BASAL CELL CARCINOMA ARISING WITHIN A TRICHOEPITHELIOMA: AN IMMUNOHISTOCHEMICAL STUDY

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A b s t r a c t

Background: Trichoepithelioma (TE) and basal cell carcinoma (BCC) of skin represent distinct tumor entities but they have a close histogenetic and phenotypic relationship.

Objective: A unique case of a BCC arising within a TE is described with an emphasis on the analysis of different and for each tumor type typical immunophenotype.

Material and Methods: A 71-year-old man presented with a subcutaneous solid tumor in the lumbar region. The resected tumor specimen was studied by immunohistochemistry.

Results: Histology revealed a coexistence of classic TE and nodular BCC. Both tumors were strongly positive for BerEP4 and negative for EMA. Neoplastic epithelium of the BCC showed a diffuse staining for Bcl-2, while the TE expressed Bcl-2 almost exclusively in the peripheral cells of tumor islands. In the BCC, neoplastic nodules exhibited a focal staining for CD10, while the peritumorous stroma did not. In contrast, the TE showed a focal immunoreactivity for CD10 in the stromal cells around the neoplastic islands which were completely negative. The TE contained intratumorous CK20-labeled Merkel cells but they were not detected in the BCC. A stromal immunoreactivity for CD34 was found in both tumors. Proliferative activity (Ki-67) was slightly higher in the BCC than in the TE.

Conclusion: Although a concomitant presence of TE and BCC in the same skin lesion is a unique finding, it may be sometimes encountered in a biopsy practice. Pathologists should provide a careful histologic examination of the whole TE lesion with precise section sampling to unveil such possible association.

Keywords: basal cell carcinoma, trichoepithelioma, trichoblastoma, immunohistochemistry

INTRODUCTION

Trichoepithelioma (TE) is an adnexal skin tumor containing epithelial structures that show a certain degree of differentiation toward hair follicle (1,2). The classic variant consists predominantly of uniform basaloid cells arranged in variably sized nests, trabeculae or cribriform patterns, situated in a background stroma of fibroblastic tissue (1,2). Despite its historical usage, the term TE has disappeared from the latest WHO classification (3). Various types of benign tumors that originate from follicular germinative cell, including TE, have been recently included under the term trichoblastoma (3,4). The concept of trichoblastoma has undergone considerable changes since the term was first proposed by Headington in 1970. The latest WHO classification (3) adopted the definition of trichoblastoma introduced by Ackerman as a generic term for a benign cutaneous tumor composed of follicular germinative cells.

Trichoblastoma is further divided into the following types: (3, 4)

- nodular
 - large (including pigmented)
 - small (including adamantinoid)

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- retiform (giant solitary trichoepithelioma)
- cribriform (conventional trichoepithelioma)
- racemiform (inconventional trichoepithelioma)
- columnar (desmoplastic trichoepithelioma)

Since the name TE is still routinely used in biopsy practice, in the present article the author works with this term according to tradition.

TE exhibits many histopathologic features similar to those of basal cell carcinoma (BCC) (1,2). Therefore, the correct diagnosis is very important because BCC is a locally aggressive malignant neoplasia (1,2,5-7) while TE is a benign tumor with excellent prognosis (1, 2). As a consequence, they require different therapeutic strategy and clinical management. The main differential diagnostic features of both entities are illustrated in Table 1. (1, 4). Considering the histomorphologic similarities, differentiating between TE and BCC is diagnostically challenging and is often not possible without the use of immunohistochemistry. In problematic cases, pathologists usually apply Bcl-2, CD10, CD34, and CK20 immunohistochemical stains to disclose a correct diagnosis. Herein, a unique case of a BCC arising within a TE is described with an emphasis on the analysis of different and for each tumor type typical immunophenotype.

Table 1 Useful histological features for distinguishingd between basal cell carcinoma and trichoepithelioma. (loosely adapted from ref. 1,4)

Trichoepithelioma	Basal cell carcinoma
symmetry	asymmetry
surrounding by a fibrous stroma	invasive growth
fibroblasts-like cell aggregates, similar to a follicular papillae	absence (or minimal presence) of a specific follicular stroma
retraction artefact rare	retraction artefact common
solar elastosis absent or rare	solar elastosis marked
horn cysts common	usually no horn cysts
usually no ulceration	often ulceration
mitoses not increased	increased mitoses

CLINICAL HISTORY

A 71-year-old man presented with a subcutaneous solid tumor in the right lumbar region. He claimed that the lesion had been present for 3–4 years. Recently, it has become painful. Clinically, it appeared as a subcutaneous nodular resistance measuring a few centimeters. A presumptive clinical diagnosis was a lipoma. A surgical exstirpation of the lesion was done and the sample was send for a microscopic examination.

MATERIAL AND METHODS

The resected tumor mass consisted of a few fragments of solid tissue, brownish in color and elastic in consistency. The obtained specimen was processed into four formalin-fixed paraffin-embedded tissue blocks which were then stained with hematoxy-

lin-eosin. The selected section was analyzed immunohistochemically with monoclonal mouse anti-human antibodies against the following antigens: EpCAM (clone BerEP4, DAKO, ready to use), EMA (clone E29, DAKO, ready to use), Bcl-2 (clone 124, DAKO, ready to use), CD10 (clone 56C6, DAKO, ready to use), CD34 (clone QBEnd/10, DAKO, ready to use), CK20 (clone Ks20.8, DAKO, ready to use), and Ki-67 (clone MIB1, DAKO, ready-to-use).

RESULTS

Microscopic examination of the sample revealed a coexistence of classic TE and nodular BCC (Figure 1). The dominant tumor component (> 95% of total tissue) was the TE showing a characteristic histomorphologic growth pattern. It composed of small branching islands of basaloid cells with focal invaginations that somewhat resembled hair papillae. Nodular BCC consisted of typical nests of basaloid cells with peripheral nuclear palisading

Fig. 1 Detail on interface between the trichoepithelioma (lower part) and the nodular basal cell carcinoma (upper part). (hematoxylin & eosin, 40x)

Fig. 2 Basal cell carcinoma. Strong diffuse positivity for Bcl-2 in the neoplastic nodules. (80x)

and clefting between tumor and stroma. No intact skin or another tissue was found. By immunohistochemistry, both tumors were strongly positive for BerEP4 and negative for EMA. Neoplastic epithelium of the BCC showed a diffuse staining for Bcl-2 (Figure 2), while the TE expressed Bcl-2 almost exclusively in the peripheral cells of tumor islands (Figure 3). In the BCC, neoplastic nodules exhibited a focal staining for CD10 (Figure 4), while the peritumorous stroma did not. In contrast, the TE showed a focal immunoreactivity for CD10 in the stromal cells around the neoplastic islands which were completely negative (Figure 5). The TE contained scattered intratumorous CK20-labeled Merkel cells (Figure 6). They were not detected in the BCC. A very strong immunoreactivity for CD34 in the peritumorous stroma was found both in the TE (Figure 7) and in the BCC. Proliferative activity (Ki-67 index) was slightly higher (up to 10%) in the BCC (Figure 8) than in the TE (< 5%) (Figure 9). Since the lesion was obviously not completely removed, re-excision was recommended. At the time of writing this article no further clinical information about the patient was available.

Fig. 3 Trichoepithelioma. Expression of Bcl-2 predominantly in the outermost layers of tumor nests. (120x)

Fig. 4 Basal cell carcinoma. Focal positivity for CD10 in the neoplastic nodules. (80x)

Fig. 5 Trichoepithelioma. Focal positivity for CD10 in the peritumorous stroma. (100x).

Fig. 6 Trichoepithelioma. Scattered CK20-positive Merkel cells in the tumor. (120x)

Fig. 7 Trichoepithelioma. Strong CD34 positivity in the peritumorous stroma. (100x)

Fig. 8 Basal cell carcinoma. Slightly increased Ki-67 proliferative index. (80x)

Fig. 9 Trichoepithelioma. Low Ki-67 proliferative index. (100x)

DISCUSSION

Although TE and BCC of skin represent distinct tumor entities with different biological behaviour, they have a close histogenetic and phenotypic relationship (2). It has been explained on the basis of an assumption that they have a common genesis from pluripotential cells which may develop toward hair structures (2). This hypothesis is supported by the fact that patched gene mutations are seen in both tumors (2). As it has already been mentioned, the pathologic distinction between them is sometimes complicated by many histomorphologic similarities (1, 2). As such, immunohistochemical analysis and adequate tissue sampling are essential in diagnostically equivocal lesions. In a routine biopsy practice several molecular markers are helpful in distinguishing TE from BCC (Table 2). (1,8–11). In the current case we analyzed a panel of selected antibodies to demonstrate an immunophenotypic diversity of these neoplasms. Our results corroborate the data found in the global literature which are summarized in Table 2. The only exception was a stromal staining of CD34 in the BCC, although it was not surprising because it developed in a background of

the TE. In spite of that, the present case is an excelent example to demonstrate a typical immunoprofile of these two neoplasms. One should keep in mind, however, among those markers there is not a single one that is absolutely effective in discriminating between TE and BCC (12). This highlights the need to use a complex panel of antibodies to improve the differential diagnosis process.

Table 2 Standard immunohistochemistry panel for differential diagnosis of trichoepithelioma and basal cell carcinoma. (loosely adapted from ref. 1,8–11). (CK, cytokeratin; AR, androgen receptor; MC, Merkel cells, PHLDA1, pleckstrin homology – like domain family; p75NTR, p75 neurotrophin receptor)

Marker	Trichoepithelioma	Basal cell carcinoma
Bcl-2	positive in peripheral tumor cells	diffusely positive in tumor nests
CD10	– positive in stroma – usually negative in tumor	– usually positive in tumor – negative in stroma
CD34	positive in stroma	negative
Ki-67	low	increased
CK15	focally positive	negative
CK20	focally positive (MC)	negative
stromelysin-3	negative	usually positive in stroma
AR	negative	usually positive in tumor
D2-40	usually positive in tumor	usually negative in tumor
PHLDA1	positive in tumor	negative in tumor
p75NTR	positive in tumor	usually negative in tumor

Very rarely, a BCC may develop within a TE in which case features of both tumors are seen in the same lesion. Only a few such cases have been published in literature until now (13–18). The concomitant occurrence of TE and BCC raises the question of whether there is a true malignant transformation or if it is only the result of two neoplasms independently developing in the same location (collision tumor) (16, 17). In our case it is unclear whether the BCC developed independently or by transformation from the TE. Considering a long-term growth of tumor containing just a small proportion of BCC component it seems more likely that this event represents a focal malignant transformation. Anyway, they were two histologically and immunophenotypically separate tumor units within a single lesion, of which the BCC was prognostically more important and should be decisive for further clinical management.

CONCLUSION

Although a concomitant presence of trichoepithelioma and basal cell carcinoma in the same skin lesion is a unique finding, it may be sometimes encountered in a biopsy practice. Pathologists should provide a careful histologic examination of the whole trichoepithelioma lesion, especially in large sized tumors, with precise section sampling to unveil such possible association.

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