Trichoepithelioma

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ABSTRACT

Trichoepithelioma—a small benign tumor derived from basal cells in the hair follicle. It may occur sporadically or as the cardinal feature of
a relatively common genetic disorder called multiple familial trichoepithelioma characterized by the presence of many small tumors
predominantly on the face, inherited in an autosomal dominant pattern. A trichoepithelioma can undergo malignant transformation into a
basal cell carcinoma.1

This is a case report of 66-year-old male patient with a rounded and mobile firm swelling of 1 cm on mandibular labial vestibule of the oral
cavity causing alarm and discomfort to the patient.

Keywords: Autosomal dominant, Basal cell carcinoma, Brooke-Spiegler syndrome (BSS), Cylindroma (CYLD), Papillary mesenchymal
bodies, Trichoepithelioma (TE).

INTRODUCTION

Trichoepithelioma (TE) is a benign adnexal neoplasm. According to some authors, trichoepithelioma may be a
superficial form of trichoblastoma. The gene involved in the familial form of trichoepithelioma is located on 9p21. Other
cases are associated with Brooke-Spiegler syndrome (BSS)
caused by mutations of the cylindromatosis oncogene (CYLD),
which maps to 16q12-q13. A 2006 study has suggested that
abnormalities in this gene may result in either of three
syndromes: BSS, familial cylindromatosis and multiple familial
trichoepithelioma.2

CASE REPORT

A 66-year-old male patient (Fig. 1) was reported to CDC and
Research Institute, Rajnandgoan, Chhattisgarh, with
asymptomatic, mobile swelling of a peanut size of 1 cm in the
vestibular mucosa of mandible of oral cavity.

On oral examination, a round to oval shape, well
circumscribed, mobile, firm swelling in the vestibular mucosa
of mandible of oral cavity was noticed. The overlying mucosa
was intact and normal.

Clinical differential diagnosis of benign soft tissue tumor
and/or peripheral odontogenic tumor was reported. The lesion
was excised under general anesthesia. The specimen was sent
to histopathological observation.

Gross specimen (Fig. 2) was an oval shaped and encapsu-
lated which was measuring about 1 × 0.5 × 0.5 cm in diameter
of yellowish white color and firm in consistency. The cut surface
showed a cheesy material. The tissue was fixed and processed
routinely and stained with hematoxin and eosin.

On histopathological examination section showed multiple
horn cysts with lamelated keratin, calcification and proliferation
of basaloid cells around (Fig. 3). Based on these findings, the
diagnosis of trichoepithelioma was made.

Fig. 1: Clinical photograph showing numerous, small papules and
nODULES close to midline (nasolabial folds)
DISCUSSION

The trichoepithelioma derives from the inferior segment of the follicle epithelium as a hamartoma. Three clinical forms of trichoepithelioma are recognized:

- A small solitary form
- A small multiple form which is inherited in an autosomal dominant fashion
- A rare giant solitary form.

Histologically all three forms of trichoepithelioma are similar but not identical. They all show demarcated tumor clearly differentiated as hair forming structures. But in this case report along with intraoral involvement patient had multiple papules and nodular lesions on his face (Fig. 1).

The occurrence of multiple trichoepitheliomas is transmitted as an autosomal dominant trait. Lesions first appear in childhood and gradually increase in number. The primary lesions of trichoepithelioma are characterized as follows:

- Rounded, skin-colored, firm papules or nodules that are 2 to 8 mm in diameter
- Located mainly on the nasolabial folds, the nose, the forehead, the upper lip, and the scalp; 50% of lesions occur on the face and scalp. Occasionally, lesions occur on the neck and the upper part of the trunk.

The gene associated with the familial type of trichoepithelioma links to the short arm of chromosome 9. Because several tumor suppressor genes (i.e. p16, p15 and the gene for the basal cell nevus syndrome) are in this region, the gene for the development of familial trichoepithelioma also encodes for a tumor suppressor. If altered, cellular proliferation may be upregulated because of a poorly functioning or absent tumor suppressor. Due to the 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 trichoepithelioma differentiates toward or derives from hair structures, particularly the hair bulge.

Trichoepithelioma is a benign skin tumor with follicular differentiation, which sometimes is difficult to distinguish clinically and histologically from basal cell carcinoma. One of the most helpful differences is the histological appearance of the stroma. CD34 is an antigen known to stain the spindle-shaped cells located around the middle portion of normal hair follicles. CD34 staining pattern differentiates between trichoepithelioma and basal cell carcinoma. CD34 stain may be helpful in distinguishing between these two tumors on small punch difficult diagnostic cases.

In this case report, the lesion excised from labial vestibular mandible area. In the autosomal dominant form, multiple trichoepitheliomas may be present, usually on the nasolabial folds. In some cases, the distribution is dermatomal. An association may exist with other cutaneous tumors (e.g. cylindroma or BSS, spiradenoma, basal cell carcinoma, ungual fibromas) or dystrophia unguis congenital.

Trichoepithelioma may be a part of the Rombo syndrome (i.e. vermiculate atrophoderma, milia, hypertrichosis, trichoepithelioma, basal cell carcinoma, peripheral vasodilatation). Solitary giant trichoepithelioma presents as a large, polypoid lesion, usually in the lower part of the trunk or in the gluteal area. This is the first case report of trichoepithelioma lesion showing involvement of oral cavity.

Familial cases appear to be related to a mutation in a gene coding a tumor suppressor located on band 9q21. Also, the gene involved in basal cell carcinoma (PTCH, human patched gene located on band 9q22.3) appears to participate in the pathogenesis of TE. BSS patients have a high incidence of multiple skin appendage tumors, such as cylindroma, trichoepithelioma and spiradenoma. These patients may show mutations of the CYLD gene (cylindromatosis gene) that maps to 16q12-q13.9

The Brooke-Spiegler syndrome is a rare, autosomally dominant disease with a predeposition to develop different adnexal tumors. Clinically, it is characterized by the presence of multiple cylindromas, trichoepithelioma and occasionally spiradenomas.

Microscopic features are well-circumscribed dermal tumor; islands, nests and cords of uniform basaloid cells; cells are set in a variably cellular fibrous stroma; epithelial structures resemble hair papillae or abortive hair follicle; small keratocytes (infundibular differentiation) lined by stratified squamous epithelium; retraction of stroma from adjacent dermis; foci of Fig. 2: Gross specimen of trichoepithelioma (TE): Cut surface showing cheesy material

Fig. 3: Cystic spaces containing calcified material and lamilated keratin (HP)
calcification are often present; few mitotic figures and apoptotic bodies. In the reported case multiple horn cysts with laminated keratin, calcification and proliferation of basaloïd cells around are significant findings in excised specimen of oral cavity.

As many as 30% of TEs connect with the overlying epidermis. In the upper dermis, multiple nodules are composed of uniform, basaloïd cells, frequently with central, keratin-filled cysts. Peripheral palisading is present, but artefactual clefting is uncommon. Apoptotic and mitotic figures are not a feature. The stroma is generally fibrous, with little myxoid component. Calcification is common, typically associated with the rupture of the keratinous cysts. A distinctive feature is the papillary-mesenchymal body (fibroblastic aggregate resembling abortive follicular papillae). Papillary mesenchymal bodies were observed in 93% of trichoepitheliomas, 7% keratotic BCC and 0% of all routine BCC.

Papillary mesenchymal bodies are important histological findings useful in differentiation of trichoepitheliomas from basal cell carcinoma. Immunohistochemical studies reveal expression of the cytokeratins associated with the outer root sheath (i.e. cytokeratins 5, 6, 8 and 17) and expression of bel-2, predominantly in the peripheral cell layer of the nests. The intervening stromal cells express CD34. Transforming growth factor beta is expressed in most TEs. Merkel cells can be detected in all TE variants. Some studies have shown that TEs frequently have Merkel cells (detectable with chromogranin or cytokeratin 20). TEs apparently lack expression of androgen receptors, while many basal cell carcinomas are positive.

Histological differentiation between basal cell carcinoma and benign trichoblastic neoplasms, such as trichoepithelioma and trichoblastoma can be difficult on small biopsies. Therefore, several attempts have been made to identify immunohistochemical differences between these entities. Recent studies have shown androgen receptor expression in a number of mature epithelial structures in the skin and in epithelial neoplasm’s including basal cell carcinoma. In contrast, androgen receptor expression was absent in mature hair follicles or the few trichogenic neoplasm’s studied to date. These findings suggested that androgen receptor expression might be a useful adjunct in the histological differential diagnosis between basal cell carcinoma and benign trichoblastic neoplasms. Focal expression of androgen receptor was detected in 78% of basal cell carcinomas. None of the trichoblastic tumors showed any androgen receptor immunoreactivity.

Although extremely rare, some TEs may develop high-grade carcinomas with aggressive behavior (including metastasis). Immature trichoepithelioma typically exhibits no horn cysts, displays fewer primitive hair structures and lacks the adenoidal growth patterns of the tumor lobules which are usually present in the classical trichoepitheliomas.

Desmoplastic trichoepithelioma is a benign neoplasm considered to follicular differentiation. Its sweat gland or sebaceous lines of differentiation have been also reported. Histologically, it shows narrow strands of tumor cells, a desmoplastic stroma and keratinous cysts. Pleomorphism, palisading or peripheral clefting are not seen. Features favoring desmoplastic TE include a rim of compact collagen around groups of epithelial cells, granulomas, calcification of cornified cells within cysts, absence of necrotic neoplastic cells are only rare mitotic figures. Fibroblasts surrounding TE nests do not express the matrix metalloproteinase stromelysin-3 (ST-3), in contrast to basal cell carcinoma.

The solitary giant variant is characterized by deep involvement of the reticular dermis and subcutaneous tissue.

CONCLUSION

Trichoepithelioma is benign adnexal neoplasm (poorly differentiated hamartoma). Commonly located on the head and neck region, solitary-nose, upper lip and cheeks, multiple-central part of the face, trunk, neck and scalp. The interesting features in this case report was its unusual site that is the vestibule of the mouth. Histological importance is the differential diagnosis, basal cell carcinoma, microcystic adnexal carcinoma, trichoadenoma, tumor of follicular infundibulum and basaloïd follicular hamartoma.

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