

Basaloid follicular hamartoma on the upper eyelid

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Basaloid follicular hamartoma (BFH) is a benign rare neoplasm of the hair follicles whose clinical and histological appearance is very similar to basal cell carcinoma. Although these hamartomas are considered to be benign lesions, malignant differentiations have been reported. It may be generalized or localized, familial or sporadic, and BFH can be accompanied by systemic diseases. Although there are many clinical forms of BFH, they all have the same histopathological features. Basaloid follicular hamartoma is a folliculocentric tumor limited to the superficial dermis. Involvement of the deep reticular dermis or soft tissue is not seen in BFH [1].

We present a 52-year-old man with a solitary, hyperpigmented, asymptomatic, slow growing skin tumor on his left upper eyelid.

A 52-year-old man presented with a slowly developing asymptomatic left upper eyelid lesion (over 4 years). Dermatological examination showed a solitary, smooth surfaced, hyperpigmented nodule measuring 1 cm in diameter (Figure 1), and there were no other similar skin lesions or significant internal diseases exhibited. He had no family history of similar lesions. The lesion was locally excised, and the specimen was grossly measured to be 1.2 × 0.7 × 0.2 cm.

Low-power light microscopy revealed a well-circumscribed and completely removed lesion in the dermis, without connections to the epidermis (Figure 2). Microscopically, the tumor revealed strands and cords of small basaloid cells emanating from the infundibular portion of the hair follicle. The tumor stroma was scant and mildly fibrocellular. There was no nuclear pleomorphism, mitotic activity, apoptotic cells, or cleft formation between the tumor and the stroma (Figure 3), and upon immunohistochemical examination, Bcl-2 stained only in the outermost basal cells (Figure 4). Cd34 was positively stained in the peritumoral stroma and blood vessels (Figure 5), and

CD10 was stained in the peritumoral stroma as well as the matrical cells (Figure 6).

Basaloid follicular hamartoma was first described in 1969 by Brown *et al.* as “generalized hair follicle hamartoma” with associated alopecia, aminoaciduria, and myasthenia gravis [2]. The term “basaloid follicular hamartoma” was first used for a patient who had a localized and solitary type of the lesion, without associated abnormalities, by Mehregan and Baker in 1985 [3]. Morohashi *et al.* described BFH as an abortive growth of secondary hair germs with a limited differentiation toward the upper follicular portion of the hair shaft [4].

Basaloid follicular hamartoma may manifest with different clinical presentations, such as a solitary lesion, or as multiple lesions with a generalized or localized distribution. Basaloid follicular hamartoma may present as individual or linearly distributed, small, skin-colored to brown papules or plaques, or as multiple lesions in a generalized distribution on the face, scalp, and occasionally, the trunk. Basaloid follicular hamartoma may be a familial, congenital, or acquired condition.

Several forms of generalized BFH have been described: (1) sporadic form, multiple BFH without systemic disease; (2) generalized acquired form, female patients with generalized BFHs associated with alopecia and autoimmune diseases, such as myasthenia gravis or systemic lupus erythematosus, in which the lesions are found mainly on the face and periorificial areas; (3) generalized familial form, an autosomal dominant disease that may or may not be associated with hypotrichosis, hypohidrosis, and palmoplantar pitting, which appears on the face and genital region; (4) generalized congenital form, generalized BFH associated with other ectodermal defects, such as hypotrichosis and punctate keratotic pits, on the palms and soles and with cystic fibrosis [1].

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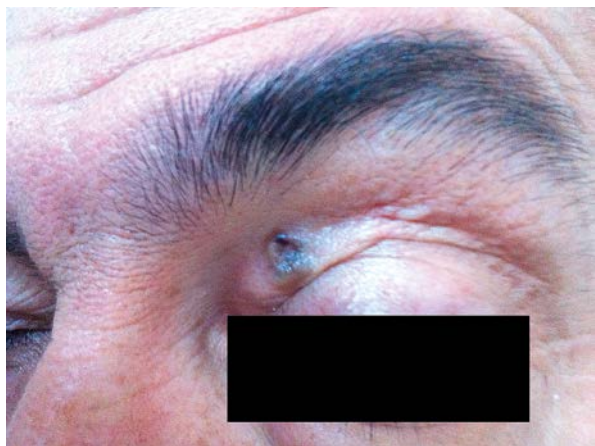


Figure 1. A solitary, smooth surfaced, hyperpigmented 1 cm nodule is located on the left upper eyelid of a 52-year-old man

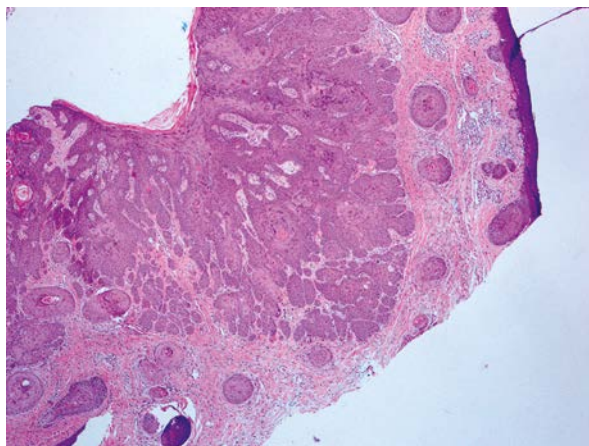


Figure 2. Low-power light microscopy revealed a well-circumscribed and completely removed lesion in the dermis, without connections to the epidermis (hematoxylin-eosin, original magnification at 40×)

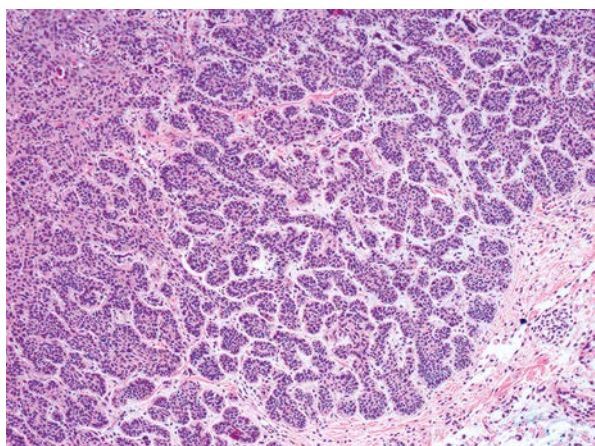


Figure 3. A biopsy specimen with basaloid follicular hamartoma shows strands and cords of small, basaloid cells emanating from the infundibular portion of the hair follicle. The tumor stroma was scant and mildly fibrocellular. There was no nuclear pleomorphism, mitotic activity, apoptotic cells, or cleft formation between the tumor and the stroma (hematoxylin-eosin, 100×)

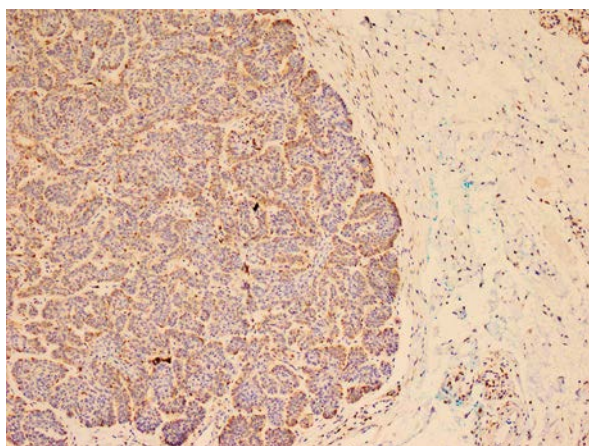


Figure 4. Bcl-2 stains only the outermost basal cells in BFH (Bcl-2, 100×)

The localized forms of BFH present as linear unilateral lesions or as plaques with alopecia [3–6]. The linear unilateral type of BFH is associated with lines of Blaschko and presents at birth or appears in early childhood [3, 5, 6]. Solitary BFH was first described in 1992 as a smooth plaque or a papule appearing most commonly on the face or scalp [7].

The pathogenesis of BFH has been linked to a mutation in the PTCH (patched) gene on chromosome band 9q23. However, this mutation is thought to be less severe than the PTCH gene mutation demonstrated in nevoid basal cell carcinoma syndrome (NBCS) [8–10].

The clinical differential diagnosis for BFH depends on its presentation. The most common misdiagnoses for in-

dividual lesions include basal carcinoma (BCC), intradermal melanocytic nevus, seborrheic keratosis, sebaceous hyperplasia, syringoma, angiofibroma, trichilemmoma, steatocystoma, trichoepithelioma (TE), basal cell hamartoma with follicular differentiation, and hamartoma of the sebaceous follicles. When presenting as a plaque, nevus sebaceous, lupus erythematosus, and sarcoidosis should be considered. Basaloid follicular hamartoma in a linear distribution may mimic linear epidermal nevus, lichen striatus, linear morphea, and basal cell nevus. The differential diagnosis of generalized BFH could include generalized follicular hamartoma syndrome, tuberous sclerosis, Cowden disease, multiple trichoepitheliomas, nevoid basal cell nevus syndrome, Rombo syndrome, and multiple tumors of the follicular infundibulum [11]. Basaloid follicular hamartoma is often misdiagnosed as trichoepithelioma or basal cell carcinoma, histopathologically [1].

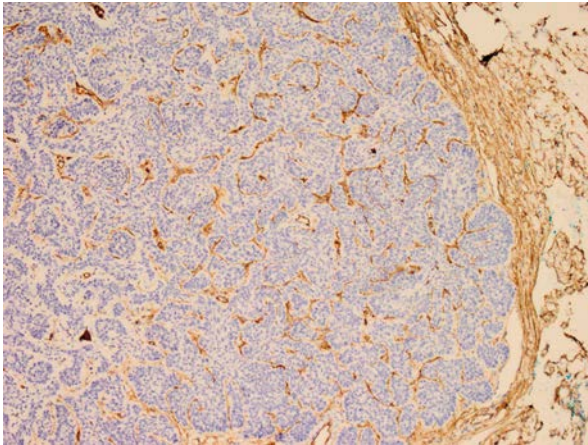


Figure 5. CD34 is positive in the peritumoral stroma and blood vessels (CD34 100×)

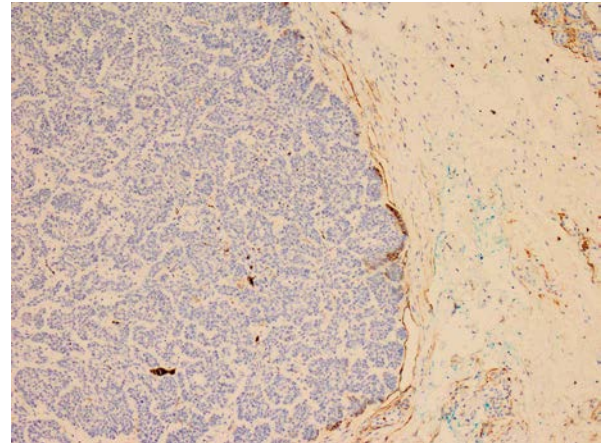


Figure 6. CD10 stains the peritumoral stroma of BFH, as well as the matrical cells (CD10 100×)

Specifically, BFH consists of malformed and distorted hair follicles composed of cords and strands of basaloid cells. These cells are arranged in a radial, anastomosing fashion and may arise from the follicles and/or show an epidermal attachment. The tumor cells are bland, without nuclear pleomorphism, and mitotic activity is rare or absent, with little to no single cell necrosis. While the presence of peripheral palisading has been reported, this feature is typically lacking to the degree seen in BCC. The stroma is scant or absent, and when present, consists of eosinophilic compact collagen with no fibrocytes. Clefts within the fibrous stroma have been reported, and minimal clefting between the tumor and stroma has been observed, but it is not a well-accepted feature of BFH. Mucinous ground substance, if present, is usually subtle; furthermore, BCC displays a variety of histological patterns. The neoplastic cells may involve and destroy pre-existing hair follicles and the interfollicular dermis, and sometimes, infiltrate the deeper dermis, subcutaneous fat, and skeletal muscle [12].

Differentiating BFH from BCC can be the most difficult aspect of the diagnosis, and additional immunohistochemical stains may help to separate BFH from BCC. Ki-67 (a proliferative marker associated with mitosis) and Bcl-2 staining are more prominent in BCC than in BFH. Bcl-2 stains only the outermost basal cells in BFH. CD 34 is an intercellular adhesion protein and cell surface glycoprotein; the ligand is CD62L (L-selectin). It is also called hematopoietic progenitor cell antigen and is a commonly used marker of hematopoietic progenitor cells and endothelial cells. CD34 also stains stromal cells and dendritic cells. In differential diagnosis it is important that the stromal cells of the BFH stain positive for CD34, but the stromal cells of BCC are negative [1, 12]. Although in BCC the stromal and tumor cells stain with CD10, in BFH, the peritumoral stroma and matrical cells stain with CD10 [13].

Histologically, TE has distinct islands of basaloid cells in a lacelike or adenoidal network and, occasionally, as solid aggregates; additionally, they exhibit a more nodular growth pattern than BFH. The tumor islands show peripheral palisading as in BCC; however, the stroma lacks the retraction artifact seen in BCC. In TE, the fibrocystic stroma is more prominent than in BFH, and it predominates over the epithelial portion. Additionally, in TE, normal follicular bulbs and papillae are seen [11]. While both BFH and TE have keratin cysts consisting of a fully keratinized center, surrounded by basophilic cells without high-grade atypia and mitoses, they are more prominent in TE.

We report a case of solitary BFH that developed on the left upper eyelid of a man. Since only a few cases have been reported, presenting case reports will increase awareness of this disorder. Although BFH is a benign rare neoplasm of the hair follicles, it is important to differentiate it due to the malignancy risk and similar characteristics to other benign tumors.

Conflict of interest

The authors declare no conflict of interest.

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