Research Paper

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UTILITY OF Ki67 IN PRE-MALIGNANT AND MALIGNANT SKIN LESIONS

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ABSTRACT Objective: The purpose of the study is to evaluate the significance of ki67 antigen expression in premalignant and malignant skin lesions. Materials and methods: This was a retrospective study that included 12 premalignant and 15 malignant skin lesions diagnosed during June 2016 to May 2018. Immunohistochemistry with ki67 was done on these 27 cases. The ki67 proliferative index was determined by counting stained nuclei among 500 tumor cells. Result: The Ki67 labeling index for keratoacanthoma was 33%, Bowen's disease was 37%, Bowen's disease with microinvasion was 40.8%, Squamous cell carcinoma was 42.2%, Basal cell carcinoma was 53%.Conclusion: IHC with Ki67 may be suggested in punch biopsies of skin in suspected malignancies to know the aggressive nature of the lesion.

KEYWORDS

Premalignant skin lesions, Malignant skin lesions, Ki67 labeling index.

ARTICLE HISTORY

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INTRODUCTION:

Pre malignant lesions of the skin are the conditions that can be recognized clinically and histopathologically and are associated with increased risk of developing invasive cancer. Pre malignant lesions of the skin include Bowen's disease, actinic keratosis and keratoacanthoma.

It is important to distinguish these lesions from the malignant lesions and treat them promptly. In our study we compared the proliferative index of premalignant and malignant skin lesions using Ki67.

AIM: Aim of our study is to compare the proliferative index of pre-malignant and malignant skin lesions.

MATERIALS AND METHODS:

This retrospective study of 2 years(June 2016 to June 2018) was undertaken in the Department of Pathology at Sree Balaji Medical College, Chennai. During this period of study, we received 154 skin biopsies out of which 114 were benign lesions, 8 were not from representative site, 12 were premalignant lesions of skin and 15 were malignant lesions of skin. Out of 27 selected cases, 12 were premalignant and 15 were malignant skin lesions.

The biopsies received were formalin fixed, embedded in paraffin, sectioned at 3microns and mounted on to poly L lysine coated slides. Ki67 immunohistochemical proliferative marker study using peroxidase-antiperoxidase technique was done with mouse monoclonal Ki67 antibody. Goat anti-mouse IgG polyclonal was used as secondary antibody. Horse radish peroxidase is used as micropolymer and Diaminobenzene(DAB) as chromogen substrate. Positive Ki67 staining was observed as brown granular nuclear staining.

For Ki67 scoring the most positive area of the tumor was selected avoiding foci of inflammation. The number of positive nuclei is counted in 500 tumor cells in a high power field(x400). The average of 3 counts over the same slide was taken and expressed as percentage of Ki67 positive cells in the tumor.

RESULTS:

Ki67 labeling index was studied in 27 cases which included 12 premalignant lesions(8 Keratoacanthoma, 4 Bowens disease) and 15 malignant lesions(5 Squamous cell carcinoma, 2 Bowens disease with invasion and 8 Basal cell carcinoma). For control normal skin was used. Control showed uniform staining of basement membrane, whereas the premalignant and malignant lesions showed uneven staining pattern. The Ki67 index of each cases are as follows: Keratoacanthoma-33%, Bowen's disease-37%, Bowens disease with microinvasion-40.8%, Squamous cell carcinoma-42.2%, Basal cell carcinoma-53.4%. Squamous cell carcinoma and Basal cell carcinoma show higher Ki 67 index than the premalignant lesions of the skin. The highest Ki67 expression was found in BCC. This confirms that its aggressive behavior is partly due to the enhanced cell proliferation.

Table 1 : ki67 index % of each skin lesion

Skin lesion	Ki67 index %
Keratoacanthoma	33%
Bowen's disease	37%
Bowen's disease with microinvasion	40.8%
Squamous cell carcinoma	42.2%
Basal cell carcinoma	53.4%

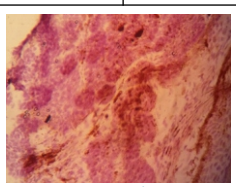

Figure : Expression of ki67 in Bowen's disease with micro-invasion

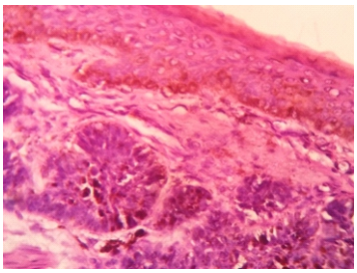

Figure : Ki67 expression in basal cell carcinoma.

DISCUSSION:

In view of the rising incidence of pre-malignant and malignant skin lesions in daily practice it is essential to assess the aggressive nature of the lesion.

The Ki67 antigen, a high molecular weight non-histone protein, is considered as the most reliable marker of proliferating cells1,2. It is expressed in all phases of cell cycle, except in G0 and is a marker of proliferation expressed in many cancers2,3,4. Positive Ki67 immunostaining had prognostic value in patients with certain types of cancers1. The Ki67 level has been shown to correlate with tumor progression, metastatic potential, and decreasing overall survival3,5.

In our study the expression of Ki67 was highest in basal cell carcinoma (53.4%) which was in concordance with the study conducted by Effat et al6.

Among the squamous cell lesions, poorly differentiated squamous cell carcinomas show higher Ki67 index which points at the aggressive behavior5,7. Pre malignant lesions show lower Ki67 index (Bowen's disease-37%, Keratoacanthoma-33%) than the Squamous cell carcinoma(42.4%) which is compatible with the study conducted by Batinacet al., (KA Ki67- 10 to 25.75% and SCC Ki67-36.5 to 46.2%)5.

The quantitative and qualitative evaluation of the expression of Ki67 may be helpful in differentiating malignant and premalignant epidermal lesions8.

CONCLUSION:

This study showed highest Ki67 expression in BCC. In SCC, particularly in poorly differentiated SCC the Ki67 expression is high. This confirms that its aggressive behavior is partly due to the enhanced cell proliferation.

IHC with Ki 67 may be suggested in punch biopsies of skin in suspected malignancies before the radical dissection of the tumor to know the aggressive nature of the tumor. These results warrant further study of modulation of cell proliferation in premalignant lesions.

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