

## Original Article

### The Usefulness of CD10 in Distinguishing between Cutaneous Basal Cell Carcinoma and Squamous Cell Carcinoma

Shahram Sabeti<sup>1</sup>, Farhad Malekzad<sup>2</sup>, Nastaran Neishaboori<sup>1</sup>  
Mihan Pourabdollah Toutkaboni<sup>3</sup>, Farahnaz Bidarizerehpoo<sup>1</sup>

1. Dept. of Pathology, Shahid Beheshti University of Medical Sciences, Tehran, Iran
2. Skin Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran
3. Chronic Respiratory Diseases Research Center, NRITLD, Shahid Beheshti University of Medical Sciences, Tehran, Iran

#### ABSTRACT

**Background & Objectives:** CD10 is a cell surface enzyme with metalloendopeptidase activity, also known as Common Acute Lymphoblastic Leukaemia Antigen, which mainly serves as a marker for acute lymphoblastic leukemia (ALL). To date and to the best of our knowledge, only few comparative immunohistochemical studies have assessed CD10 expression in cutaneous epithelial neoplasms. Our goal was to determine whether CD10 can be used in pathologic distinction of cutaneous basal cell carcinoma (BCC) and squamous cell carcinoma (SCC).

**Methods:** This study included 27 BCC and 17 SCC cases immunohistochemically stained for CD10. Cytoplasmic +/- cell membrane staining was considered as positive. Each slide was studied by two pathologists and scored semi-quantitatively as follows: negative (<10%); 1+ (10-50% positive cells); and 2+ (>50% positive cells).

**Results:** The rate of CD10 expression in tumor cells was significantly higher in BCCs in comparison to SCCs. (20/27 vs., 2/17;  $P < 0.0001$ ).

**Discussion:** Our findings suggest CD10 as a useful adjunct marker in distinguishing cutaneous BCC and SCC.

**Keywords:** Basal Cell Carcinoma, Squamous Cell Carcinoma, Antigen CD100

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Address Communications to: Dr. Mihan Pourabdollah Toutkaboni, Chronic Respiratory Diseases Research Center, NRITLD, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

E mail: mihan\_p@yahoo.com

## Introduction

The incidence of skin cancer is rising rapidly in most parts of the world; BCC is the most prevalent form, followed by Squamous cell Carcinoma (SCC). Differentiating between SCC and Basal Cell Carcinoma (BCC) is clinically important as there is a significant difference in their rate of aggressiveness and metastatic potential. This distinction is usually made without significant difficulty on routine microscopic examination. But, it occasionally poses difficulties, especially in small biopsy samples. Difference in biologic behavior mandates application of more accurate diagnostic methods in such cases.

CD10 (CALLA) is expressed in a large percentage of cases of acute lymphoblastic leukemia, follicular lymphoma, Burkitt lymphoma, and some other hematopoietic tumors (1). In addition, CD10 is also widely expressed in normal tissues, such as lymphoid precursor cells, the brush border of enterocytes, renal tubules and glomeruli, myoepithelial cells of the breast, hair follicles, eccrine glands, and sebaceous glands (2). The function of CD10 is to reduce cellular response to peptide hormones by regulating local peptide hormone concentrations (3). CD10 may be an indicator of tumor invasiveness if it is expressed in stromal cells, as can be found in the peritumoral stromal cells of the invasive component of malignancies such as carcinomas of the prostate, breast, colorectal and lung (4), while it may be a marker of follicular differentiation if it is expressed in tumor cells of cutaneous epithelial neoplasms. There are reports showing that the stromal expression of CD10 in cutaneous epithelial neoplasms may be an indicator of malignancy (5). CD10 may also be beneficial in differentiating benign adnexal tumors from BCC (6).

Recent studies support the usefulness of CD10

as a marker of early BCC, especially when SCC cannot be excluded clinically or by conventional stains (7). Other immunohistochemical stains that may be of use in differential diagnosis as reported in prior studies include BerEP4, epithelial membrane antigen (EMA), bcl-2, Cam 5.2, CK20, carcinoembryonic antigen and p53 (8).

In this study, we immunohistochemically stained unequivocal cases of cutaneous SCC and BCC for CD10 marker to clarify the usefulness of this method in their pathologic distinction.

## Materials and Methods

### Tissue samples

This study enrolled 44 formalin-fixed paraffin embedded tissue samples of SCC and BCC cases obtained from archives of pathology wards of Loghman and Shohadaye Tajrish hospitals, Tehran, Iran. Specimens were either incisional or excisional biopsies taken between 2010 and 2013. They included 27 cases of BCC (nodular, adenoid, pigmented and metatypical types) and 17 cases of SCC. Ethical consent requirements had been fulfilled before performance of any procedure on the blocks.

Two contiguous 5  $\mu$  thick sections were cut from each block, one mounted for routine (H&E) staining and re-evaluated by 2 general pathologists to confirm the prior histopathologic diagnosis and adequacy of specimens and the other mounted on a poly-L-lysine-coated slide for immunohistochemistry.

### Immunohistochemical staining methodology

Tissue sections were de-paraffinized in xylene, re-hydrated in a series of graded alcohols and washed in distilled water. Heat-induced antigen retrieval was carried out by microwave pretreatment in citrate buffer (10 millimolar, pH 6.0), boiling for three 2-min periods separated by 2 min. Intervals at room temperature. The slides were then washed 3 times in 1% PBS and treated with peroxidase block for 10 min to

neutralize endogenous peroxidase activity. For CD10 staining, primary antibody (Novocastra product RTU-CD10-270) was applied to the slides and incubated for 10 to 15 min. Post primary block (Novocastra product RE7111) was used to enhance penetration of the subsequent polymer reagent for a 30 min period and, after washing the slides in PBS buffer, incubation with novo link polymer (Novocastra product RE7112) was performed. The sections were then incubated with 3, 3'-diaminobenzidine (DAB) working solution for 5 min. Hematoxylin counter stain was performed, followed by dehydration, clearing, and mounting.

Sections from formalin-fixed, paraffin-embedded normal human intestinal and testicular tissues were used as positive and negative controls, respectively. CD10 stains the cytoplasm of the surface epithelial cells of small intestine.

#### CD10 immunostaining interpretation

Positive CD10 staining was identified as brown cytoplasmic staining with or without coexisting membrane staining. Each case was examined at high magnification independently by 2 pathologists and the percentage of positive cells was averaged and reported as follows:

0-10%: negative; 10-50%: (+) and >50%: (++)  
Staining pattern of tumor cell nests (central +/- peripheral) and of peritumoral stroma was also assessed and reported.

#### Statistical analysis

The collected data were tabulated and statistically analyzed using 'Statistical Package for the Social Sciences, version 11.5. Differences were considered statistically significant when ( $P \leq 0.05$ ) and highly significant when ( $P \leq 0.01$ ).

## Results

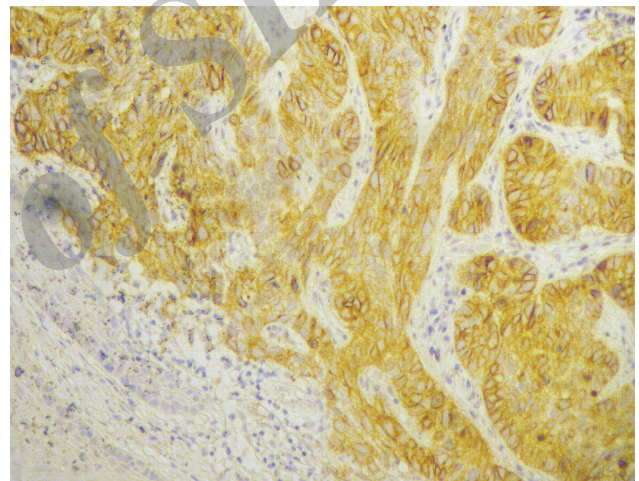
#### Epidemiologic data

This study was performed on 44 cases, including 9 females and 35 males with an average age of

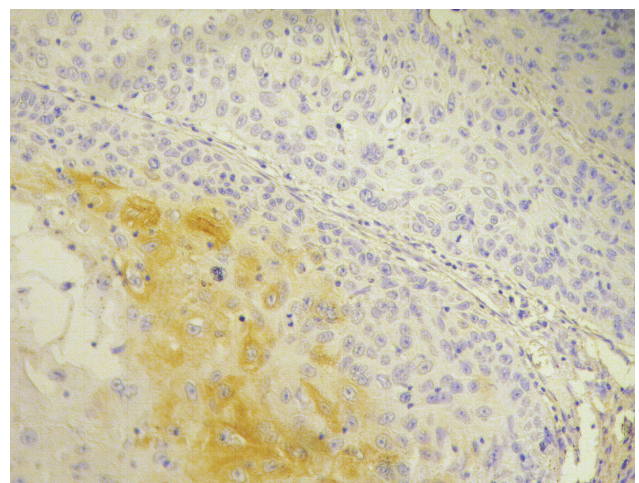
64 years. The BCC cases (19 male patients and 8 female patients) were between 46 to 88 years of age (mean= 65 years). The SCC cases (1 female and 16 male patients) were between 40 to 82 years old (mean=62 years). The majority of lesions were located at the head and neck region.

#### Immunohistochemical staining

Positive reaction was noted in 20 out of 27 cases of BCC. Of these, 6 cases showed 2+ and the remainder showed 1+ staining reaction with cytoplasmic +/- membranous pattern (Fig. 1). In CD10 positive tumor cell nests, there was a trend toward more peripheral rather than central staining. In contrast, only 2 SCC cases exhibited weak focal positivity (Fig. 2).



**Fig.1:** Diffuse cytoplasmic/membranous CD10 staining in a case of BCC ( $\times 400$ )



**Fig.2:** Focal cytoplasmic CD10 staining in a case of SCC ( $\times 400$ )

The peri-tumoral stroma showed positive reaction in 74% of BCCs (20/27) and 71% of SCCs (12/17).

Fisher exact test was used for comparison of CD10 reaction data in BCC and SCC cases (Table 1) and showed a significant difference in the

neoplastic ( $P=0.0001$ ) but not in the stromal component ( $P=1.0000$ ).

Normal skin components showing positive CD10 reaction were the basal layer of epidermis, inner root sheath, hair matrix and perifollicular fibrous sheath. Sebaceous lobules were immunopositive with weak, cytoplasmic staining.

**Table 1-**Comparison of the CD10 profile between BCC and SCC cases

	Staining percentage and intensity			Total
	None	Weak	Strong	
<b>BCC</b>	7	14	6	27
<b>SCC</b>	15	2	0	17
<b>Total</b>	22	16	6	44

### Discussion

In most cases, differentiation of SCC and BCC is straightforward in routine H&E stained slides. Difficulties mainly arise in differentiating between basaloid SCC and keratinizing BCC and between cases of superficial SCC and BCC. The distinction of these neoplasms is clinically important because of the more aggressive behaviour and metastatic potential of SCC which mandates more radical treatment and closer follow-up.

Nowadays, Immunohistochemistry has become an important diagnostic tool in Dermatopathology. With regard to CD10 expression, some authors suggest that CD10 may be an indicator of tumor invasiveness if expressed in stromal cells, while it may be a marker of follicular differentiation if it is expressed in the epithelium of tumors (5). It can also be predictor of tumor invasiveness and metastasis in tumors such as malignant melanoma (9).

Justin Wagoner *et al.* supported the utility of CD10 as a marker for early BCC, especially when SCC could not be excluded clinically or by conventional stains (7). Similarly, Aiad *et al.* concluded that CD10 might be a useful

immunohistochemical marker to differentiate between BCC and SCC; At least, if tumor cells were CD10 positive, this would favor BCC over SCC (10). Furthermore, CD10 has been shown to assist in differentiation between basal cell carcinoma and trichoepithelioma. The expression of CD10 in trichoepithelioma was in the stroma of tumor papillae, and notably lacking in the epithelial component, whereas in basal cell carcinoma, CD10 was expressed peripherally in the basaloid nests and was absent in the stroma (11).

With regard to other markers, cytoplasmic bcl-2 expression is rare in SCC but present in most BCCs (12-14). p53 mutations are usually present in cutaneous SCC and implicated in its pathogenesis but are not of value in differentiation of cutaneous SCC from BCC (15). When SCC and BCC were compared, p53 and p63 staining intensities were significantly higher in the former (16).

In our study, we observed a statistically significant difference in CD10 expression between SCC and BCC. These results support CD10 as a useful adjunct marker in distinguishing between these tumors. Our study enrolled more cases compared

to known previous studies and was representative of a larger population.

Given the positive staining of the inner root sheath, hair matrix and perifollicular fibrous sheath, our results also support the hypothesis that BCCs may be of follicular derivation.

### Conclusion

Our findings suggest CD10 as a good adjunct marker in distinguishing between BCC and SCC.

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