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Research Paper

Malignant Transformation Within Benign Adnexal Skin Tumour- A Rare Malignant Trichogenic Tumor

Medical Science

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ABSTRACT

Trichoepithelioma is a rare benign skin lesion that originates from hair follicles. Trichoepitheliomas are mostly seen in the scalp, nose, forehead, and upper lip. Trichoepithelioma is histologically similar to basal cell carcinoma and has a rare risk of malignant transformation. In addition, most frequent incidence of this disease in young to elderly women may lead to social and psychological issues. Precise diagnosis and management of this rare disease seem necessary.

We report to you an unusual adnexal tumor on the scalp of a 24-years-old woman with trichoepithelioma. Histologic examination of the tumor showed it to merge with adjacent areas of classic trichoepithelioma. The tumor showed cytologic atypia, mitotic figures, necrosis, deep infiltration, pseudoglandular pattern and areas of squamous differentiation . The differential diagnosis of this malignant follicular neoplasm included malignant trichoepithelioma and basal-cell carcinoma with matrical differentiation. The unique clinicopathologic features, however, raised consideration of a "malignant trichoepithelioma."

Introduction

Trichoepithelioma 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 band 9p21.[1] Other cases are associated with Brooke-Spiegler syndrome caused by mutations of the cylindromatosis oncogene (*CYLD*), which maps to 16q12-q13.[2, 3, 4] A 2006 study has suggested that abnormalities in this gene may result in one of 3 syndromes: Brooke-Spiegler syndrome, familial cylindromatosis, and multiple familial trichoepithelioma.[5]

A 2009 study reports a novel missense mutation in the *CYLD* gene, heterozygous nucleotide G-->A transition at position 2,317 in exon 17, in a Chinese family with multiple familial trichoepithelioma.[6] Additionally, a novel splicing mutation in the*CYLD* gene (IVS12 + 1 G-->A) has been reported in a Taiwanese family with multiple familial trichoepithelioma.[7]

The gene associated with the familial type of trichoepithelioma links to the short arm of chromosome 9. Because several tumor suppressor genes (ie, 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 up-regulated because of a poorly functioning or absent tumor suppressor. Studies have indicated that *CYLD* encodes a deubiquitinating enzyme that negatively regulates the nuclear factor (NF)–kappaB and c-Jun N-terminal kinase (JNK) pathways.[8] 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. Rare instances of tumors resembling trichoepithelioma have been reported in animals.[9]

Familial cases appear to be related to a mutation in a gene encoding a tumor suppressor located on band 9q21. Additionally, the gene involved in basal cell carcinoma (*PTCH,* human patched gene located on band 9q22.3) appears to participate in the pathogenesis of trichoepithelioma.[12]

Brooke-Spiegler syndrome 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 map to 16q12-q13. [13]

Case Details

A twenty-four(24) years old Indian lady presented to our hospital with history of scalp swelling for two years.The swelling was insidious in onset with initial size of about 2 x 2 cm. it was gradually increasing in size. There was rapid increase in size in the last 6 months. History of ulceration over swelling present from 2 weeks. There were no other swellings elsewhere in the body.

On physical examination, she was moderately built and nourished. Vital signs were normal. Local examination revealed a 9 x 8 cm swelling in right parietal region, irregular in shape, with ulcerations over the skin. Surrounding skin was normal. There were no signs of inflammation. It was firm in consistency and did not appear to be fixed to underlying skull. No regional lymph nodes palpable. Other systemic examination was unremarkable.

Laboratory tests were unremarkable. Plain skull X-ray did not reveal involvement of skull. Biopsy of the lesion was suggestive of trichoepithelioma with suspicion of malignancy.

On surgical intervention the growth was found to infiltrate the periosteum. Wide local excision of the tumor was done; along with excision of outer table of skull.

Defect was covered using locally advanced flap and skin grafting.

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Discussion

Skin adnexal tumours (SAT) are a large and diverse group of benign and malignant neoplasms, which exhibit morphological differentiation towards one of the different types of adnexal epithelium present in normal skin: pilosebaceous unit, eccrine and apocrine. SAT may display more than one line of differentiation (hybrid/composite tumours), rendering precise classification of these neoplasms difficult. The diagnosis of these mixed SAT relies on histological evaluation, and they are usually classified according to the predominant morphological component. The histogenesis of mixed adnexal tumours is still uncertain; however, the possibility of origin from a pluripotent stem cells is suggestive.

Most SAT are benign, and local complete surgical excision is curative. However, diagnosing some of these tumours has important implications, as they might be markers for syndromes associated with internal malignancies, such as trichilemmomas in Cowden disease and sebaceous tumours in Muir–Torre syndrome. A malignant counterpart of almost every SAT has been described. These tumours are rare, locally aggressive, and have the potential for nodal involvement and distant metastasis, with a poor clinical outcome. Therefore, establishing a diagnosis of malignancy in SAT is important for therapeutic and prognostic purposes. A vast variety of differential diagnosis has to be kept in consideration while treating such sclap tumours viz

- Basal cell carcinoma
- Microcystic adnexal carcinoma
- Trichoadenoma
- Tumor of follicular infundibulum
- Basaloid follicular hamartoma

To conclude, a very high index of suspicion and a competent pathological support is mandatory and highly beneficial in the diagnosis of this rare scalp tumor entity.

FIGURES

FIGURE 1

FIGURE 2

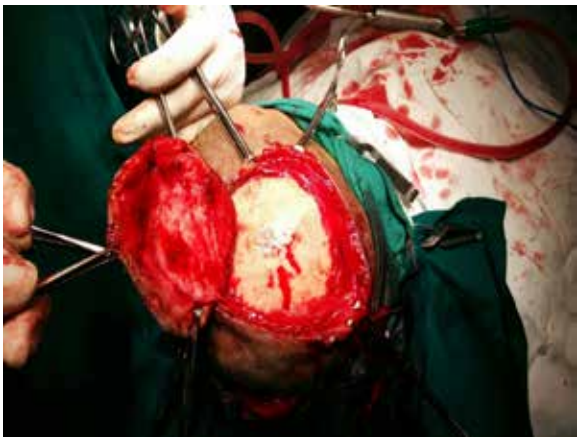

FIGURE 3

FIGURE 4

FIGURE 5

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