Expression of S100A7 in oral potentially malignant disorders: An immunohistochemical study

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Abstract

Context: Oral potentially malignant disorders (OPMDs) are a group of heterogeneous lesions with an increased risk of malignancy. S100A7 expression serves as a biomarker to identify the dysplastic lesion.

Aims: To study the status of S100A7 antigen in healthy oral mucosa and OPMDs.

Settings: Bharati Vidyapeeth (Deemed to be University) Dental College and Hospital, Pune.

Design: S100A7 antigen in healthy oral mucosa and OPMDs.

Methods: Biopsies were collected of clinically diagnosed OPMDs as well as of healthy oral mucosa and analysed for the malignancy potential.

Material: Polyclonal rabbit S100A7 25 µl, BioGenex detection system, hydrogen peroxide, non-streptavidin biotin-HRP, wash buffer, DAB chromogen, TRIS buffer, Harris haematoxylin and eosin.

Statistical Analysis Used: Data analysis was performed using Statistical Package for Social Sciences Version 27.0. Qualitative data variables expressed were analysed using frequency and percentage. Quantitative data variables were expressed using mean and standard deviation. The Chi-square test was used to compare the grade of intensity, where P value <0.05 was considered significant.

Results: Healthy oral mucosa did not reveal any immunopositivity. Oral leukoplakia showed some focal expression till middle middle third of epithelium. Oral erythroplakia was found with maximum expression while submucous fibrosis showed increased intense staining in six cases.

Conclusions: S100A7 antigen showed significant immune expression in OPMDs and may be used as a marker for early diagnosis and precision therapy.

Keywords: Malignancy potential, oral potentially malignant disorders, S100A7

INTRODUCTION

The term ‘potentially malignant disorders’ was defined by the World Health Organization (WHO) as the risk of malignancy being present in a lesion or condition either during the time of initial diagnosis or at a future date.

Oral potentially malignant disorders (OPMDs) are a group of heterogeneous lesions associated with various risks of transformation into invasive cancer. The potential of S100A7 expression was underestimated to serve as a biomarker for dysplastic lesions which were at high risk.\(^1\)

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Subjects
Five subjects of healthy oral mucosa were considered as control.
Each of 15 oral leukoplakia, oral erythroplakia and oral submucous fibrosis was considered as an experimental group. Clinically obvious oral squamous cell carcinoma (OSCC) was excluded.

**METHODS**

Five healthy oral mucosal tissues were collected along with 15 from clinically diagnosed oral leukoplakia, oral erythroplakia and oral submucous fibrosis. Histopathological grading of dysplasia was done with haematoxylin and eosin [Figures 1‑3]. Anti-S100A7 antibody was used to evaluate the malignancy potential by assessing the expression at the nuclear and cytoplasmic level in all the layers of the epithelium [Figures 4‑6].

**Ethical Clearance Number**
EC/NEW/INST/2019/329.

**RESULTS**

In the category of oral erythroplakia, 11 cases of severe dysplasia consisting of 73.33% of the total were observed, indicating the significant potential of conversion to malignancy owing to the highest intensity of staining with anti-S100A7 [Figure 4]. It was followed by four cases consisting of 26.66% that took up the minimal intensity of stain against anti-S100A7 suggestive of the least probable chances of malignancy.

In the study group of oral leukoplakia, six cases of severe dysplasia consisting of 40% of the total subjects had taken up the maximum stain of anti-S100A7 that led to the utmost prominent staining [Figure 5], indicating that amongst the 15 cases of oral leukoplakia those 6 cases have the paramount potential to undergo malignancy transformation. This was followed by five cases of low-grade dysplasia consisting of 33.33% of the entire subjects that took up the minimal intensity of stain suggesting of least malignancy potential, while the minimum quantity of cases was found in moderate dysplasia with four cases having a fair susceptibility to transform into severe and therefore a high potential of malignancy transformation.

In the study group of oral submucous fibrosis, nine cases were diagnosed to be mild dysplasia which was imperative of the fact of its low potential of malignancy transformation, while the rest 40% consisting of six cases of severe dysplasia were representative of high susceptibility to malignancy [Figure 6].

**DISCUSSION**

In a workshop coordinated by WHO, it was decided to use the term ‘Potentially Malignant Disorders’ to convey that not all disorders described under this term may transform into cancer, rather this is a family of morphological alterations which may have an increased potential for malignant transformation. Etiological factors can be identified and patients can be warned of the potential malignant changes. Primarily S100A7 (psoriasin) was detected in psoriatic keratinocytes. S100A7 has a distinct expression that gets bound to different receptors in a zinc-dependent manner. Dysregulation is associated with the multitude of malignancies apart from OSCC like osteosarcoma, ovarian cancer (S100A7) and cervical cancer (S100A7).

**Anti-S100A7 antibody in OPMDs**

Comparison of S100A7 in OPMDs versus control group

S100 A7 was not detected in oral healthy mucosa. Comparison of immunopositivity of anti-S100A7 [Figure 7] in OPMDs with the control group shows that expression of anti-S100A7 was identified which is the preliminary stage for neoplastic change eventually leading to malignancy.

**Assessment of anti-S100A7 status in oral leukoplakia**

Amongst the 15 subjects in the category of oral leukoplakia, 40% of them were detected with severe dysplasia, which took up immunexpression of Anti-S100A7 antibody at the nuclear and cytoplasmic level till the upper one-third of the epithelium [Figure 5]. Thus those six subjects are suggested to have the highest potential to undergo a malignant transformation in this particular clinical strata. It was followed by four cases that showed immunexpression till just the middle one-third of the epithelium. The last of all five cases showed mild expression which extended to the lower one-third of the epithelium. Therefore, we concluded from the above information that 40% of cases
may have the potential to transform into malignancy. The genotypic composition, habits, micronutrient deficiency and lack of awareness, especially in a certain stratum of the Indian population, are considered. Lastly, the molecular genetics seems to be the significant factor that enables a significant quantity of high dysplasia cases which may have elevated the percentage of malignant potential.

**Assessment of anti-S100A7 status in oral erythroplakia**

The study data confirmed that around 11 cases constituting 73.33%, which were diagnosed with severe dysplasia, had taken up the highest expression of anti-S100A7 at the nuclear and cytoplasmic level in all the layers of the epithelium. The intensity of the stain at the nuclear and cytoplasmic level detected in the epithelium was suggestive of high malignant potential. As per this study, data mentioned that mild dysplasia was detected in just four cases, which formed 26.66% of the 15 erythroplakia lesions. Immunopositivity showed mild patchy stains in focal areas of the epithelial lining and some on just the stratum basale of the epithelium, while none of the 15 subjects showed moderate dysplasia. It was confirmed from the above study data that oral erythroplakia had the maximum cases of expression of anti-S100A7 [Figure 4] which suggested the highest transformation potential amongst the three experimental groups [Figure 7].

**Assessment of anti-S100A7 status in oral submucous fibrosis**

Amongst the 15 participants, 40% showed the highest immunopositivity to anti-S100A7 suggestive of maximal potential for malignant transformation. The immunopositivity was observed in all three layers of the epithelium at the nuclear and cytoplasmic level [Figure 6]. The rest 60% consisting of 9 patients had lesser immunopositivity as patchy focal areas of the epithelium signalling the diminished potential for malignancy. The immunopositivity was assessed similar to the other two study groups by observing the shade with each layer of the epithelium. The percentage of malignancy potential will be compared to the grades of dysplasia. Accumulated data with the statistical results were equivocal with the given aims and objectives of the research showing P value to be less than 0.05 (0.014) using the Chi-square test which was a significant finding. The sample size of the study could be increased further and significant data on the immune expression could be compared to the grades of dysplasia.

**Key messages**

S100A7 may predict the potential of malignant transformation in OPMDs.

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**Conflicts of interest**

There are no conflicts of interest.

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