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Original Article

CD10 expression helps to differentiate basal cell carcinoma from trichoepithelioma *

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Abstract

BACKGROUND: The distinction between basal cell carcinoma (BCC) and trichoepithelioma (TE) may be very difficult in some cases because of the close similarities of these two lesions clinically and histopathologically. The purpose of this study is to investigate the usefulness of CD10 in distinguishing BCC and TE.

METHODS: The immunohistochemical expression of CD10 was evaluated in an archived group of 30 BCCs and 12 TEs in a retrospective cross sectional study. The localization of anti-CD10 to the tumoral and/or stromal cells was determined in each case and was compared between these two tumors using Fisher's Exact Test.

RESULTS: In BCC cases, the expression of CD10 was noted in tumoral cells in 26 cases (83.2%). Of these, 3 cases showed positivity of the stromal and basaloid cells, two cases demonstrated stromal expression alone and two BCCs were not immunoreactive. On the other hand, 10 out of 12 (83.3%) TEs showed positive stromal immunoreactivity. Of these, one case also showed positivity of the basaloid cells. One TE demonstrated epithelial expression alone and one TE was not immunoreactive. The pattern of staining of basaloid cells and stromal cells in BCC and trichoepithelioma was statistically different ($p < 0.001$).

CONCLUSIONS: We conclude that CD10 is a useful marker in the differential diagnosis of BCC versus TE.

KEYWORDS: Basal Cell Carcinoma, Trichoepithelioma, CD10.

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Trichoepithelioma (TE) is a benign tumor derived from basal cells in the hair follicle. It may be sporadic or as the principal feature of a common genetic disorder called multiple familial trichoepithelioma characterized by the presence of many small tumors predominantly on face, inherited in an autosomal dominant pattern. Histologically, TE is characterized by a well circumscribed dermal tumor composed of islands, nests and cords of uniform basaloid cells in a cellular fibrous stroma. The tumor may be associated with epithelial structures resemble hair papillae or abortive hair follicle, small keratocysts (infundibular differentiation) lined by stratified squamous epithelium and foci of calcification. Retraction of stroma from adjacent dermis and few mitotic figures are two characteristic features of this tumor. The tumor in some instances may take on a pattern, resembling basal cell carcinoma (BCC), so the differential diagnosis of BCC versus TE can be problematic based on clinical presentation and routine hematoxylin and eosin stained sections.[1]

CD10 is a cell-surface zinc metalloproteinase of 100 KD that is also known as common acute lymphoblastic leukemia antigen (CALLA).[2] It was originally found to be expressed on the cell surface of most cases of acute lymphoblastic leukemia,[3,4] and was soon found in

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many other types of neoplasms.[5,6] CD10 expression has been shown in tumors of follicular differentiation, including trichoepithelioma, pilomatricoma, basaloid follicular hamartoma and BCC.[7-9] The limited information pertaining to the pattern of this marker expression in different studies made us investigate more closely its differential pattern in these two tumors. A few studies have indicated its expression in BCC and TE but this marker has not been used routinely for differentiating BCC and TE because of the limited number of available studies.

Methods

The studied group included 30 cases of BCC and 12 cases of TE selected from histopathologic archive of Al-Zahra hospital, Isfahan University of Medical Sciences, Iran. The samples were selected by a simple sampling method. Paraffin-embedded tissue sections were obtained from archival tissue blocks of the hospital. Hematoxylin and eosin sections were reviewed to confirm diagnosis. Since there is no absolutely objective external validator of the rendered diagnosis, we selected the cases that their history and histologic pattern were typical. For immunohistochemical staining, 3µm-thick sections were prepared from formalin-fixed, paraffine-embedded tissues. The sections were collected on glass slides coated with poly-l-lysine. They were deparaffinized by immersion in xylene, and this was followed by immersion in alcohol and then immersion in citrate buffer, pH 9.0, for 15 minutes at 95°C for antigen retrieval. Next, the sections were incubated with 3% hydrogen peroxide for 10 minutes. The slides were then incubated with the primary antibody at room temperature for 60 minutes. After washing in Phosphate Buffer Saline (PBS), the sections were treated with polymer envision for 30 minutes. The sections were then incubated with Diaminobenzidine (DAB) in a chromogen solution for 5 minutes at room temperature. Finally, the sections were stained with hematoxylin and were mounted. Normal intestinal biopsy was used as positive control. CD10 stained the cytoplasm of the surface epithelial cells of small intestine. Negative control was performed by omitting the primary antibody step. Positive CD10 staining was identified as brown cytoplasmic staining with or without cell membrane staining. Localization of anti-CD10 to the stroma and/or tumor cells was determined in cases with immunoreactivity.

The data were collected and analyzed with chi-square test using SPSS software (version 16). BCC and TE were compared for proportion of CD10 expression in tumoral cells using Fisher's Exact Test and Odds ratio for tumor type was calculated. The proportions of CD10 expression in basaloid and stromal cells for these two tumors were compared.

Results

This study included 30 cases of BCC (13 solid type, 5 morphea type, 6 adenoid type and 6 pigmented type), and 12 cases of TE. The average age (± SD) of the BCC cases in this study was 59 ± 9 years, with a 44-77 years range. The BCC group included 17 males and 13 females. In TE cases (7 males and 5 females), the average age was 30 with a 20-45 years range. Two patients had a history of multiple TEs while the others had solitary lesions. CD10 was positive in 28 out of 30 BCCs (93.3%), most demonstrating strong and/or diffuse staining of basaloid cells (26/30, 76.6%) (Figure 1). Of these, 3 cases (10%) showed staining of the stromal cells too. In 2 cases (6.6%) just stromal cells were positive and 2 BCCs (6.6%) were not immunoreactive.

Eleven of twelve cases of TE were Immunoreactive. Ten cases (75%) showed strong CD10 staining of the stroma surrounding nests of basaloid cells (Figure 2). Of these, one case (8.3%) also showed staining of the basaloid cells. one TE (8.3%) demonstrated basaloid cell staining alone and one case (8.3%) was not immunoreactive. The pattern of staining of basaloid cells and stromal cells in BCC and trichoepithelioma was statistically different; more basaloid cells were stained in BCC and more stromal cells were stained in trichoepithelioma ($p < 0.001$). Accordingly, CD10 ex-

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pression in stromal cells around basaloid nests was useful for differentiating TE from BCC. In contrast, CD10-positive basaloid cells and negative stromal cells were diagnostic for BCC (Figure 3). Odds ratio for tumor type was 32.50.

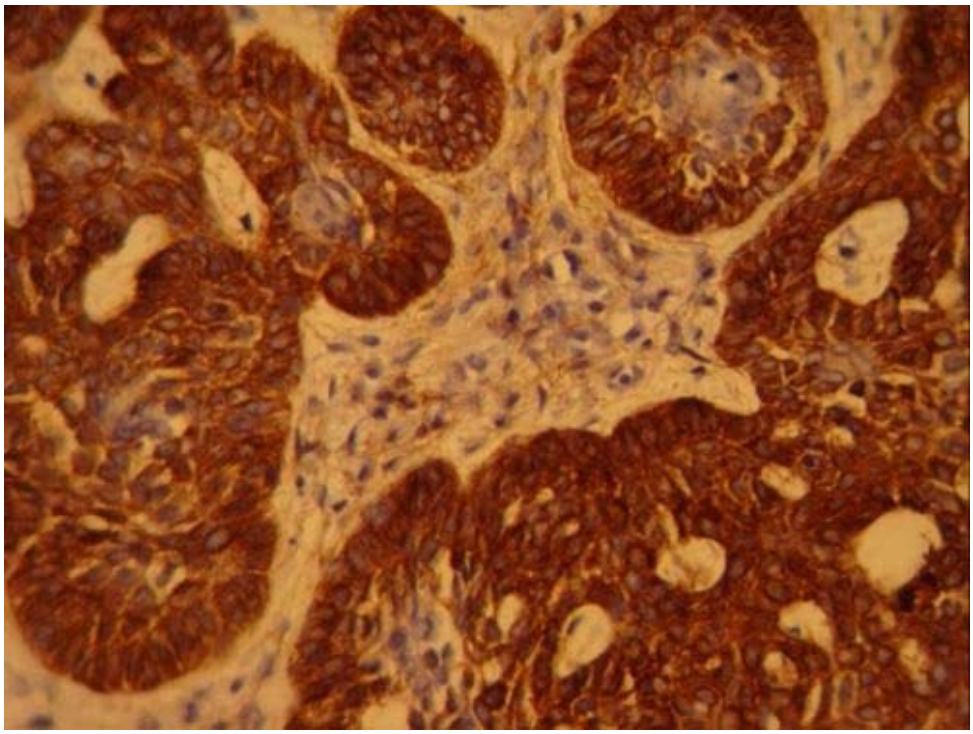

Figure 1. CD10 expression in basal cell carcinoma (× 400)

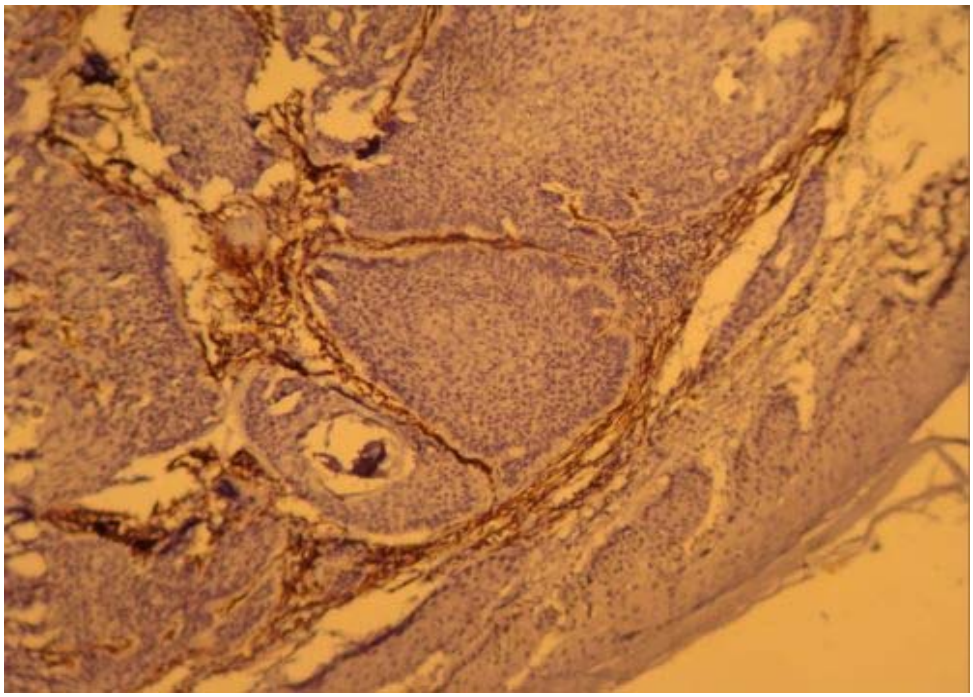

Figure 2-A. CD10 expression in trichoepithelioma (× 100)

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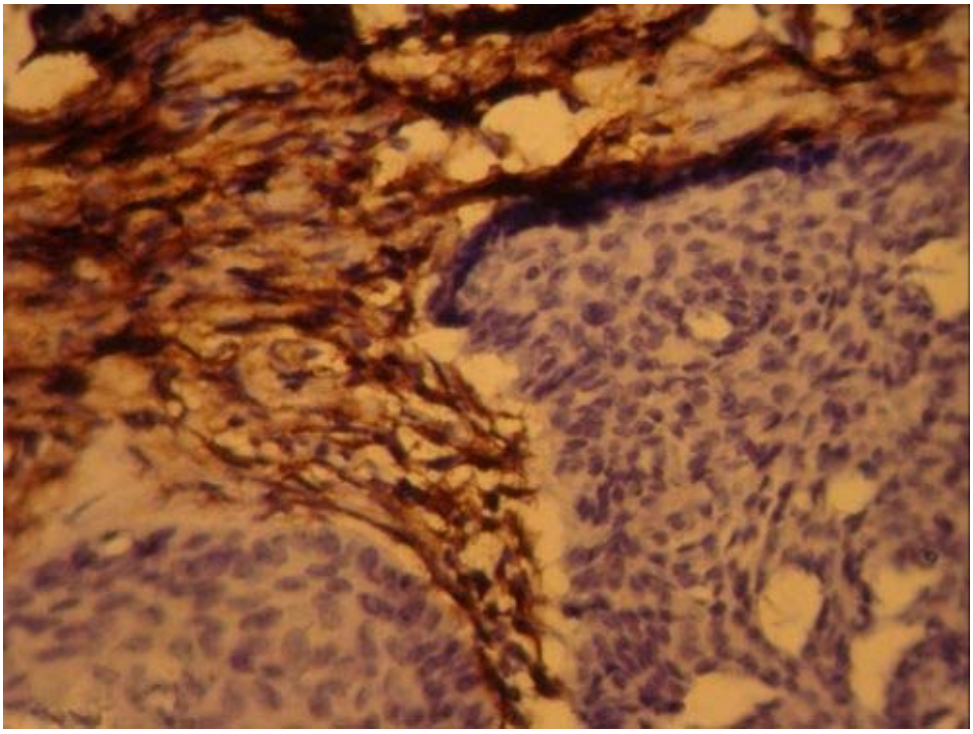

Figure 2-B. CD10 expression in trichoepithelioma (× 400)

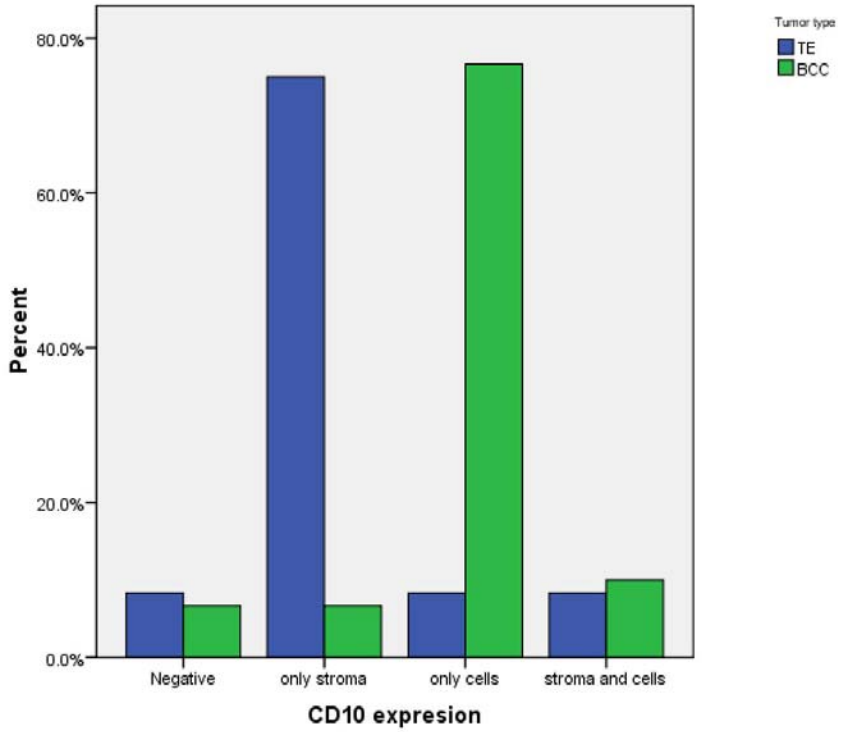

Figure 3. The comparison of CD10 expression in stromal and basaloid cells related to tumor type

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Discussion

The results of the present study indicate that CD10 is a useful marker in the immunohistochemical evaluation of cutaneous neoplasms including TE and BCC. Different staining patterns of CD10 staining in these tumors, that is basaloid cells staining in BCC and stromal staining in TE, may be useful in resolving the existing problem in clinicohistological differentiation of these two entities.

Trichoepithelioma is a benign skin tumor with follicular differentiation, whose distinction from basal cell carcinoma is sometimes difficult, clinically and histologically. Both tumors are composed of nests of basaloid cells with follicular differentiation. Sometimes it may be impossible to make a histopathologic differentiation on the basis of routine hematoxylin and eosin staining. Such distinction is clinically important because of the differences in prognosis and treatment of these tumors.[1] Therefore, several laboratory techniques have been investigated as an aid in this differentiation. In these instances, immunohistochemical examinations may provide further information.

In the past, several antibodies were used to differentiate between BCC and TE,[10-20] although most were not specific for each of these tumors. A study in 2008 by Costache M,[10] showed that CK20 and androgen receptor were helpful in differentiation between BCC and TE, but interpretation was difficult in some cases. In the same study, there was not any difference in staining with Bcl-2 and CD34 between BCC and TE. It was in contrast with Kirchmann et al. [11] and Illueca et al.[12] studies that showed the usefulness of CD34 by showing the lack of CD34 expression by tumor stroma in BCC, but positive in TE. In another study by Katona et al.[13], the usefulness of CK20 and androgen receptor in differentiation of these tumors was further confirmed. They showed that the AR-, CK20+ immunophenotype was sensitive (87%) and specific (100%) for TE. But the AR+, CK20- immunophenotype was specific (100%) and moderately sensitive (61%) for BCC. In another study, Choi et al.[14] showed that elastic fiber staining and cytokeratin 15 expression pattern may help in the differentiation of TE from BCC. Carvalho et al.[15] investigated the expression of CD23 in desmoplastic trichoepithelioma and morpheaform BCC and found no statistically significant difference in expression of this marker in these tumors. In addition, there are other immunohistochemical markers which may be helpful in differential diagnosis of TE and BCC, including Bcl-2, TGF-β and Ber-EP4.

Bcl-2 is an oncogene associated with apoptosis, and can be overexpressed in some malignancies. There are some studies which stated that Bcl-2 diffusely stains the tumor nests in BCC while it stains the outermost cell layers in trichoepithelioma.[16, 17] In contrast, there exist a number of other studies which question the reliability of Bcl-2 in distinguishing TE from BCC.[21-24]

Recently increasing evidence has suggested that androgen receptor and transforming growth factor-β (TGF-β) may be useful in differentiating TE from BCC. Verhaegh *et al.*[16] showed a diffuse cytoplasmic TGF-β staining in TE tumor cells, whereas negative staining was observed in BCCs. Izikson *et al.* [25] found positive androgen receptor immunostaining in BCC cells compared with negative staining in TE. Ber-EP4 is a monoclonal directed against two glycopolypeptides found in most human epithelial cells. Krahl *et al.* [26] did not find any consistent difference in the staining pattern of Ber-EP4 in BCC and TE.

The results of other previous studies were consistent with the results of our study.[7, 8] Moreover, Cordoba et al.[27] reported the same pattern of CD10 expression in different forms of BCC. Based on these results CD10 can be used routinely for differentiating BCC and TE.

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Conflict of Interests
Authors have no conflict of interests.

Authors' Contributions
MH and PR participated in the design of the study and examined histologic sections. FS prepared and processed the specimens and retrieved data from the archive. All authors read and approved the final manuscript.

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