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To compare and correlate the ki-67 and p53 expression in odontogenic keratocyst, in dentigerous cyst and ameloblastomas

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Abstract

Introduction: Cell proliferation is an essential process in all living organisms because of its roles in cell growth and the maintence of tissue homeostasis. The control of proliferation is completely in neoplasms. For this reason the assessment of cell proliferation activity by immunohistochemistry analysis has become an important tool to provide useful information about the behaviours of several tumours. As we know that irreversible increased cellular proliferation is a phenomenon of tumor, so in our study we are comparing and correlating proliferative marker ki-67 and p 53 expression in odontogenic keratocyst, in dentigerous cyst and in ameloblastomas.

Keywords: Ki 67, P53, Odontogenic keratocyst, Ameloblastoma, Dentigerous cyst.

Background: To compare and correlate the ki-67 and p53 expression in odontogenic keratocyst, in dentigerous cyst and ameloblastomas.

Method: A 10 cases of odontogenic keratocyst ,10 cases of dentigerous cysts and 10 cases of ameloblastomas were selected and examined morphologically and immunohistochemically for p53 and Ki 67 markers.

Results: p53 labeling index was highest in ameloblastoma group followed by keratocystic odontogenic tumor and minimal in dentigerous cyst group. The expression of ki-67 proliferative marker in keratocystic odontogenic tumor was highest and close to ameloblastoma group and was minimal in dentigerous cyst group. The result clearly depicted a very high proliferative potential of cystic epithelium of keratocystic odontogenic tumor and was comparable to a tumor i.e ameloblastoma.

Conclusion: The high proliferative potential of odontogenic keratocystic epithelium definitely stand it out from other developmental odontogenic cyst and the newer adopted WHO terminology keratocystic odontogenic tumor warrants it as aggressive lesion and also suggest a proper management.

Keywords: Ki-67, P-53, HRP

Introduction

Ki-67 antigen is present in all active parts of cell cycle, rises during later half of S phase and reaches a peak in G2 and M phase and rapidly degrades after mitosis with a half-life of detectable antigen being an hour or less[1]. So it correlates with other variables of cell proliferation p53 is a mutated product of tumor suppressor gene p53. It has a short half-life in normal cells and cannot be detected immunocytochemically, but when it mutates, the p53 protein product is more stable and can be detected immunocytochemically. It has been widely used for diagnosis of malignant tumors [2]. As we know that irreversible increased cellular proliferation is a phenomenon of tumor, so in our study we are comparing and correlating proliferative marker ki-67 and p 53 expression in odontogenic keratocyst, in dentigerous cyst and in ameloblastomas.

Materials and methods

The study material comprised of archival formalin fixed paraffin embedded specimens of patients from private oral pathology laboratory as 10 cases of odontogenic keratocyst,10 cases of dentigerous cysts and10 cases of ameloblastomas. All cases were histopathologically diagnosed. Standard histochemistry staining protocol was performed using primary antibody monoclonal mouse anti – human p 53 (1: 100 prediluted) and Monoclonal mouse anti – human Ki -67 (1: 100 prediluted) and super sensitive poly horse radish peroxidase (HRP) secondary antibody kit(biogenex india private limited). Slides were checked for positive staining as crisp, brown nuclear staining for ki-67 and p53 in respective sections. Counting of positive cells was done on all slides using counting grid. The cases were scored by counting the positive cells per minimum of 500 tumour cells per specimen.

Statistical analysis

Descriptive statistical analysis was performed for each group of lesions by statistical software program SPSS (version 16.0). The mean labeling indices were compared by using an analysis of variance test (ANOVA) for p53 and Ki 16 markers. Kruskal-Wallis Test were then performed to determine statistically significance. The keratocystic odontogenic tumor group showing a higher Ki-67 labeling index than the ameloblastoma ($P < .003$) and a highly significant difference was found with dentigerous cyst group ($p<0.000$). However the mean-percentage labeling index of p53 was highest in ameloblastoma group followed by keratocystic odontogenic tumor and minimal in dentigerous cyst group ($P > .05$) (TABLE 1 /GRAPH 1)

Discussion

Keeping the concept of tumor in mind the most common property is excessive proliferation of tumor cell thought

to be arising from mutation of p53 tumor suppressor gene or its product, we carried out this study with selection of ki-67 epithelial proliferative marker and p53 marker to put the concept of tumor proliferation due to mutated p53 gene in tumorigenesis by comparing the expression of ki-67 and p53 in epithelial lining of all the three groups.

Result of this study showed that cellular proliferative activity among dentigerous cyst, keratocystic odontogenic tumor (KCOT) and odontogenic tumor group varied uniquely.

Labeling index was assessed of ki-67 and p53 in all three groups and was correlated. Obviously it was lowest to minimal in dentigerous cyst group followed by sharp rise seen in keratocystic odontogenic tumor (KCOT) group almost equaling to group ameloblastoma. This result is in accordance to W Thosaporn et al study who used IPO-38 as novel cell proliferative marker [3].

Keratocystic odontogenic tumor (KCOT) showed markedly increased cellular proliferation and p53 expression as compared to dentigerous cyst group and was almost invariably equal to ameloblastoma group (Figure 1, 2 &3).

Immunostaining pattern of ki-67 and p53 was unique in keratocystic odontogenic tumor (KCOT) as both stained mostly in basal and suprabasal layer and not in upper layers. This result is in accordance with studies of (Matthews et al, 1988; Li et al, 1994, 1995; Slootweg, 1995; Piattelli et al, 1998) [4]. However only two cases were immunopositive for p53, a definite correlation was not made for p53 expression.

Ameloblastoma group showed variable expression of ki-67 and p53 in among histopathological variants of ameloblastomas. Two cases were of unicystic ameloblastoma and they showed high proliferative activity and p53 expression. One case of Follicular variant showed intense and high proliferative activity.4 cases of plexiform ameloblastoma expressed intense and high proliferative activity as follicular variant. Two case of granular cell variant was included and showed minimal cellular proliferation and p53 expression and might be due to loss or inactivation of signaling pathways related to cell proliferation and differentiation in the granular cells, suggesting that these cells are functionally inactive and their synthesis and secretion activities have become irregular (Sathi Gul San Ara, 2007).

Variation in labeling index among clinical and histopathological variants of ameloblastomas are unclear although possible explanation for this variation in mean labeling index may be due to difference in methodology, especially the counting protocol, used. Unfortunately it is very difficult to compare these parameters because published reports frequently fail to provide sufficient detail or explanation. Another possible reason might be the difference in the morphology of the tumors, with the solid lesions providing large follicles or plexiform sheets for analysis, whereas only a thin lining is available in the unicystic cases [4]. This may have resulted in the inclusion of greater numbers of basal and parabasal cells in the unicystic group, thus resulting in higher mean labeling indices. This is unlikely as cells in the entire thickness of the epithelial linings of the unicystic lesions were included in the count (Meer et al, 2003). Inclusion of granular cell variant has resulted in decreased overall expression of both markers and is well reflected in statistics as significantly less expression of ki-67 in ameloblastomas than odontogenic keratocysts [5].

The high proliferative potential of odontogenic keratocystic epithelium definitely stand it out from other developmental odontogenic cyst and the newer adopted WHO terminology keratocystic odontogenic tumor

warrants it as aggressive lesion and also suggest a proper management.

Results

The expression of ki-67 proliferative marker in keratocystic odontogenic tumor was highest and close to ameloblastoma group and was minimal in dentigerous cyst group. The result clearly depicted a very high proliferative potential of cystic epithelium of keratocystic odontogenic tumor and was comparable to a tumor i.e ameloblastoma. There was a significant difference in epithelial proliferation between dentigerous cyst and keratocystic odontogenic tumor depicting a much higher epithelial prolifertive potential of keratocystic odontogenic tumor than dentigerous cyst.

The expression of tumor suppressor gene p53 was although highest in ameloblastomas but due to only two immunopositive cases of keratocystic odontogenic tumor, a definite correlation was not made, but the two immunopositive keratocystic odontogenic tumor mean labeling index of p53 expressed almost equal to ameloblastoma group. Expression of p53 in dentigerous cyst was minimal.

Although use of tumor suppressor gene marker p53 is widely and routinely employed in diagnosis of routine tumors, but their use in odontogenic tumor diagnosis is still not employed confidently. The reason given for this uncertainty is to p53 over expression rather true mutation occurring in these lesions. So odontogenic lesion may take a p53 independent pathway for tumorigenesis.

The high proliferative potential of odontogenic keratocystic epithelium definitely stand it out from other developmental odontogenic cyst and the newer adopted WHO terminology keratocystic odontogenic tumor warrants it as aggressive lesion and also suggest a proper management. (FIGURE 1-4).

Conclusion

The high proliferative potential of odontogenic keratocystic epithelium definitely stand it out from other developmental odontogenic cyst and the newer adopted WHO terminology keratocystic odontogenic tumor warrants it as aggressive lesion and also suggest a proper management.

References

1. Merva Soluk-Tekkesin, John M. Wright. The world health organization classification of odontogenic lesions: a summary of the changes of the 2017 (4th) edition. Turkish Journal of Pathology; 2018:34(1-16)

2. Funaoka K, Arisue M, Kobayashi I, Iizuka T, Kohgo T, Amemiya A, Totsuka Y. Immunohistochemical detection of proliferating cell nuclear antigen (PCNA) in 23 cases of ameloblastoma. Oral Oncol, Eur J Cancer 1996; 32B:328±332.

3. Kim J, In Yook J. Immunohistochemical study on proliferating cell nuclear expression in ameloblastomas. Oral Oncol, Eur J Cancer 1994; 30B:126±131.

4. Reichart PA, Philipsen HP, Sonner S. Ameloblastoma: biological profile of 3677 cases. Oral Oncol, Eur J Cancer 1995; 31B:86±99.

5. SB RAHMAN, SMA SADAT, IA HAIDER, M AHMED: Analysis of Histological Variants of Ameloblastomas of Jaws in Relation to their Clinical Presentations: Journal of Bangladesh College of Physicians and Surgeons Vol. 35, No. 2, April 2017.

Figures and tables

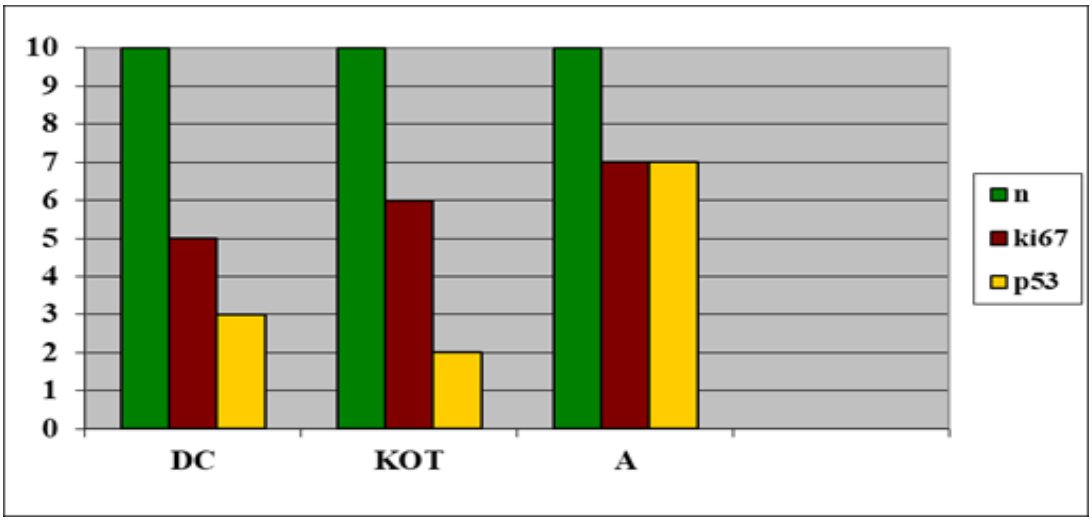
Table 1:

Multiple Comparisons

Tukey HSD

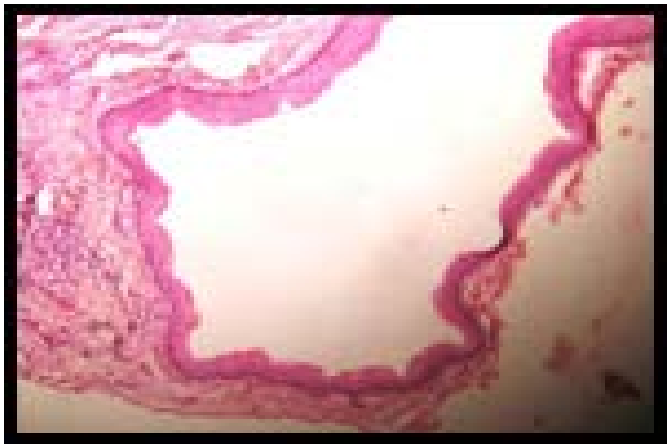
Dependent Variable	(I) GROUP	(J) GROUP	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Ki-67 expresssion - I	Dentigerous Cyst Group	Keratocystic Odontogenic Tumor Group	-33.7967	4.4250	.000	-44.655	-22.939
		Ameloblastoma Group	-19.2943	4.2789	.000	-29.794	-8.795
	Keratocystic Odontogenic Tumor Group	Dentigerous Cyst Group	33.7967	4.4250	.000	22.939	44.655
		Ameloblastoma Group	14.5024	4.0656	.003	4.526	24.479
	Ameloblastoma Group	Dentigerous Cyst Group	19.2943	4.2789	.000	8.795	29.794
		Keratocystic Odontogenic Tumor Group	-14.5024	4.0656	.003	-24.479	-4.526
Ki-67 expresssion - II	Dentigerous Cyst Group	Keratocystic Odontogenic Tumor Group	-33.2833	4.2942	.000	-43.820	-22.746
		Ameloblastoma Group	-18.8571	4.1524	.000	-29.046	-8.668
	Keratocystic Odontogenic Tumor Group	Dentigerous Cyst Group	33.2833	4.2942	.000	22.746	43.820
		Ameloblastoma Group	14.4262	3.9454	.002	4.745	24.107
	Ameloblastoma Group	Dentigerous Cyst Group	18.8571	4.1524	.000	8.668	29.046
		Keratocystic Odontogenic Tumor Group	-14.4262	3.9454	.002	-24.107	-4.745
P53 expression - I	Dentigerous Cyst Group	Keratocystic Odontogenic Tumor Group	-31.1333	14.4162	.102	-67.470	5.204
		Ameloblastoma Group	-37.5190	10.8976	.007	-64.987	-10.051
	Keratocystic Odontogenic Tumor Group	Dentigerous Cyst Group	31.1333	14.4162	.102	-5.204	67.470
		Ameloblastoma Group	-6.3857	12.6619	.870	-38.301	25.530
	Ameloblastoma Group	Dentigerous Cyst Group	37.5190	10.8976	.007	10.051	64.987
		Keratocystic Odontogenic Tumor Group	6.3857	12.6619	.870	-25.530	38.301
P53 expression - II	Dentigerous Cyst Group	Keratocystic Odontogenic Tumor Group	-33.1667	14.6170	.083	-70.010	3.676
		Ameloblastoma Group	-36.6238	11.0494	.009	-64.475	-8.773
	Keratocystic Odontogenic Tumor Group	Dentigerous Cyst Group	33.1667	14.6170	.083	-3.676	70.010
		Ameloblastoma Group	-3.4571	12.8382	.961	-35.817	28.903
	Ameloblastoma Group	Dentigerous Cyst Group	36.6238	11.0494	.009	8.773	64.475
		Keratocystic Odontogenic Tumor Group	3.4571	12.8382	.961	-28.903	35.817

Graph 1: Immunopositive samples among the groups.



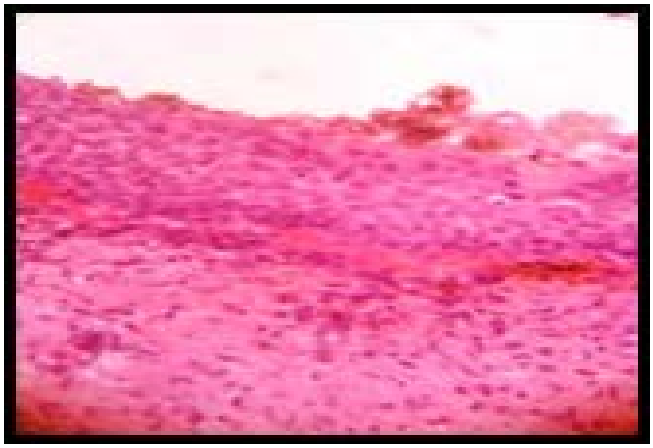
DC - Dentigerous cyst, KOC - Keratocystic odontogenic tumor, A – Ameloblastoma.

Fig.1: keratocystic odontogenic tumor (40x)

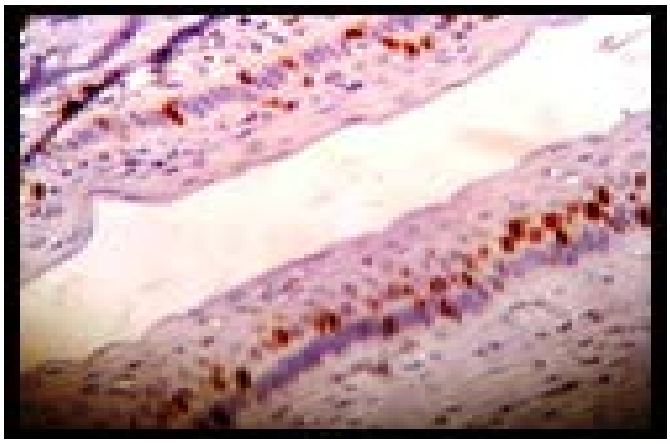


Hematoxyline And Eosin.

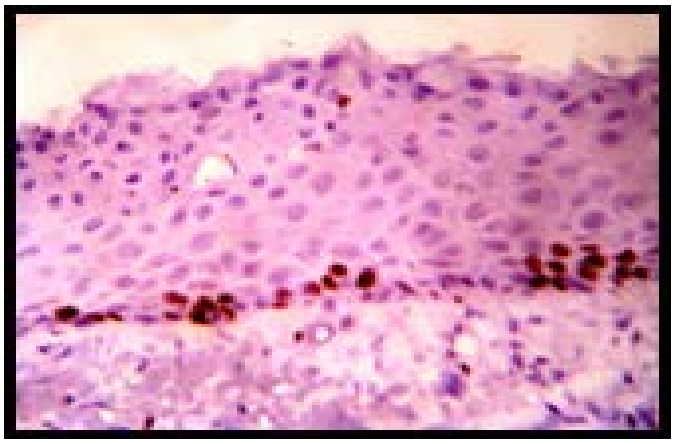
Fig.2: dentigerous cyst (40x).



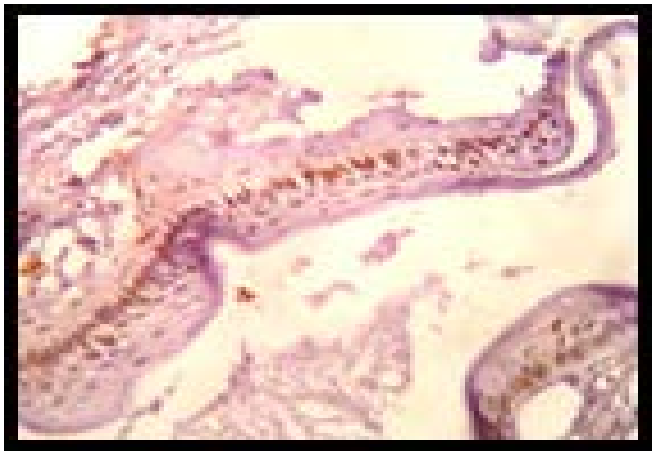
Hematoxyline And Eosin.



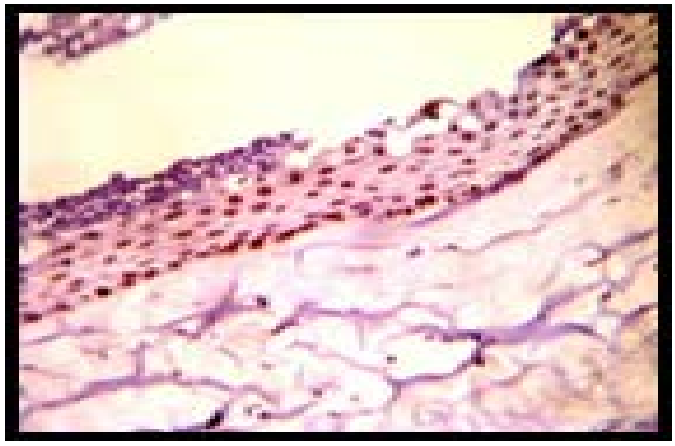
Positive Ki-67 Expression.



Positive Ki-67 Expression.

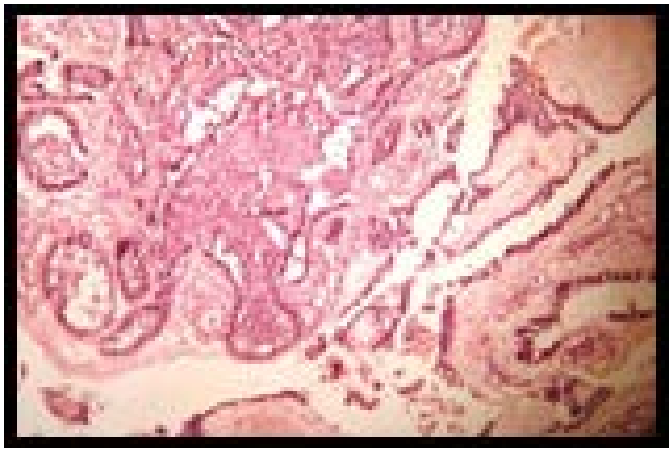


Positive p53 expression.

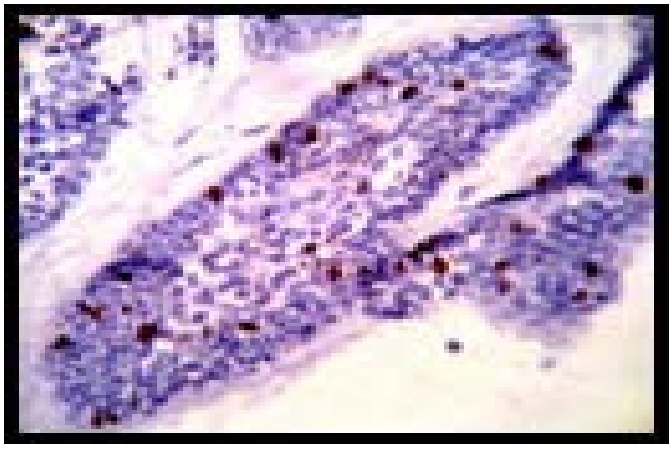


Positive p53 expression.

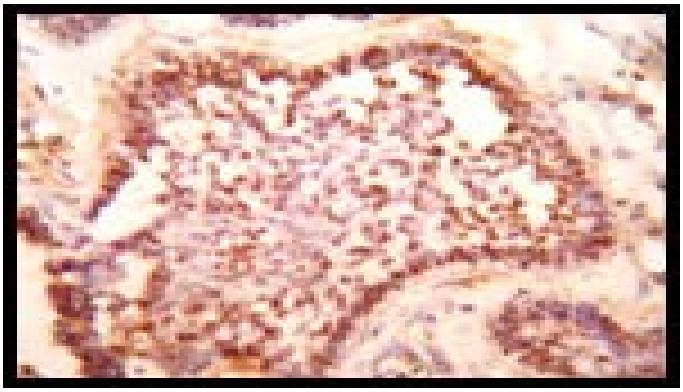
Fig.3: Ameloblastoma (40x).



Hematoxyline And Eosin.



Positive Ki-67 Expression.



Positive p53 expression.