Cd 34 Glycoprotein as A Differentiating Marker Between Basal Cell Carcinoma and Trichoepithelioma

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Abstract

Trichoepithelioma (TE) is a benign skin tumor with follicular differentiation, which is sometimes difficult to distinguish clinically and histologically from basal cell carcinoma (BCC). One of the most helpful differences is the histologic appearance of the stroma. CD34 is an antigen known to stain the spindle shaped cells located around the middle portion of normal hair follicles. We selected twenty clinically confused cases. After routine histopathological staining by haematoxylin and eosin, all cases showed typical diagnosis in seventeen cases (9BCC & 8TE) while the remaining three cases revealed overlapped features. Immunoperoxidase technique using anti-CD34 antibody carried out in all cases displayed two out of the three overlapped cases had a staining pattern similar to the typical BCC cases; the immediate tumor stroma together with the spindle cells intermixing the tumor nests were CD34 negative. Moreover, the remaining uncertainly diagnosed case had a pattern resembling the typical TE cases; the immediate tumor stroma as well as the spindle cells surrounding the tumor islands were focally CD34 positive.

From our study, we concluded that the CD34 staining pattern can be considered as a helpful tool in differentiation between TE and BCC particularly when these lesions are in doubt about the clinical or routine histologic diagnosis.

Key words: CD34 antigen- Immunohistochemistry- Trichoepithelioma- Basal cell carcinoma.

Introduction

Trichoepithelioma (TE) and basal cell carcinoma (BCC) are basaloïd neoplasms (Poneicka and Alexis, 1999). The differentiation between TE & non-ulcerated BCC can be difficult for the clinician as well as the pathologist. Both tumors can present as a solitary slowly growing, firm, skin-colored papule, or nodule with a pearly appearance commonly located on the face (Mackie and Calonje, 2004). Moreover, some lesions of TE may become quite large with telangiectasias and ulceration, making the distinction from BCC even more challenging (Pham et al., 2006).

Some histologic criteria can help to differentiate between TE and BCC. The presence of necrotic cells, mitotic figures, stromal retraction, and deposition of mucin in the stroma are characteristic of BCC, however, the presence of papillary mesenchymal bodies strongly suggests the diagnosis of TE (Brooke et al., 1989). On the other hand, there are some cases in which the histologic distinction between TE and BCC may be difficult, especially in small biopsy specimens (Kirchman et al., 1994).

CD34 is an antigen known to stain the spindle-shaped cells located around the middle portion of normal hair follicle (Kirchmann et al., 1995). Also, CD34 has been detected in the endothelial cell, in perivascular dendritic cells and in spindle shaped cells in the basement membrane zone of the eccrine glands (Nickololff, 1991).

Trichoepitheliomas are tumors believed to be derived from follicular epithelium. The hypothesis was made that the stroma around the TE tumor nests also
might be stained positively by immunohistochemical techniques for CD34. On the other hand, BCC forms a histologically distinct mucinous stroma that might not contain the CD34 glycoprotein. Therefore, the immunohistochemical stromal CD34-positive cells would be useful in distinguishing those two tumors (Kirchman, et al., 1994).

The aim of this work is to detect the CD34 staining pattern in TE & BCC, thus, facilitating the discrimination of overlapped cases of both neoplasms.

Material & methods

The material of this work is consisted of twenty selected clinically confused cases of basal cell carcinoma (BCC) versus trichoepithelioma (TE) presenting as a firm papule with pearly appearance located in the face. The cases were collected from Dermatology Department, Al-Hussein University Hospital during the period from January to August 2006. All patients were males whose ages ranged from 39 to 55 years (mean; 48.2 ± 2.1). Formalin-fixed & paraffin-embedded blocks were sectioned at 5µm thickness and examined microscopically using H&E stain to confirm the clinical diagnosis. In addition, immunohistochemical study was carried out as the sections were deparafinized, hydrated & incubated with 3% H2O2 for 5 minutes to block the endogenous peroxidase activity to investigate the expression of CD34 marker from the tumor cells. Mouse monoclonal primary antibody for CD34 (Biogenex Cat. No; AM 236-5M) was applied. Antigen retrieval was done by microwave heating in citrate solution. Secondary antimouse antibody using peroxidase labeled biotin streptavidin complex detection system (Dako, Copenhagen, Denmark) for CD34 was used. Positive reactions for CD34 appeared as a brownish cytoplasm sometimes nuclear, granular staining of the tumor cells.

Results

Microscopic examination of the routinely stained sections diagnosed 9 cases as typical BCC showing the presence of different sized and shaped islands of tumor basaloid cells, with peripheral palisading of their outer rows, found in a fibrous stroma. The islands are separated from the stroma by a clear cleft (Figs 1-A& B). Also, 8 cases revealed the features of typical TE including the presence of proliferated basaloid cell islands with follicular differentiation embedded in a fibrous stroma. The tumor islands showed a peripheral palisading of their outer rows but without a separating cleft from the stroma (Figs 2-A& B). However, the remaining three cases displayed overlapping criteria between both tumors involving the presence of follicular differentiation as well as cleft formation (Table 1).

Immunoperoxidase staining (Table 2) showed that the pattern of two out of the three overlapped cases was mimicking that of the nine typical BCC where the immediate tumor stroma did not stain for CD34, however, the surrounding stroma was positive. In addition, a clear demarcation was found between the mesenchymal component intermixed with the epithelial tumor islands being negative for CD34 and those stromal cells peripheral to the tumor being CD34-positive (Figs 3-A& B).

In contrast, the remaining overlapped case gave a pattern resembling what was revealed in the typical eight TE cases as the immediate mesenchymal stromal cells adjacent to the tumor island, the spindle cells around and within the papillary mesenchymal bodies as well as the more fibrotic areas of the tumor stroma were CD34 positive. In addition, there was no buffer zone of negatively stained cells separating CD34 reactive epithelial islands from the positive mesenchymal stromal cells (Figs 4-A, B& C).
Table 1: Routine histopathological diagnosis of all studied cases (n=20):

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>No; of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Typical basal cell carcinoma (BCC)</td>
<td>9</td>
</tr>
<tr>
<td>Typical trichoepithelioma (TE)</td>
<td>8</td>
</tr>
<tr>
<td>Indefinite diagnosis</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>20</td>
</tr>
</tbody>
</table>

Table 2: CD34 immunoreactivity in all studied cases (n=20):

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Differentiating CD34 expression pattern</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No;</td>
</tr>
<tr>
<td>Basal cell carcinoma</td>
<td>11</td>
</tr>
<tr>
<td>(BCC)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Trichoepithelioma</td>
<td>9</td>
</tr>
<tr>
<td>(TE)</td>
<td></td>
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Fig (1-A): A case of BCC revealed multiple tumor islands occupied the upper dermis of different sizes & shapes composed of basaloid cells. Tumor islands are separated from the stroma by a cleft. Fig (1-B): Revealed the peripheral palisading of the outer row of the basaloid cells in the tumor islands (Hx&E. x 200).

Fig (2-A): A case of TE showed a pathology similar to that described in BCC except for the absence of the cleft (Hx&E. x 100). Fig (2-B): Showed palisading of the outer row of tumor islands (Hx&E. x 400).
Fig (3-A): A case of BCC revealed negative CD34 staining in the tumor islands and intermixing stromal mesenchymal cells but positive in the surrounding stroma (Immunoperoxidase [IP] x 100). Fig (3-B): Revealed negative staining for CD34 around tumor nests, however, the endothelial cells stained positive (IP x 200).

Fig (4-A): A case of TE revealed positive staining for CD34 of tumor cells in the middle of the follicles more than that at the periphery (IP x 200). Fig (4-B): Showed CD34 immunopositivity in the stromal cells admixed with tumor islands (IP x100) Fig (4-C): Revealed positive CD 34 staining around & within the papillary mesenchymal bodies as well as the fibrotic area of tumor stroma (IP x 200).
Discussion

Basal cell carcinoma is a malignant neoplasm necessitating complete surgical excision as opposed to the benign behavior of TE (Poniecka and Alexis, 1999). The histopathologic discrimination of TE and BCC often represent a diagnostic challenge. The distinction is of clinical significance due to differences in prognosis and treatment (Pham et al., 2006). It has been suggested that adnexal tumors are characterized by an accompanying stroma that attempts to recreate the normal relationship between the adnexae and their surrounding mesenchyme (Swanson et al., 1998). TE can display two distinct stromal patterns (1) spindle-shaped cells associated with abundant collagen and (2) papillary mesenchymal bodies (Brooke et al., 1989). Focally, TEs may exhibit cleft formation occurring between the fibrous stroma and the surrounding connective tissue, but usually not between the epithelium and the stroma (Mehregan and Hashimoto, 1991).

Trichoepitheliomatous stroma is similar to the stroma surrounding hair follicles in normal skin. In contrast, in the stroma surrounding BCC, there is a deposition of mucinous material and often cleft formation (Mehregan and Hashimoto, 1991). Cleft formation in BCC is ascribed to several factors including (1) glycosaminoglycan production, (2) collagenase production by peritumoral fibroblasts and (3) decreased tumor cell-basement membrane and basement membrane-stromal connections (Miller, 1991).

CD34 is a 115-kd glycoprotein initially detected on human hematopoietic progenitor cells. It has been detected by immunohistochemical techniques on vascular endothelial cells in non-hematopoietic organs (Chu et al., 2000). The function of CD34 is unknown, but some authors consider it to be involved in cell interactions adhesion or migration (Fina et al., 1990).

In this study, CD34 immunostaining had a significant role regarding the accurate diagnosis and the distinction between difficult clinical and routine histopathological cases of BCC and TE. By haematoxylin and eosin stain, we found that seventeen cases were definitely diagnosed as typical BCC (9 cases) and typical TE (8 cases) while three cases revealed overlapped features between both neoplasms. After CD34 staining, one of the overlapped cases displayed the same pattern like that of the typical eight TE cases including positive immediate stromal cells adjacent to the positive tumor islands, positive spindle-shaped cells of the papillary mesenchymal bodies and the positive fibrotic areas of the tumor stroma. However, the remaining two overlapped cases showed a staining pattern resembling the nine typical BCC in which there was an absence of any positivity either in the immediate tumor stroma or in the cell islands while the surrounding tumor stroma was CD34-immunoreactive.

Our results coincided with those reported by Kirchmann et al. (1994) and Kirchmann et al. (1995) who stated that all their cases of BCC and TE revealed the characteristic previously mentioned CD34 pattern in either lesions.

Based on our and Kirchmann et al. (1995) study’s observation that the stroma around BCC was devoid of anti-CD34 positive cells while the stroma immediately adjacent to TE was positive, this may provide an additional in vivo support to the hypothesis that the stroma is different among these neoplasms. Also, Kirchmann et al. (1995) speculated that benign TE had a stroma closely resembled the mesenchymal component of the normal skin while BCC were surrounded by a stroma containing cells not normally found in the dermis. Moreover, they suggested that loss of CD34 stromal staining might be related to some inherent feature of the stromal cells surrounding the epithelial islands in these tumors.

We can concluded that a more practical application of our observations may be the ability to use anti-CD34 staining of stromal cells in order to help in differentiating BCC from TE since these
tumors are occasionally similar both clinically and histologically.

References


سي دي 34 جليكوبروتين كدليل تميزي بين الورم الظهاري القاعدي والخلايا والورم الظهاري الشعري

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1 قسم الأمراض الجلدية والتناسلية والذكورة ، 2 قسم الباطولوجي
كلية طب بنيين الأزهر فرع القاهرة واسيوط.

الورم الظهاري الشعري هو ورم حميد وفي بعض الأحيان من الصعب التفرقة بينه وبين الورم الظهاري القاعدي الخلايا من حيث تحليل الأنسجة أو حتى من الناحية الإكلينيكية. وقد تم اختيار عشرة حالات غير واضحة التشخيص اكلينيكيا وبعد تشخيصها روتوينيا بصباغة الهيماتوكسيلين والأيويوسين وجدنا ان تسعة حالات كانت نموذجة للورم الظهاري القاعدي الخلايا وثمانى حالات نموذجة للورم الظهاري الشعري بينما تشابهت الثلاث حالات الباقية في التشخيص. وبعد استخدام سي دي 34 اضطر أن حالات من هذه الحالات الثلاث تشابه في نمط الصباغة مع النمط الأولي للورم الظهاري القاعدي الخلايا حيث تغير الصباغة في النسيج الضام القريب من الورم وكذلك في الخلايا المضغزية التي تميز بين مجموعات خلايا الورم بينما اظهرت الحاله الثالثة نفس نمط الصباغة مثل الثمانية حالات النموذجة للورم الظهاري الشعري حيث وجدت بور ايجابية من السي دي 34 في النسيج الضام القريب من الورم وكذلك في الخلايا المضغزية التي تحتوي حجز خلايا الورم

لذا يستطيع من هذا البحث أن ننصح بصباغة سي دي 34 يعتبر وسيلة مساعدة للتمييز بين الورم الظهاري القاعدي الخلايا والورم الظهاري الشعري خصوصا تلك التي يشك في تشخيصها اكلينيكيا وبايثولوجيا بالصباغة الروتوينية.