Original Article

CD10 immunoreactivity in cutaneous squamous and basal cell carcinoma

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ABSTRACT

Objective: The aim of this study was to compare CD10 expression in tumoral and stromal cells of cutaneous squamous cell carcinoma (SCC) and basal cell carcinoma (BCC) in order to differentiate SCC from BCC in problematic cases.

Methodology: Twenty six SCC and 30 BCC cases were retrieved randomly from Al-zahra hospital pathology archive and CD10 expression was determined in tumoral and stromal cells (fibroblasts around tumoral nests) of each case based on immunohistochemical method.

Results: 25 of 26 SCC samples (96.2%) failed to stain with CD10 in tumoral cells whereas CD10 expression of stromal cells was identified in all SCC cases (100%). In contrast, 26 of 30 BCC cases (86.7%) were positive in tumoral cells and only 5 of 30 BCC samples (17.7%) were positive in stromal cells. Accordingly, the staining pattern of tumoral and stromal cells in BCC and SCC was statistically different (p< 0.001).

Conclusion: These findings support CD10 expression as a differential marker for BCC and SCC. CD10 staining pattern is mostly tumoral in BCC and stromal for SCC.

KEY WORDS: Basal Cell Carcinoma, Squamous Cell Carcinoma, CD10, Immunohistochemistry.

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INTRODUCTION

BCC and SCC are the most common skin cancers respectively. BCC usually originate from basal cell layer or outer root sheath of hair follicles and it is considered as an adnexal tumor in WHO classification.[1] Basal cell carcinoma usually grows slowly with local invasiveness.[2] Keratinocytes are recognized to be the source of SCC. Distinguishing BCC from SCC is critical because these have different treatments based on their different prognosis, recurrence and metastasis.[1] The SCC recurrence rate is approximately double than for basal cell carcinoma. Moreover metastasis is seen at least in 2% of SCC cases whereas it's very rare in BCC.[3] It is sometimes difficult to differentiate them clinically as well as histopathologically.[1,4] Especially some intermediate cases demonstrate similar morphological patterns on Hematoxylin and Eosin (H&E) prepared slides.

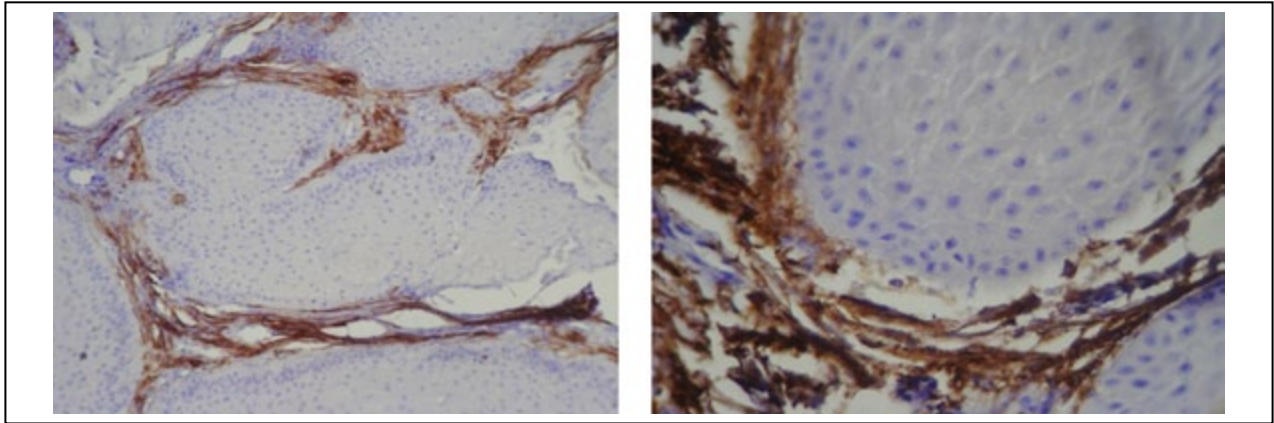The CD10 antigen also known as ''CALLA'' is a cell-surface metalloendopeptidase which is

Fig.1: CD10 immunostaining is only positive in stromal cells of SCC but not in tumoral cells. (A x100, B x400).

expressed in various normal and neoplastic cells. CD10 Antibody (clone 56C6) preserves reactivity even in paraffin embedded material.[5] In normal skin CD10 immunostainting is present in sebaceous glands, myoepithelial cells of eccrine and apocrine glands, periadnexal dermis, and inner root sheath cells of vellus hair follicles and occasional endothelial cells.[6-8] CD10 has been recognized as a useful marker to differentiate BCC from trichoepithelioma (TE).[9,10] It is not routinely used to differentiate BCC from SCC but it has been claimed in some articles that CD10 can be utilized as a specific marker to distinguish BCC from SCC.[4,11-13]

This study was done to compare CD10 expression in tumor and stromal cells of BCC and SCC in order to determine a suitable specific immunohistochemical marker for definite distinction of these two tumors.

METHODOLOGY

This is a descriptive-analytical cross-sectional study in which 30 cases of BCC and 26 SCC in small shave or punch biopsy specimens were randomly retrieved from surgical pathology archive of Isfa-

han Al-Zahra hospital within 2010. Patients' data including sex, age and final diagnosis were recorded. H&E slides were reviewed microscopically and only those with definite and characteristic patterns for BCC or SCC were included in the study. Ethical approval for use of all specimens was obtained from the research ethics committee of the Isfahan University of Medical Sciences.

Each paraffin-embedded block was cut for two 3-4 μ thick sections and mounted on glass slides for H&E staining and poly-l-lysin coated slides for IHC staining. Slides were dried in an oven at 60°C for 60 minutes. Thereafter, sections were deparaffinized, rehydrated and rinsed in tap water before antigen retrieval. After inactivation of endogenous catalyses by using 3% hydrogen peroxide, the sections were incubated with primary antibody for 24 hours (clone 56C6, RTU-CD10-270 Novacastra Lot:6004843) diluted at a 1:150 concentration and then secondary antibody (N-vision, Dako system) for 40 minutes at room temperature. After each step of antibody treatment, slides were drained with phosphate buffered saline (PBS). Finally, the diami-
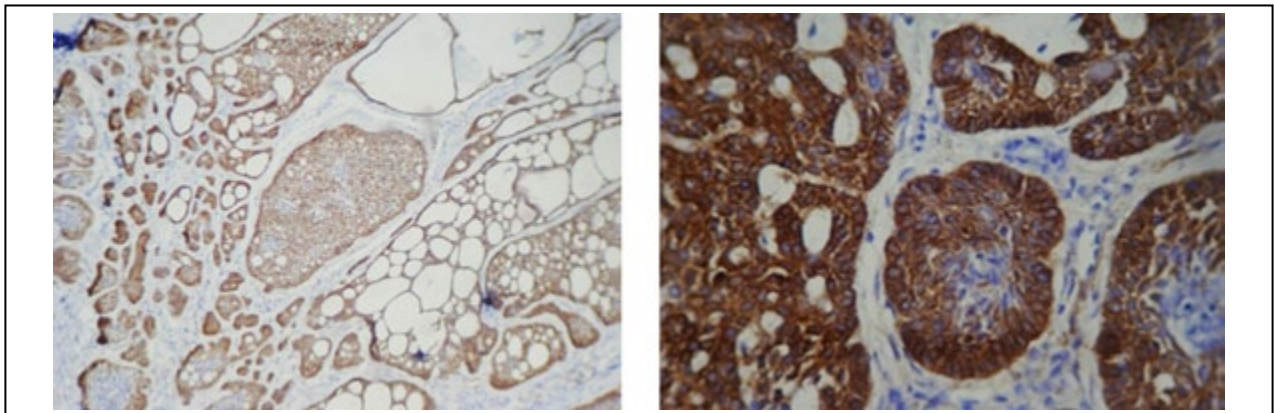

Fig.2: CD10 immunopositivity in BCC tumor cells.
Peripheral palisading cells are stronger in CD10 expression (Ax100, Bx400)

nobenzidine (DAB) applied on slides for 5 minutes and the specimens were counterstained with hematoxylin. Normal duodenal biopsy was used as positive control in which brush border epithelial cells were stained. Negative control was considered by omitting primary antibody phase.

CD10 positivity was considered as brown cytoplasmic and/or membrane staining. 10 high power fields were examined for each case and mean percentage of positive cells were calculated as follow: <10% as negative and ≥ 10% as positive.[11,12] Stromal or tumoral cells CD10 immunostaining was determined for each case and results were compared by Fisher Exact Test. The data were collected in prepared checklist which included all the studies' variables. SPSS-18 statistical software was used for data analysis. Chi-square test was applied to compare quantitative variables. Statistical significance was predetermined as $P \leq 0.05$.

RESULTS

This study included 26 cases of SCC; their ages were between 36-96 years, with median age of 70 and mean (±SD) age of 66 (±14) years. 77% of SCC cases were males. At histopathological examination, 2 of 26 cases were diagnosed as poorly differentiated, 5 cases as moderately differentiated and the others were well differentiated. 30 cases of BCC were involved in this study. Their age ranged from 42 to 78 years with median age of 62 and mean age of 64 (±8.7) years from which 57% of cases were males. Microscopic study of slides showed 13 of 30 cases as nodular subtype, 5 of 30 cases as infiltrative, 6 of 30 cases as adenoid and 6 of 30 cases as pigmented subtypes of BCC. Some

parts of normal skin including inner root sheath of hair follicles, hair matrix and periadnexal dermis expressed CD10 which was considered as positive internal control in this study.

In all SCC cases (100%), CD10 immunopositivity was detected in stromal cells. CD10 was negative in tumoral cells of 25 of 26 cases (96.2%) (Fig.1). Only in one case (1/26 or 3.8%), peripheral tumoral cells next to stroma were positive although central tumoral cells were negative (Table-I). In the BCC group, CD10 expression was noted as below: CD10 was positive in tumoral cells of 11 of 13 cases in nodular subtype (84.61%), stromal cells were negative in 11 of 13 cases (84.61%) of nodular subtype. In infiltrative BCC cases, 4 of 5 cases (80%) were positive for tumoral cells whereas 1 of 5 cases (20%) were positive for stromal cells, CD10 positivity was detected in all adenoid BCC cases and 1/6 (16.66%) of such cases in stromal cells. CD10 positivity of tumor cells was seen in 5/6 (83.33%) and CD10 stromal positivity in 1/6 (16.66 %) of pigmented cases. Totally 26/30 (87.7%) of BCC samples were positive in tumoral cells (Fig.2) and 5/30 (16.66%) were positive in stromal cells (Table-II).

There was a statistically significant difference between SCC and BCC in CD10 expression. Tumoral cell CD10 positivity was seen in 1/26 (3.8%) of SCC samples versus 26/30 (86.7%) of BCC samples. In contrast, CD10 was positive in 26/26 (100%) of SCC cases and 5/30 cases of BCC in stromal cells (P value <0.001). There was no statistically significant association in CD10 positivity of SCC or BCC cases with age, sex and subtypes in either tumoral or stromal cells (Table-III).

Table-I: CD10 immunostaining among SCC different grades in tumor and stromal cells.

SCC differentiation grades	CD10 in tumor cells		CD10 in stromal cells	
	Positive	Negative	Positive	Negative
Well differentiation	1	18	19	0
% within subtype	5.3%	94.7%	100%	
% within CD10 in tumor cells	100%	72%	-	
% within CD10 in stromal cell	-	-	73.1%	
Moderate differentiation	0	5	5	0
% within subtype	0%	100%	100%	
% within CD10 in tumor cells	0%	20%	-	
% within CD10 in stromal cells	-	-	19.2%	
Poorly differentiation	0	2	2	0
% within subtype	0%	100%	100%	
% within CD10 in tumor cells	0%	8%	-	
% within CD10 in stromal cells	-	-	7%	
Total	1	25	26	0

Table-II: CD10 immunostaining among BCC histopathological subtypes in tumor and stromal cells.

BCC subtypes	CD10 in tumor cells		CD10 in stromal cells	
	Positive	Negative	Positive	Negative
Nodular count	11	2	2	11
% within subtype	84%	15.4%	15.4%	84.6%
% within CD10 in tumor cells	42.3%	50%	-	-
% within CD10 in stromal cells	-	-	40%	44%
Infiltrative count	4	1	1	4
% within subtype	80%	20%	20%	80%
% within CD10 in tumor cells	15.4%	25%	-	-
% within CD10 in stromal cells	-	-	20%	16%
Adenoid count	6	0	1	5
% within subtype	100%	0%	16.7%	83.3%
% within CD10 in tumor cells	23.1%	0%	-	-
% within CD10 in stromal cells	-	-	20%	20%
Pigmented count	5	1	1	5
% within subtype	83.3%	16.7%	16.7%	83.3%
% within CD10 in tumor cells	19.2%	25%	-	-
% within CD10 in stromal cells	-	-	20%	20%
Total	26	4	5	25

DISCUSSION

It is critical to differentiate SCC from BCC clinicopathologically. Because of higher incidence of local recurrence and metastasis (especially to lymph nodes), SCC needs more aggressive treatment in comparison with BCC. Although the distinction between SCC and BCC is readily based on histological criteria on H&E prepared microscopic slides and is fairly easy, but there are similar morphological patterns which make it difficult to differentiate them only histologically, occasionally.[1,2,12] Some accepted criteria like basophilic/eosinophilic stains, peripheral palisading, keratin pearls and retraction from stroma are not characteristic and can be seen in either of BCC or SCC. For example, keratotic BCC and metatypical BCC are very similar to basaloid SCC in H&E prepared microscopic

Table-III: Comparative final results of CD10 immunostaining in tumor and stromal cells of BCC and SCC.

	BCC (n=30)	SCC (n=26)	Statistical significant test	Pvalue
Tumor cells:				
Positive	26(86.7%)	1(3.8%)	Fisher's	Pv<0.001
Negative	4(13.3%)	25(96.2%)	Exact Test	
Stromal cells:				
Positive	5(16.7%)	26(100%)	Fisher's	Pv<0.001
Negative	25(83.3%)	0(0%)	Exact Test	

slides.[1,4] Some immunohistochemical markers have been introduced including Involucrin, CEA and EMA. These markers were not specific enough to be superior to conventional staining in differential diagnosis.[2,14-16] BerEP4 is a sensitive but not specific marker for BCC and its variants.[8,17,18] To differentiate BCC from SCC, an immunopanel with BerEP4, EMA and Ulex europaeus has been advised.[2,8] BerEP4 positivity is present invariably at least in 50% of BCC tumoral cells, whereas EMA or Ulex europaeus are negative. BerEP4 expression has not been reported in SCC yet but EMA and Ulex europaeus are positive variably.[2,3,8,17]

As it has been claimed in some limited studies, CD10 expression may be helpful in strong distinction of these two tumors.[4,11,12,13] CD10 expression in cutaneous tumors has been investigated in some studies but our knowledge about CD10 expression is rather limited especially in various types of SCC. In this study, CD10 immunostaining in tumoral and stromal cells of BCC and SCC was determined.

According to our findings, tumoral cells failed to stain in 25/26 (96.2%) of SCC cases. This finding is in accordance with some previous studies.[4,11-13,19] CD10 positivity of stromal cells was noted in 100% of SCC cases. This is rather different from findings of Wagoner et al. Wagoner et al reported CD10 positivity in stromal cells of 2/13 (13.38%) of SCC cases. In comparison, Aiad et al reported CD10 positivity in 16/16 (100%) and Yada et al in all SCC cases.[4,11,12] CD10 expression was detected in tumoral cells of

26/30 (86.7%) of BCC cases, in contrast only 5/30 (17.7%) of BCC cases were positive in stromal cells. These data are in accordance with some previous studies about BCC tumoral cells' CD10 positivity. Aiad et al reported 47.6% (10/21) positivity in tumoral cells and 95.2% (20/21) positivity in stromal cells (the latter is contrary to our findings). Wagoner et al[4] and Yada et al reported 14/16 (87.3%) and 86% positivity of tumoral cells respectively. Yada et al revealed a negative correlation between the expression of CD10 in tumoral and stromal cells in BCC.[11]

There is a reverse correlation in CD10 immunostaining between SCC and BCC. On the other hand, no significant statistical difference was detected among BCC variant histopathological patterns or SCC different grades and CD10 immunoreactivity.

Based on this study CD10 is a useful marker to distinguish SCC from BCC. CD10 positivity in tumoral cells supports BCC as final diagnosis and at least SCC can be ruled out. Our results about CD10 immunostaining of stromal cells were not completely in accordance with previous studies, especially Aiad findings (17.7% positivity in this study versus 95.2% in Aiad report). Probably more studies must be done with more samples to exclude one of these findings.

CONCLUSION

CD10 expression can be utilized as a differential marker in which CD10 immunopositivity of tumoral cells is in favor of BCC rather than SCC. In contrast stromal cells positivity for CD10 is more suggestive of SCC.

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