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Trichoepithelioma (TE) with Aggressive Characters: A Case Report

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Abstract

Trichoepithelioma (TE) is a benign adnexal neoplasm that may be of superficial form. The gene associated with TE links to short arm of chromosome 9p21. The gene for the development of familial trichoepithelioma also encodes for tumor suppressor gene. Its altered cellular proliferation may be up-regulated because of a poorly functioning or absent tumor suppressor gene. This is due to presence of significant numbers of Merkel cells within the tumor nest and the detection of a sheath of CD34 positive dendrocytes around the tumor nests. It appears that TE differentiates towards or derives from hair structure, particularly the hair bulge.

TE is reported with equal frequency in male and female. TE is seen in young age adults. The hereditary form, however, may be seen in younger individuals. Here we report a case of TE with aggressive characters, studied with histopathology and immunohistochemistry, that shows unusual aggressive features manifested by high mitotic index. This case is reported to alert the pathologist and clinician to the existence of such lesion.

المستخلص

التركوبيتليوما Trichoepithelioma (TE)ورم ظهاري وشعري هو ورم الملحقات الجلدية الحميدة التي قد تكون ذات شكل سطحي. وترتبط الجينات المرتبطة مع TE إلى الذراع القصير للكروموسوم 9p21. إن الجينات التي تؤدي لظهور ورم ظهاري شعري عائلي تُرمِّزُ أيضا الجين الكابت للورم. قد يؤدي تغيير الانتشار الخلوي إلى تعديل بسبب سوء أداء، أو، غياب الجينات الكابتة للورم. ويرجع ذلك إلى وجود أعداد كبيرة من خلايا ميركل داخل عش الورم والكشف عن غلاف dendrocytes إيجابي CD34 حول أعشاش هذا الورم. ويبدو أن TE يتمايز نحو أو مستمد من بنية الشعر، وخاصة انتفاخ الشعر. وتفيد التقارير أن TE يتواجد بتواتر متساو في الذكور والإناث. وقد وجد TE في الشباب البالغين. إن الشكل الوراثي، مع ذلك، يمكن أن يظهر في الأفراد الأصغر سنا. ونوثق هنا حالة TE مع بروز غير معتاد، عدواني الملامح ، وهو ما يتضح من مؤشر الإنقسامية العال. إن توثيق هذه الحالة جاء لتنبيه الطبيب الشرعي والطبيب الفاحص إلى وجود مثل هذه الآفة .

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Keywards: Trichoepithelioma (TE); Mitotic index; Ki67; Immunohistochemistry; Metastasis.

Introduction

Trichoepithelioma is a rare tumor, arising from hair germinal layer. It is usually clinically presented as single or multiple papules or nodules. Lesions first appear in childhood and gradually increase in number [1]. The primary lesion of TE is characterized by rounded, skin colored, firm papule or nodule about 2-8mm in diameter (Fig.1). It is located mainly on the nasolabial folds, forehead, upper lip, and scalp. Fifty per cent of lesions occur on face and scalp.

Occasionally lesions also occur on the neck and upper trunk. Ulceration is rare in the autosomal dominant form of a multiple TE which may present on nasolabial folds. In some cases there is dermatomal distribution, associated with other cutaneous tumors like cylindroma in Brook-Spiegler syndrome, spiradenoma, basal cell carcinoma, ungual fibroma or dystrophia unguis congenital [2].

TE may also be part of Rombo Syndrome (i.e., vermiculate atrophderma, miliahypertichosis, TE, basal cell carcinoma and peripheral vasodilation). However, solitary giant TE presents as a large polypoidal lesion usually in trunk or gluteal area [1]. Occurrence of multiple TE is transmitted as an autosomal dominant trait but familial cases appear to be related to a mutation in tumor suppressor gene located on 9p21. The gene which is located on 9q22.3 and is involved in basal cell carcinoma appears to participate in the pathogenesis of TE. A 2006 study [4] has suggested that abnormalities in this gene may result in one of 3 syndromes: Brooke-Spiegler syndrome, familial cylindromatosis, and multiple familial trichoepithelioma [1,3,4].

Brooke-Spiegler syndrome, familial cylindromatosis and multiple familial trichoepithelioma are due to germ line mutations in the cylindromatosis (CYLD) gene on chromosome 16q12 [5,6]. In differential diagnosis, this clinically may include basal cell carcinoma, colloid milium, cylindroma, follicular infundibulum tumor, Milia-Miliaria, pilar cyst, steatocytoma multiplex, syringoma trichlemmoma, and trichofolliculoma. Histologically, basal cell carcinoma, microcysticadenexa carcinoma, trichoadenoma, is a tumor of follicular infundibulum, basoloid follicular hamartoma.

TE shows histologically in upper dermis, with multiple nodules composed of uniform basoloid cells arranged peripherally in palisaded manner (Fig. 2), frequently, with central keratin-filled cysts. Artefactual clefting is uncommon, apoptotic and mitotic figures are rarely present and central necrosis or atypical mitotic figures are not a feature. The stroma is generally fibrous with very little

myxoid component. Calcification is very common typically associated with the rupture of the keratinous cysts. A very distinctive feature is papillary–mesenchymal body (fibroblastic aggregate resembling abortive follicular papillae) [7,8].

Fig. 1. Rounded colored skin papule.

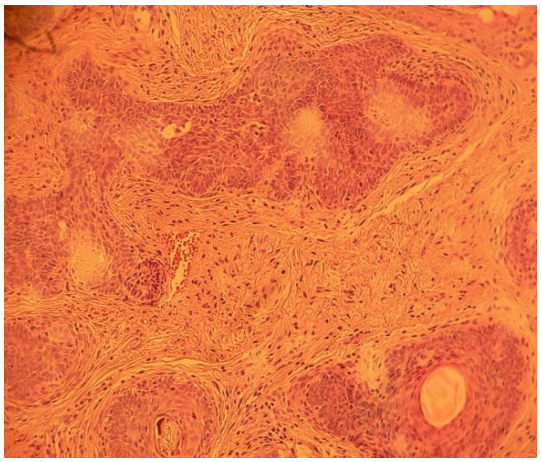

Fig. 2. Multiple nodules composed of uniform basoloid cells arranged peripherally in palisaded manner.

Immunohistochemical studies reveal expression of the cytokeratins associated with the outer root sheath CK(5,6,8,17) and expression of bcl-2 predominantly in the peripheral cell layer of the nests. The intervening stromal cells express CD34. Transforming growth factor–b is expressed in most TE. Merkel cells can be detected in all TE variants [5]. TE variants involve desmoplastic variant as its name indicates. It is characterized by a prominent sclerotic stroma. It occurs in the same population as in the classic type and presents as a plaque located in the same anatomic areas as in the classic form. Histologically, it shows narrow strands of tumor cells; desmoplasticstroma and keratinous cysts.

Pleomorphism, palisading or peripheral clefting are not seen. Feature favouring desmoplastic TE includes a rim of compact collagen around groups of epithelial cells. It shows Granulomas calcification of cornified cells within cysts, absence of necrotic neoplastic cells and only rare mitotic figures. Fibroblasts surrounding TE nests do not express the matrix metalloproteinase stromelysin-3(ST3), in contrast to basal cell carcinoma. Solitary giant variant is characterized by deep involvement of the reticular dermis and subcutaneous tissue. In contrast, basal cell carcinoma is characterized with palisading peripheral basoloid cells with clefting, mitotic figures, necrotic keratinocytes and myxoidstroma but without papillary-

mesenchymal body. Microcystic adenexal carcinoma shows small keratinous cysts in the upper, and in the deep portion. Small ducts and syringoma-like show infiltrated pattern. Trichoadenoma is similarly sized clusters of basaltic cells containing numerous keratin cysts. Tumor of follicular infundibulum has plate-like growth of basaltic cells having several points of attachement to the epidermis and follicles [8].

Basaloid follicular hamartoma is solitary, localized, linear nevoid of generalized papules or plaques. Thin anastomosing cods of basaltic cells, sometimes with peripheral palisading and occasional keratin cyst formation exist [9].

In this paper, we present a case report of TE showing aggressive characters (i.e. misleading cancer symptoms). This is done in order to increase awareness of such rare case and to avoid its mischaracterization and, hence, treatment.

Material Method and Case Report

A 35 year old Libyan female was referred for excision of a mass in the nasofold region. The tumor was growing slowly, but it did not cause subjective symptoms. No palpable lymph nodes. On inspection a subcutaneous tumor measuring 1x1cm was found. The tumor was sharply demarcated, solid in consistency, white in color and lobulated in nature. Grossly, the tumor was found to be entirely subcutaneous with normal overlying epidermis. Microscopically, using H&E stain, it revealed skin sections that are composed of lobules with anastomosing streaks of uniform basaltic cells arranged in palisaded uniform. Some cells show atypia (Fig. 3). All the lobules were surrounded by a fibroxyoidstroma. In this case abnormal mitosis appeared in large number up to 8 mitotic indices per 10 HPF. Proliferating marker using Ki67 was done and appeared to be positive (Fig. 4).

Discussion

Trichoepithelioma is an unusual neoplasm of the hair germinal layer. Recurrence has been described. Classification of this tumor is difficult due to its rarity.

Hair germ tumors are one heterogeneous biological manifestation of epithelial and mesenchymal interaction and have been classified according to the relative predominance of either component [10,11]. Another classification was according to categories on which part of the developing hair follicles they resemble [12]. Ackerman classified the benign hair follicle tumors after the most prominent morphological part [5].

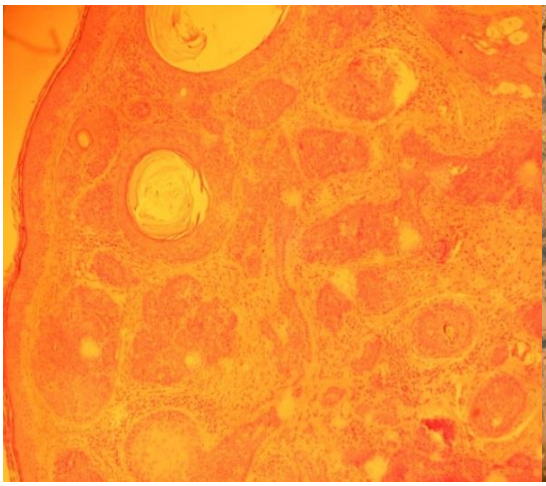

Fig. 3. Well circumscribed-orgnoid lobules composed of clusters of basaltic cells within a fibrous stroma.

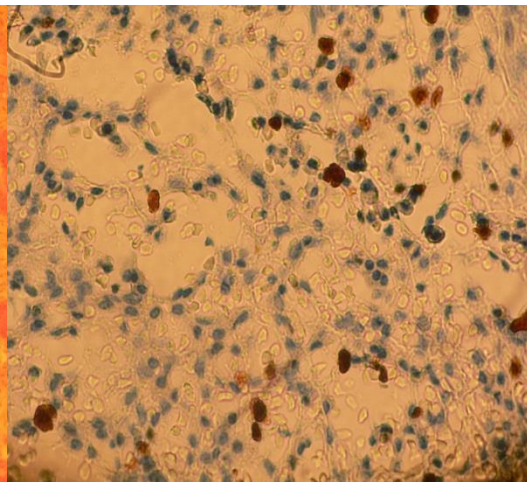

Fig. 4. Ki67 positive, formalin/PFA-fixed paraffin-embeded section.

Three clinical forms of TE are recognized and are histologically similar [1,7,13,14]. They, histologically, include solitary a small form, multiple a small form (inherited as in autosomal dominant fashion), while the solitary giant form is rare. Trichoepitheliomas in general are benign tumors but recurrence was reported in one of nine published cases of giant solitary forms. In the present case, the mitotic index is high. Proliferation marker Ki67 is highly positive denoting cytological aggressiveness of TE calling for increased clinical awareness for medical follow up due to the possibility of recurrence or metastasis. No similar cases were found in literature.

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