Original Article

COMPARATIVE ANALYSIS OF p53 & PCNA IN ORAL EPITHELIAL DYSPLASIA, ORAL LICHEN PLANUS AND ORAL SQUAMOUS CELL CARCINOMA – AN IMMUNOHISTOCHEMICAL STUDY

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ABSTRACT

Background: The strong indicator of malignant transformation potential of certain lesion is the change in the expression of proteins which are related to cell proliferation and apoptosis. Earlier studies suggest that oral lichen planus shows a possibility of malignant transformation to squamous cell carcinoma, therefore the diagnosis of oral lichen planus in the initial stages is not an error in diagnosis but it shows that in due course of time it has transformed into squamous cell carcinoma.

Aim & Objective: The aim is to analyze the expression of p53 and PCNA in oral epithelial dysplasia,oral squammous cell carcinoma.Both the differences and combined immunoexpressions was studied.

Methodology: 40 cases were taken, 10 cases each of dysplastic tissue, oral lichen planus, oral squamous cell carcinoma and buccal mucosa. Immunohistochemistery was done to analyze p53 and PCNA expression.

Result: The results of this study exhibited the alterations in the expression of these proteins as observed in Lichen planus and epithelial dysplasia conforming the potential for malignant transformation of both lesions.

KEYWORDS : p53 & PCNA, Oral Epithelial Dysplasia, Oral Lichen Planus, Oral Squamous Cell Carcinoma, Immunohistochemical Study

INTRODUCTION

Oral Squamous Cell Carcinoma is the 6th most frequent cancer in the world and the 8th most common cause of cancer related to deaths worldwide.5 year survival rate of OSCC is just 40-50%.15.8 to 48% of OSCC patients were associated with premalignant lesions and conditions when diagnosed.WHO in 2005 workshop included premalignant lesions and conditions under the term “potentially malignant disorders” which were defined as the risk of malignancy being present in a lesion or condition either at time of initial diagnosis or at a future date.Oral leukoplakia is the most common potentially malignant disorder where malignant transformation rate of leukoplakia is 0.6 % to 20% and malignant potential of Oral lichen is 0.04 to 1.74%.Histological examination of tissue remains the gold standard for diagnosis and identification but the molecular level changes in the lesion occur before any clinical and histopathological changes. Identification of high-

risk potentially malignant disorders and intervention at premalignant stages could constitute one of the keys in reducing the mortality, morbidity associated with OSCC.

AIMS & OBJECTIVES

1.To analyze the quantitative and qualitative immunoexpression of p53 and PCNA in oral epithelial dysplasia, oral lichen planus and OSCC.

2.To correlate the difference in the immunoexpression of p53 and PCNA in different grades of epithelial dysplasia and OSCC

3.To correlate the combined immunoexpression of p53 and PCNA in oral epithelail dysplasia,oral lichen planus and OSCC.

METHODOLOGY

It is a retrospective study and the samples were selected histopathologically from confirmed cases after H&E staining from the archives of the Department of Oral Pathology, I.T.S greater Noida.The Total Sample Size is 40 cases:

- 10 cases - Varying grades of Epithelial dysplasia
- 10 cases - Varying clinical forms of Oral lichen planus
- 10 cases - Varying stages of OSCC
- 10 cases – Normal Buccal mucosa

4 μm thick sections were taken and immunohistochemistry was performed using monoclonal antibody (DO-7) p53 and monoclonal PCNA antibody. Evaluation of Staining was done where:

- Only cells with brown-colored staining were considered positive.
- PCNA is a nuclear stain
- P53 is a cytoplasmic and nuclear stain

Labelling Index was done where Counting of positive cells out of total 500 cells at X400 magnification from 4 representative areas. The Intensity of staining was as follows:

- Negative (no color) = 0
- Mild (light brown) =1
- Moderate (dark brown) = 2
- Intense (very dark brown) = 3

The Distribution of staining is done below:

DISTRIBUTION	SCORE
Negative	0
Only basal layer **OR** Only peripheral cells in OSCC islands and nests	1
Basal and Suprabasal layer OR Peripheral and few central cells in OSCC	2
All the layers of epithelium OR All the cells in OSCC epithelial islands	3

RESULTS

Figure 1 : 40x view of p53 in Mild dysplasia

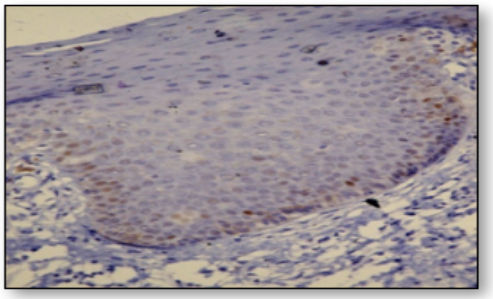


Figure 2 : 4x view of p53 in moderate dysplasia

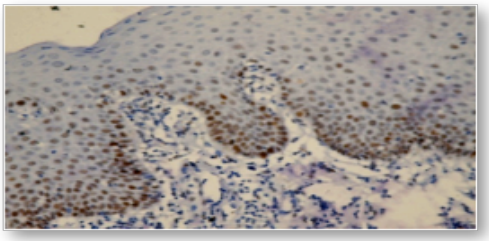


Figure 3 : 4x view of p53 in severe dysplasia

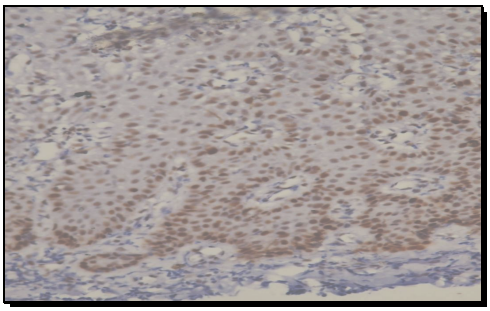


Figure 4 : 40 x view of p53 in oral lichen planus

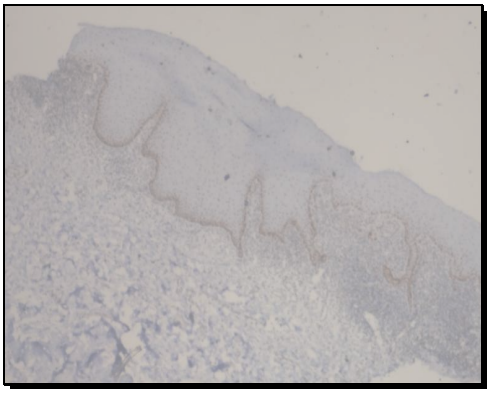


Figure 5 : 40 x view of p53 in well differentiated OSCC

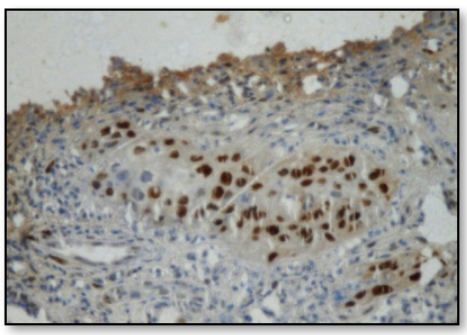


Figure 6 : 40x view of p53 in moderately differentiated OSCC

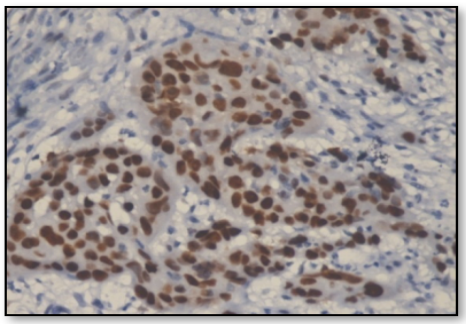


Figure 7 : 40x view of p53 in poorly differentiated OSCC

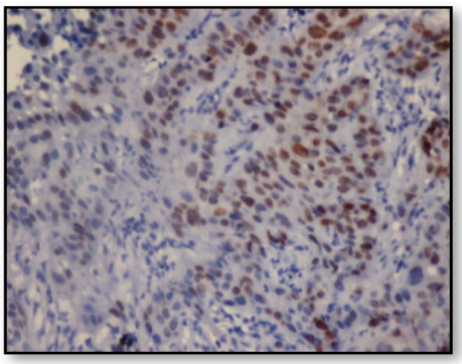


Figure 8 : Mild Dysplasia PCNA

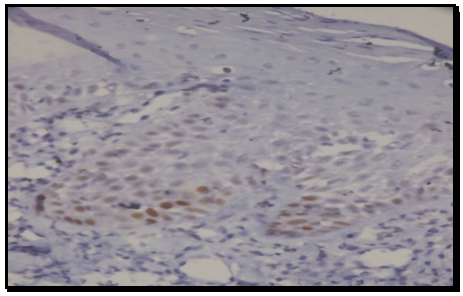


Figure 9 : Moderate Dysplasia PCNA

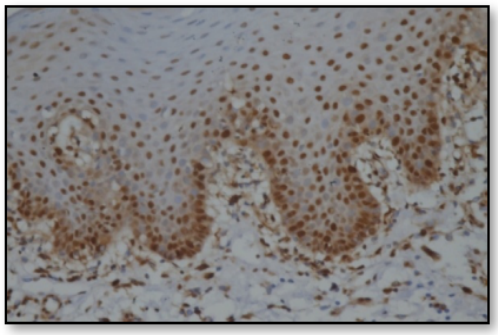


Figure 10 : Severe Dysplasia 40X

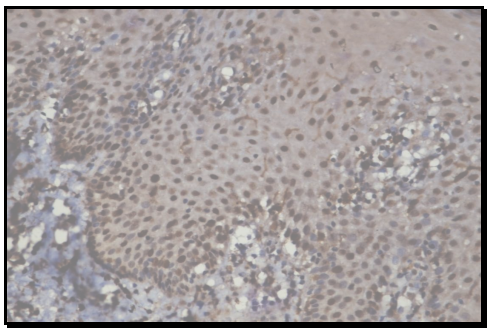


Figure 11: Moderately diff OSCC PCNA 40 x

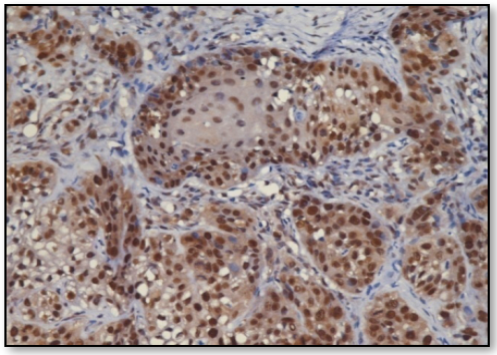
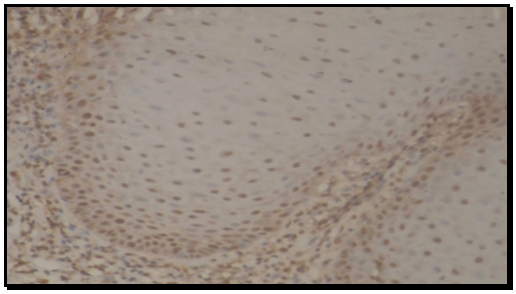


Figure 12: 40 x view of PCNA in Oral Lichen Planus



DISCUSSION

The strong indicator of malignant transformation potential of certain lesion is the change in the expression of proteins which are related to cell proliferation and apoptosis. Earlier studies suggest that oral lichen planus shows a possilbility of malignant transformation to squamous cell carcinoma,therefore the diagnosis of oral lichen planus in the initial stages is not an error in diagnosis but it shows that in due course of time it has transformed into squamous cell carcinoma.The accumulation of the genetic alterations leading to cancer development favours the index which shows increased cell proliferation index in epithelial dysplasia and oral lichen planus, this also suggests that epithelium of epithelial dysplasia is more susceptible than oral lichen planus, but when compared to normal mucosa oral lichen planus shows more susceptibility towards the malignant transformation[1] this goes completely in accordance with our study which resulted that p53 and PCNA labelling indices were seen higher in OLP and dysplasia when compared with normal buccal mucosa. With increase in grade of epithelial dysplasia the indices of p53 labelling increased suggesting that alterations in the expression of p53 are essential for carcinogenesis indicating an important step in transformation from normal to malignancy.p53 is basically a nuclear protein whose mutation is strongly associated to cancer[2,3,4,5].Our study suggested that suprabasal p53 immunoexpression can be highly predictive for malignant disorders. p53 labeling index is 0.44 in OLP ,PCNA labeling index is 0.52 in OLP .Earlier studies suggested that there is a possibility that increased cell proliferation is probably a secondary phenomenon due to epithelial cells damage caused by infiltrating lymphocytes in OLP. Combined p53/ PCNA expression could be a relevant marker of increased malignant potential or aggressiveness and biologic behavior of lesions [6,7,8,9,10,11].High combined P53/ PCNA index confirmed in highly invasive cancer; had high risk of tumor recurrence; Indicator of poor prognosis in OSCC patients. In general the data obtained in the present study goes in agreement to those authors who evaluated the expression of PCNA,p53 in relation to cell proliferation and apoptosis in oral lichen planus.for all the earlier studies expression of these proteins act as a strong indicator of malignant transformation of lichen planus as they participate with oral carcinogenesis.

CONCLUSION

The results of this study exhibited the alterations in the expression of these proteins as observed in lichen planus and epithelial dysplasia conforming the potential for malignant transformation of l both lesions.need for a long follow up is need to keep a check on any alteration that indicate possible malignant transformation.

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