Solitary trichoepithelioma: clinical, dermatoscopic and histopathological findings

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Abstract
Trichoepithelioma is part of the adnexal carcinomas. It is a benign, small tumor, usually under a centimeter in diameter, which develops in the basal cells of the hair follicle. Case report: We present the case of a 30-year-old female patient, from rural area, which was hospitalized in the Clinic of Dermatology, Emergency County Hospital, Craiova, Romania, in March 2015, for the presence of a skin tumor, with round-oval shape, 0.5 cm in diameter, brownish colored, located on the left cervical region. The patient had no past medical history. The skin tumor appeared two years ago, and it was slowly increasing in size. Physical examination was in normal ranges. The dermatoscopic examination revealed a pearly white background covered with tumor islands that were oval shaped, with hyperpigmentation, centered by keratin cysts and surrounded by collagen. During hospitalization, we performed tumor biopsy. The histopathological examination showed microscopic structure of trichoepithelioma. After history taking, physical examination, dermatoscopic examination and histopathological result, our diagnosis was left cervical trichoepithelioma. Conclusions: Trichoepithelioma is a rare trichogenic tumor, which appears at any age, including newborns, with potential for local recurrence. Our case report represents a classic dermatoscopic aspect of trichoepithelioma, that can have close resemblance to basal cell carcinoma and other skin adnexal tumors, clinically, dermatoscopic and histopathological.

Keywords: trichoepithelioma, skin adnexal tumors, dermatoscopy, solitary lesion.

Introduction
Trichoepithelioma (TE) is a rare benign tumor of skin that originates from benign proliferation of epithelial-mesenchymal origin cells [1–6]. It is commonly located on the face and hairy skin [7, 8]. Trichoepithelioma can generally appear as solitary papule or nodule with dimensions between 2 to 8 mm with skin color in the sporadic type [1, 9], or as multiple lesions in the autosomal dominant type [1, 4]. The gene for the development of familial trichoepithelioma encodes a tumor suppressor and links to the short arm of chromosome 9 [10, 11]. Harada et al., in 1996, reported a mutation in this tumor suppressor-encoding gene situated on band 9p21 in multiple familial trichoepithelioma [12].

It can appear at any age, but most common presentations are noted in the 4th decade [4]. In the case of this tumor, the diagnosis is not possible with clinical examination only and dermatoscopic and histopathological diagnosis is essential for ruling out other close differential diagnosis of basaloid epitheliomas and basal cell carcinomas [4, 13, 14].

The aim of this paper was to highlight the clinical and practical dermatoscopy characteristics of trichoepithelioma but also the histopathological and immunohistochemical ones.

Case report
We present the case of a 30-year-old female patient, from rural area, which was hospitalized in the Clinic of Dermatology, Emergency County Hospital, Craiova, Romania, in March 2015, for the presence of a skin tumor, with round-oval shape, 0.5 cm in diameter, brownish colored, located on the left cervical region (Figure 1).

The patient had no past medical history.

The skin tumor appeared two years ago, and it was slowly increasing in size.

Physical examination revealed in cervical region a tumor of 0.5 cm diameter, brownish colored and round-oval shape with no other pathological findings.

Dermatoscopic examination was performed with Heine Delta 20 and highlighted the following aspects: pearly white background covered with tumor islands that were oval shaped, with hyperpigmentation, centered by keratin cysts and surrounded by collagen (Figure 2). During hospitalization, we performed tumor biopsy.

The histopathological examination, using Hematoxylin and Eosin (HE)-stained paraffin cross-sections, showed microscopic structure of trichoepithelioma. Histopathological examination showed the following aspects: normal epidermis and the presence of horny cysts in the dermis bounded by a small number of cell layers, made
up of cells with eosinophilic cytoplasm and oval nuclei. Solid tumor islands are composed from basaloid-type cells, small, monomorphic, with rare pale, vesicular nuclei, palisading at periphery, which is a very important element that makes difficult to distinguish between trichoepithelioma and basal cell carcinoma. Also, complete keratinized horny cyst, steep and complete keratinization are the main elements for differential diagnosis with squamous cell carcinoma. Adjacent to the cysts, are present solid tumor islands and branched cords composed of basal type cells. On the image, it can see two rudimentary hair follicles. Tumor stroma is rich in fibroblast-type cells (Figures 3–7).

For immunohistochemical analysis, we used the following antibodies’ panel (Table 1).

In these cases, we followed sequential protocols, the LSAB2-HRP system (code K0675, Dako) and LSAB2-AP system (code K0674, Dako) were used for the reactions amplification and 3,3’-diaminobenzidine (DAB, code 3467, Dako) was used to see the reactions. For the validity of positive reactions, there were used negative external controls, by omitting the primary antibody.

For the reaction analysis, we used a quantification of positivity: intense, moderate or weak positive reaction.

<table>
<thead>
<tr>
<th>Antibody</th>
<th>Clone/Source</th>
<th>Dilution</th>
<th>Antigen retrieval</th>
</tr>
</thead>
<tbody>
<tr>
<td>BerEp4</td>
<td>VU-1D9/Leica</td>
<td>1:100</td>
<td>Pepsin, 2 minutes</td>
</tr>
<tr>
<td>CD34</td>
<td>QBEnqband-10/Dako</td>
<td>1:100</td>
<td>Citrate buffer, 5 minutes</td>
</tr>
<tr>
<td>CK20</td>
<td>PW31/Leica</td>
<td>1:100</td>
<td>Citrate buffer, 5 minutes</td>
</tr>
<tr>
<td>Bcl2</td>
<td>124/Dako</td>
<td>1:50</td>
<td>Tris-EDTA, 7 minutes</td>
</tr>
</tbody>
</table>

The immunohistochemical analysis showed: Bcl2 positive in tumor cells and stroma, CD34 positive in vessels and stromal cells, BerEp4 negative, CK20 negative (Figures 8–14).

Thus, corroborating physical examination, dermatoscopic and histopathological examination, our diagnosis was trichoepithelioma.
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Figure 5 – Stroma containing many fibroblasts and inflammatory cells – lymphocytes. HE staining, 100×.

Figure 6 – Cords of basaloid-type cells. HE staining, 200×.

Figure 7 – Rudimentary hair follicles. HE staining, 40×.

Figure 8 – Bcl2 positive in tumor cells and stroma, 40×.

Figure 9 – Bcl2 positive in tumor cells and stroma, 100×.

Figure 10 – BerEp4 negative, 40×.
Discussion

Trichoepitheliomas are benign tumors developed from skin annexes. They affect young adults, more frequently women.

From the clinical point of view, the lesion is unique and may look like papule or nodule, round-oval shape, small size, typically 2–8 mm in diameter, skin color or with pigments. In 50% of cases, it can be found on the face (forehead, nasolabial groove, upper lip) and the cervical region [15].

Trichoepithelioma (TE) was first described by Brooke as *epithelioma adenoides cysticum*, in 1892 [16]. Brooke showed the histogenesis of this tumor from the epidermis and the epithelium of hair sacs. Pinkus work [17] presented the idea that all skin epitheliomas had as origin adult pluripotential cells, in a majority percent, and less in embryonic rests or other specific part of the epithelial system. Lever, in 1967 [18], described the origin from a primary epithelial germ or a pluripotential embryonic cell, and Montgomery, in 1967 also [19], from the outer walls of the fair follicle and hair matrix. The immunoreactivity of the epithelial nests and the keratinous cysts, in the classic solitary TE, dermoplastic TE, trichoblastic fibroma, trichogenic trichoblastoma and giant solitary trichoepithelioma are like to those of the outer root sheath and the infundibulum of normal hair follicles. It is reported that all trichogenic tumors differentiate mainly toward the outermost layer of the exterior root sheath and other parts of them towards other parts of the follicle. No specific immunoreactivity or staining pattern for each kind of trichogenic tumor has been demonstrated, fact that highlights the idea that all neoplasms of follicular germinative cells should be grouped as a single entity [20].

As reported in studies published previously, there are three forms of TE: solitary, multiple and dermoplastic [21].

The solitary form is found more often in young adults. It locates on the middle facial area and in some cases around nasal area. This location is mainly due to the high number of sebaceous glands in these areas.

TE rarely can reach sizes of over 1 cm diameter and can it be found on the neck, scalp or trunk [22].

We may encounter multiple trichoepitheliomas in Brooke–Spiegler syndrome and Rombo syndrome.

Brooke–Spiegler syndrome had autosomal dominant transmission. Mutation of the gene CYLD on chromosome 16q12–13 is involved, which acts as a tumor suppressor by preventing the uncontrolled cell growth and division [23]. This syndrome is characterized clinically by the presence of multiple trichoepitheliomas, cylindromas (type of epithelial tumor characterized by islands of neoplastic
cells embedded in a cylindrical hyalinized stroma formed from ducts of glands) and spiradenomas (benign tumor of eccrine sweat gland origin) at the face and cervical region.

The Rombo syndrome is dominantly inherited disorder characterized by verruculat atrophoderma (symmetrical vermiform facial atrophy with time, the lesions developed into pit-like depressions), hypotrichosis (less than normal amount of hairs), milia (benign, keratin-filled cysts), trichoepitheliomas, basal cell carcinomas and peripheral vasodilatation with cyanosis [24].

The definite diagnosis of trichoepithelioma is established by histopathological examination, used also in our case. Other conditions that need to be excluded are mostly represented by basal cell carcinoma and pigmented nevi.

Regarding the differentiation between basal cell carcinoma and trichoepithelioma that can be done considering the clinical findings, sustained by dermacoscopic and histopathological findings. Clinical examination of trichoepithelioma reveals the appearance of the tumor in young adults, as solitary of multiple tumors, with a fine translucent aspect, sometimes with telangiectasias on the surface, with a very slow rate of growth.

Basal cell carcinoma usually appears in people over 50-year-old, usually as a translucent pearly papule, pink-red, that develops gradually a central ulceration and telangiectasia on the surface area; also, we notice a significant increase, gradually.

Performing dermatoscopy, in case of TE, we notice a white background with thin arborize vessels and multiple cysts on the surface; for basal cell carcinoma, the background is pink-red with the presence of blue-gray ovoid cysts and multiple globules with the same color.

Concerning the histopathological features, in trichoepithelioma we can find a cribriform pattern with discrete aggregation of germinative cells and pale fibrocytic stroma, papillary mesenchymal body with hair bulb formation and the epithelial–connective tissue units can be surrounded by a cleft.

In nodular basal cell carcinoma, the histopathological exam can reveal a relatively circumscribed mass of large basoid aggregation that may have a jagged outline and large zone of necrosis, stroma reaction artifact with mucin deposits and clefts between the germinative cells and the periphery.

In literature, we found studies were Bcl2 expression was positive in TE and also in basal cell carcinoma [25, 26]. CD34 that in our case was also positive has been considered useful for the differential diagnosis between TE and basal cell carcinoma because the stroma is positive in TE and negative in basal cell carcinoma [27].

The curative treatment consists in surgical excision of skin tumor, attitude approached for our case.

Cases of relapses were reported if the surgical excision was incomplete. Extremely rare cases of malignancy were reported by previous studies. Trichoepithelioma may transform, very rare, in a basal cell carcinoma [28, 29].

Conclusions

TE is a rare trichogenic tumor, which appears at any age, including newborns, with potential for local recurrence.

It can appear at any age, including at birth. Our case report represents a classic dermoscopic aspect of trichoepithelioma, that can have close resemblance to basal cell carcinoma and other skin adnexal tumors, clinically, dermoscopic and histopathological. Corroborating all the data, we can establish the final, certain diagnosis, and apply the proper therapeutic measures.

Conflict of interests

The authors declare that they have no conflict of interests.

Acknowledgments

This paper was published under the frame of European Social Fund, Human Resources Development Operational Programme 2007–2013, Project No. POSDRU/159/1.5/136893.


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