Original Article

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

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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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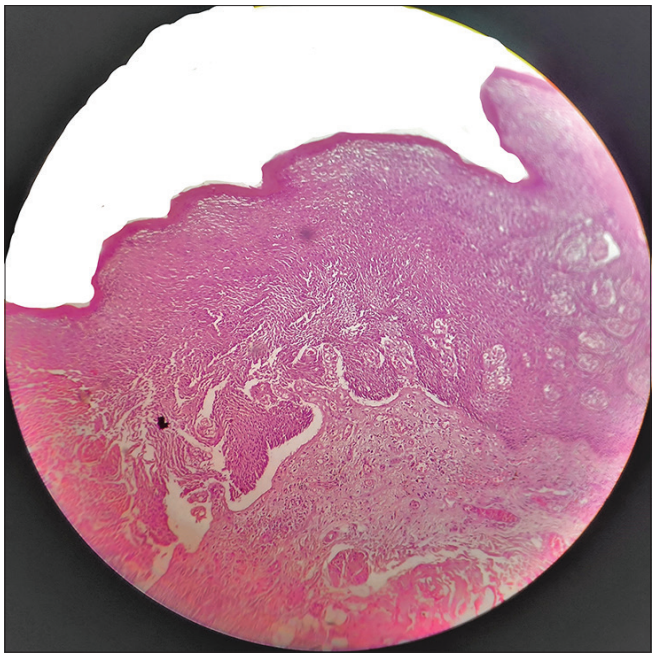

Figure 1: erythroplakia with dysplasia in H AND E

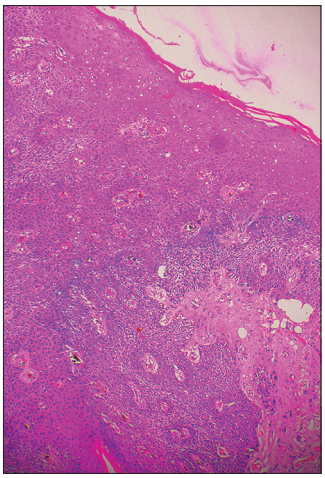

Figure 2: Leukoplakia with dysplasia H AND E 10X

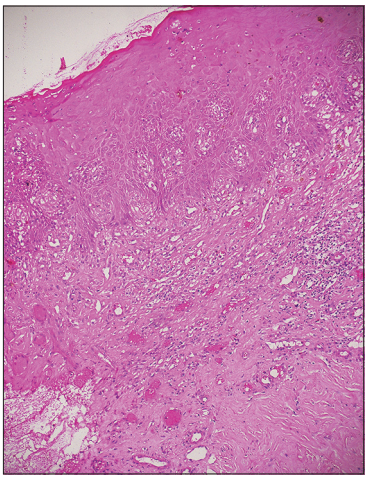

Figure 3: OSMF WITH DYSPLASIA HAND E 10X

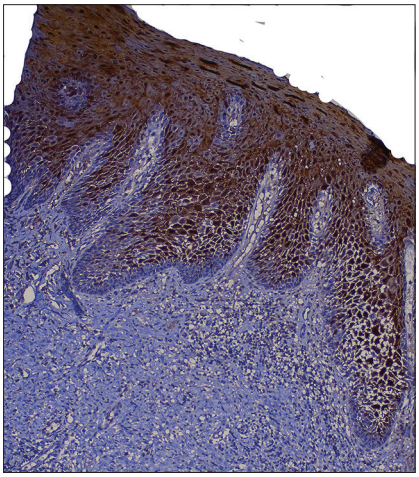

Figure 4: Erythroplakia with dysplasia in S100A7

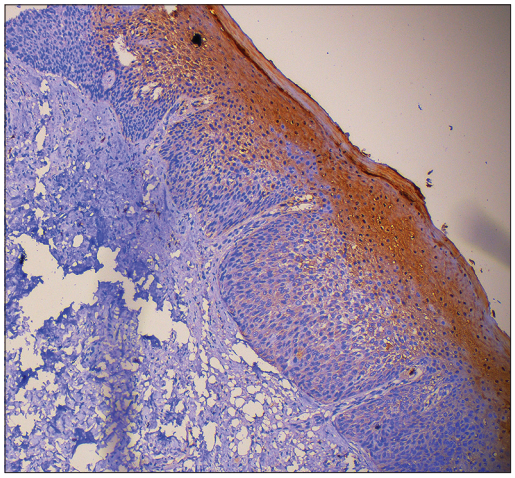

Figure 5: Leukoplakia with dysplasia IHC 10X

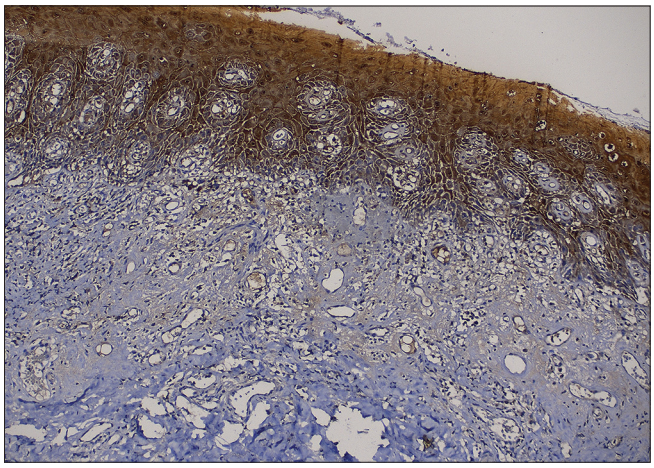

Figure 6: OSMF WITH DYSPLASIA IHC

Subjects

Five subjects of healthy oral mucosa were considered as control.

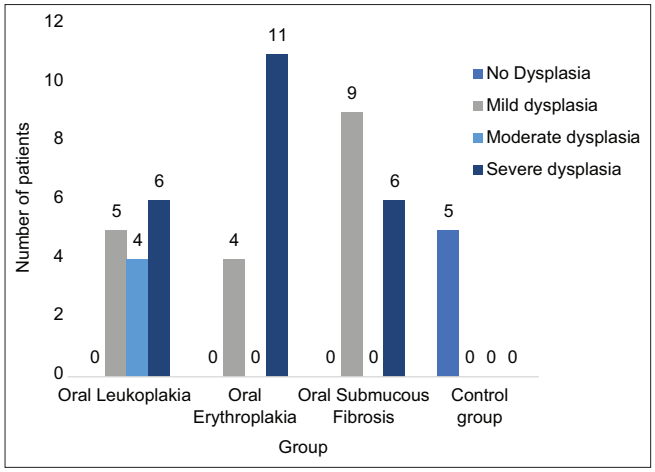

Figure 7: Gradation of dysplasia with study vs control group

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.[2] 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%[3] of them were detected with severe dysplasia, which took up immunoexpression 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 immunoexpression 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. Immunoexpression 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 immunoexpression 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 immunoexpression 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 vary with etiological factors, molecular pathogenesis and epithelial–mesenchymal transitions happening at the cellular level specific to every individual. The staining intensity with anti-S100A7 shows conducive results by Muhammad Arsalan Raffat, Naila Irum Hadi *et al.* 2020 who state that higher levels of S100A7 protein level were seen in stage I oral submucous fibrosis group in comparison to the healthy individuals.[4]

CONCLUSION

The aim to study the status of S100A7 in OPMDs was substantiated by the intensity levels of expression found at the nuclear and cytoplasmic level. Severe dysplasia corroborated with the maximum levels of immunopositivity. Depending upon the severity we could gauge the potential for malignant transformation. As per Thorburn and Darling 2020, anti-S100A7 or psoriasin has been gaining increased recognition for its proposed correlation to poor prognosis in OSCC patients and emerging as the favoured predictive biomarker for oral pre-cancer progression.[4] In case of disparities in the grading of dysplasia, S100A7 can provide a better perspective histopathologically via its immunoexpression at the nuclear and the cytoplasmic level about the futuristic possibilities of malignancy transformation.

Anti-S100A7 antibody may predict the potential of malignant transformation in the given categories of oral leukoplakia, oral erythroplakia and oral submucous fibrosis. The study has been exclusively conducted amongst the Indian local population to analyse their pattern of staining intensity given the respective 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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Nil.

Conflicts of interest

There are no conflicts of interest.

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