptibility for malignant transformation in the range of 5-18%.⁴ The histopathological study is the best predictor in the evaluation of malignancy in OPMDs. The objective of our study was to evaluate the relevance of histopathological findings in lesions presenting as oral leukoplakia and erythroplakia.

Materials and Methods

A retrospective study was conducted in the Department of Oral Pathology from January 2013 to December 2015, in which the cases were selected based on inclusion and exclusion criteria. The cases, which were clinically diagnosed as leukoplakia and erythroplakia and associated with tobacco habit, were included for the study. The cases which did not have the clinical records were excluded from the study. Pathologic report of 20 cases of the patients was retrieved and reviewed in detail which fulfilled the preset criteria. Clinical features, which were
recorded, include age, gender, site, clinical diagnosis, and their histopathological findings. The presence of epithelial dysplasia was graded using the WHO 2005 grading. They were graded as: Mild epithelial dysplasia, moderate epithelial dysplasia, severe epithelial dysplasia, and carcinoma in situ. Architectural changes, which involved the lower one-third of the epithelium along with the cytological atypia, were considered as mild epithelial dysplasia. Architectural changes, which involved the middle third of the epithelium, were graded as moderate epithelial dysplasia. Architectural changes extending more than 2/3rd of the epithelium and the increased number of the cytological atypia were graded as severe epithelial dysplasia. Full thickness of the epithelium exhibiting architectural disturbances, abnormal superficial mitosis, and atypical figures was included under carcinoma in situ.\(^5\) Results were then correlated with the clinical diagnosis.

**Results**

A total of 20 cases were selected for the study which met the inclusion criteria. The age ranged from 27 to 77 years, with a mean age of occurrence was seen involving 54 years. The age group commonly affected was 40-60 years. Male predilection was seen in the ratio of male to female of 7:3. Table 1 summarizes the patient’s age distribution in the study group.

Clinical presentation was seen to involve a single site, commonly affected was buccal mucosa and next the tongue. In 3 patients, it was observed that there was multiple site involvement. The site of involvement is shown in Table 2.

In the clinical presentation, out of the 20 cases, 12 presented with homogenous leukoplakia [Figure 1], 5 being erythroplakia, and 3 were speckled leukoplakia.

Histopathology report of 12 cases of homogenous leukoplakia showed hyperkeratosis in 9/12 [Figure 2], and mild epithelial dysplasia was seen in 3/12 [Figure 3]. Histopathology report of 5 cases of erythroplakia was diagnosed as mild dysplasia in 3/5, severe dysplasia in 1/5, and 1 case of SCC were reported (1/5) [Figure 4]. The histopathology report of 3 cases of speckled leukoplakia was diagnosed as mild epithelial dysplasia in 2/3 and severe dysplasia in 1/3 as depicted in the Table 3.

**Discussion**

Leukoplakia is defined as “A white plaque of questionable risk having excluded (other) known diseases or disorders that carry no increased risk for cancer.” Leukoplakia can present in any location in the oral cavity. Leukoplakia can be divided clinically as a homogenous type (flat, thin, uniform white) and a non-homogeneous type. The non-homogeneous type has been defined as erythroleukoplakia/speckled (a white and red lesion) that may be either irregularly flat or nodular.\(^6\) Leukoplakia has the prevalence rate of approximately 2%. The rate of malignant transformation in oral leukoplakia varies among studies, ranging from <1% to 20%.

Figure 1: Clinical picture: It shows homogenous leukoplakia on the right buccal mucosa

Figure 2: Hyperkeratosis with no dysplasia (H and E, ×100)

Figure 3: Mild epithelial dysplasia: Dysplastic feature seen in basal and suprabasal cell layer of stratified squamous epithelium (H and E, ×400)
Erythroplakia is defined as “A fiery red patch that cannot be characterized clinically or pathologically as any other definable disease.” The clinical presentation may be flat or depressed with a smooth or granular surface. Non-homogeneous leukoplakia (“erythroleukoplakia”) presents as a mixed red and white lesion. The important etiologic factors are considered to be tobacco and alcohol use. Studies conducted in South- and Southeast-Asia has reported a prevalence rate of erythroplakia to vary in the range of 0.02% and 0.83%.\(^7\)

Erythroplakia cases on histopathologic study most often show epithelial dysplasia of varying grade and may even show carcinoma in situ or SCC.\(^8\) The cases presenting clinically as erythroplakia are rare, and hence, there are very few documented data that would reliably predict its malignancy potential.\(^6\)

The concept of oral cancer development being a two-step process that is the initial presence of a precursor lesion which subsequently develops into cancer has been accepted. Oral leukoplakia and erythroplakia are well-known precursor lesions hence our aim was to find a clinicopathologic correlation of these common precursor lesions.

Our study showed leukoplakia and erythroplakia cases presented mainly in the fifth decade of life. However, in a study done by Scott and Cheah (1989),\(^9\) the result showed that the sixth and seventh decades as the common age of occurrence. Liu et al., in 2010,\(^10\) conducted a study on potentially malignant lesions which showed a higher incidence in fifth decade; this finding was similar in our study, which is a decade earlier than the previous studies. There was one case seen in a 27 year old this could be attributed to the easier access to gutka/pan masala, smoking, peer pressure, and advertisement in media, e.g., television and the internet may be the cause for a change in the trend that we have seen.

In our study, there was an increase presentation seen in males compared to females in a ratio of male to female that is 7:3. Studies conducted by Liu et al.,\(^10\) Dietrich et al.,\(^11\) and Misra et al.\(^12\) also showed increase incidence in males. The reason for greater incidence in males is due to increase use of tobacco in males.

We found that most of the cases presented with lesions involving a single site which was seen on the buccal mucosa most commonly and then on the lateral border of the tongue. Similar result was seen in studies conducted by Misra et al.\(^12\) and Lee et al.\(^13\) but not in accordance with results of Liu et al.,\(^10\) in which the common site of involvement was the tongue.

In our study, the most common case was of homogenous leukoplakia (12) followed by erythroplakia (5) and speckled leukoplakia (3). Histopathological finding of homogenous leukoplakia was mainly hyperkeratosis followed by mild epithelial dysplasia. In cases diagnosed as speckled leukoplakia, histopathological study showed mild and severe dysplasia, and in erythroplakia cases, its histopathologic diagnosis was mild epithelial dysplasia, severe epithelial dysplasia, and one case of SCC. A study conducted, in 2006, by Holmstrup et al.\(^14\) showed, out of 236 patients, there were 39 cases of homogenous

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**Table 1:** The age distribution of patients in the study group

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>21-30</td>
<td>2</td>
</tr>
<tr>
<td>31-40</td>
<td>2</td>
</tr>
<tr>
<td>41-50</td>
<td>2</td>
</tr>
<tr>
<td>51-60</td>
<td>8</td>
</tr>
<tr>
<td>61-70</td>
<td>5</td>
</tr>
<tr>
<td>71-80</td>
<td>1</td>
</tr>
</tbody>
</table>

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**Table 2:** The site of involvement

<table>
<thead>
<tr>
<th>Site of the lesion</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buccal mucosa</td>
<td>10</td>
</tr>
<tr>
<td>Tongue</td>
<td>3</td>
</tr>
<tr>
<td>Gingival</td>
<td>2</td>
</tr>
<tr>
<td>Vestibule</td>
<td>1</td>
</tr>
<tr>
<td>Retromolar trigone</td>
<td>1</td>
</tr>
<tr>
<td>Multiple sites</td>
<td>3</td>
</tr>
</tbody>
</table>

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**Table 3:** Correlation of histopathology with clinically diagnosed cases of leukoplakia and Erythroplakia

<table>
<thead>
<tr>
<th>Cases</th>
<th>Number of cases</th>
<th>Hyperkeratosis</th>
<th>Mild epithelial dysplasia</th>
<th>Severe epithelial dysplasia</th>
<th>Squamous cell carcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Homogenous</td>
<td>12</td>
<td>9</td>
<td>3</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Speckled</td>
<td>3</td>
<td>0</td>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Erythroplakia</td>
<td>5</td>
<td>0</td>
<td>3</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

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leukoplakia, 46 cases were non-homogenous leukoplakia, and 9 cases were erythroplakia. Epithelial dysplasia was seen in 71% of the cases. 20% of non-homogenous leukoplakia showed malignant development and only 3% of the homogenous leukoplakia developed malignancy. The present study showed that most of the cases presented as homogenous leukoplakia while erythroplakia was uncommon which was similar to the previous studies. Lee et al.\[13\] conducted a study, in which 1046 patients were selected who were diagnosed as oral leukoplakia, 408 cases showed only epithelial hyperplasia, and/or hyperkeratosis, 477 cases presented with epithelial dysplasia. Out of 477 cases, 200 cases showed mild dysplasia, 234 showed moderate, 43 showed severe, and 135 cases showed invasive SCC. The incidence of malignancy in our study was seen in only one case that is in case of erythroplakia.

Above finding necessitates the need for taking biopsies and histopathologic diagnosis of cases which are clinically diagnosed as speckled leukoplakia and erythroplakia. In our study, tobacco was the only habit recorded since it was a retrospective study some of the files did not have detailed information of the duration and frequency of the habits. Tobacco was the most prevalent of the habits recorded.

Future prospects for the study would be to consider all the OPMD which are clinically diagnosed and histopathologically studied using a larger sample and with better evidence.

**Conclusion**

Our study result showed that the incidence of leukoplakia and erythroplakia was higher in males in the ratio of 7:3. Age of presentation was commonly seen in the fifth decade. Clinical presentation commonly showed homogenous leukoplakia. Histopathological evidence showed a wide range of presentation ranging from hyperkeratosis to epithelial dysplasia of varying grade to frank SCC. Hence, we would emphasize that follow-up of the patients and counseling regarding cessation of the risk factors are measures to be taken and biopsy is the gold standard for diagnosis or to rule out malignancy, especially in cases of erythroplakia and speckled leukoplakia.

**References**
