CASE REPORT

Basaloid follicular hamartoma: A case report and review of the literature

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Abstract Basaloid follicular hamartoma (BFH) is a rare, benign, skin adnexal tumor. Several clinical patterns have been reported, but they all share the same histopathological features. BFH may be hereditary or nonhereditary and can be accompanied by systemic diseases. Microscopic examination of BFH shows branching cords and anastomosing strands of basaloid cells in a loose, fibrous stroma. The most important pathological differential diagnosis is infundibulocystic basal cell carcinoma. These two lesions must be differentiated carefully based on clinical presentation and histopathological picture, and even molecular studies may be needed. We present a report of a 78-year-old woman with a solitary, asymptomatic, slow-growing skin tumor on her left scalp. No associated systemic disorders were found. On the basis of an excisional biopsy performed on the tumor, a pathological diagnosis of sporadic BFH was made.

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Introduction

Basaloid follicular hamartoma (BFH) is a malformation of a hair follicle and is restricted to the superficial dermis [1,2]. BFH can be associated with several systemic diseases, such as myasthenia gravis, systemic lupus erythematosus, and alopecia. There is a likelihood that the incidence of BFH may be underestimated because of its benign course and also because the occurrence of BFH is very rare. In this article, we present a case of a solitary BFH on the left scalp in a patient and review the clinical presentation and histopathological differential diagnosis.

Case presentation

A 78-year-old woman had a skin tumor on her left scalp for more than 2 years. The tumor was stable and asymptomatic without itching or tenderness. She presented to the Department of General Surgery at Shin-Kong Wu Ho-Su Memorial Hospital for management in December 2009. Physical examination showed a smooth surfaced,
erythematous papule measuring 0.6 cm in diameter on the temporofrontal area of the left scalp. It was well defined and elastic on palpation. There was no other similar skin lesion. The patient did not have alopecia, ptosis, dysphagia, or diplopia. She had no family history on record for similar lesions. An excisional biopsy of the tumor was done, and the specimen was sent for histopathological examination.

Microscopically, the tumor was characterized by branching cords and anastomosing strands of basaloid cells embedded in a loose, fibrous stroma. The tumor was well demarcated and located in the superficial dermis (Fig. 1). The cords and strands were formed by two to four layers of basaloid cells (Fig. 2). Peripheral palisading was not seen. Horn cysts and abortive hair follicle–like structures were present in the tumor (Fig. 3). No mucinous areas were identified. There were no cleft-like spaces between the stroma and the epithelial strands. The epidermis was atrophic but intact. The tumor was not associated with the hair follicles nor was it connected with the epidermis. The tumor cells were uniform with bland-looking nuclei and eosinophilic cytoplasm. No squamoid cell was identified. Mitoses were absent. Immunohistochemical stains for Ki-67 (Cellular marker for proliferation), Bcl-2 (B-cell lymphoma 2), CD34, and CD10 were performed (Fig. 4). Very few tumor cells showed nuclear positivity for Ki-67, and only the peripheral tumor cells showed weak cytoplasmic positivity for Bcl-2. The stromal cells showed positive staining against CD34. CD10 stained weakly for the stromal cells but not the tumor cells. Based on the histopathological features, immunohistochemical studies, and stable clinical presentation, a diagnosis of a solitary BFH was made.

Discussion

BFH is a unique, benign, skin adnexal tumor. In 1969, this tumor was first reported under the title "generalized hair follicle hamartoma" with associated alopecia, aminoaciduria, and myasthenia gravis [3]. Mehregan and Baker [1] first used the term "basaloid follicular hamartoma" to
report of similar skin tumors in 1985. Since then, only a few cases have been reported. Morohashi et al. [2], based on ultrastructural and immunohistochemical studies, thought that BFH was an abortive growth of secondary hair germs with a limited differentiation toward the upper follicular portion of the hair shaft.

The pathogenesis of BFH is found to be associated with the patched (PTCH: Protein patched homolg) gene mutation on chromosome 9q23. The PTCH gene encodes a receptor involved in the sonic hedgehog-patched-Gli (Products of Glioma-associated oncogene) signal pathway [4]. Mutations in this signal pathway can lead to abnormal growth and patterning of cells.

BFH may manifest in multiple clinical presentations, such as multiple lesions with a generalized or localized distribution, or as a solitary lesion. Several forms of generalized BFH have been described: (1) sporadic form: multiple BFHs without systemic disease [5]; (2) acquired form: female patients with generalized BFHs associated with alopecia and autoimmune diseases, such as myasthenia gravis or systemic lupus erythematosus [6,7]; (3) familial form: an autosomal dominant disease that may or may not be associated with hypotrichosis, hypohidrosis, and palmoplantar pitting [8–10]; and (4) congenital form: generalized BFHs associated with alopecia and cystic fibrosis [11].

The localized forms of BFH present as linear unilateral lesions or as plaques with alopecia [1,2,12,13]. The linear unilateral type of BFH is associated with lines of Blaschko and presents at birth or appears in early childhood [1,12,13].

Solitary BFH was first described in 1992 as a smooth plaque or a papule appearing most commonly on the face or scalp as in our case [5]. The incidence of solitary BFH may be underestimated because solitary BFH is usually asymptomatic and stable.

Although there are many clinical forms of BFH, they all share the same unique histopathological features as previously described in our case. BFH is a folliculocentric tumor limited to superficial dermis. Deep reticular dermis or soft tissue involvement is not typical of this disease. In early lesions, the branching cords of basolaid cells connecting the central pilosebaceous structures can be seen. In longstanding cases, the central pilosebaceous structures may be totally replaced by the tumor [14].

Histopathological differential diagnosis includes (1) trichoepithelioma, (2) fibrofolliculoma, (3) fibroepithelioma of Pinkus, (4) folliculocentric basaloid proliferation, and (5) infundibulocystic basal cell carcinoma (IFBCC).

Trichoepitheliomas are usually larger than BFH. The tumor islands of basolaid cells may have “swiss cheese” or lace-like pattern with no branching tumor strands. The stroma of trichoepithelioma is more cellular than that of BFH [5,15].

Fibrofolliculoma is another type of tumor with epithelial strands embedded in a fibrous stroma. Compared with BFH, fibrofolliculoma has much more prominent stroma and less amount of epithelial strands [5]. In some areas, no epithelial strands can be found [15].

Fibroepithelioma of Pinkus is a variant of basal cell carcinoma (BCC), which is characterized by arborizing cords of basolaid cells from epidermis and may be identical to
BFH microscopically. However, eccrine ducts, which are not seen in BFH, may be present in some epithelial cords of fibroepithelioma of Pinkus. In addition, fibroepithelioma of Pinkus is surrounded by more prominent fibrous stroma [10,15].

Folliculocentric basaloid proliferation occurs in the skin adjacent to a BCC [16]. It is a reactive lesion characterized by folliculocentric, vertically oriented basaloid aggregates with histologically unaltered stroma [16]. Most of the basaloid aggregates are surrounded by a prominent hyaline basement membrane. The folliculocentric basaloid proliferation has no keratin cysts, which is the most notable difference from BFH [16].

The most important histopathological differential diagnosis of BFH is the IFBCC. IFBCC is formed by cords and strands of basaloid cells embedded in a loose, fibrous stroma, as in BFH [15]. Horn cysts can also be found in IFBCC. IFBCC is not a folliculocentric tumor like BFH and may be located in the interfollicular dermis [10]. Pilosebaceous structures are usually destroyed by the tumor cells and, thus, are not seen in IFBCC. Deep infiltration, epidermal ulceration, and clinical rapid growth also imply a diagnosis of IFBCC [10,15]. Immunohistochemical stains using proliferative antibodies, such as Ki-67, and proliferating cell nuclear antigen have a more intense reaction in IFBCC than in BFH [14]. Bcl-2 stains only the outermost tumor cells of BFH but is more prominent in BCC [17]. The stromal cells of the BFH stain positive for CD34, but the stromal cells of BCC are negative. CD10 stains both the stromal and tumor cells of BCC, whereas it stains only weakly in the stromal cells of BFH [17]. At the molecular level, both IFBCC and BFH have abnormal PTCH signaling pathways. However, the degree of aberrant overexpression of PTCH mRNA is higher in IFBCC [14].

The clinical significance of BFH is that it may be mistaken for BCC clinically and histologically, especially the IFBCC subtype. They must be differentiated carefully because BFH may be located in the interfollicular dermis [10]. Folliculocentric, vertically oriented basaloid aggregates with histologically unaltered stroma [16]. Most of the basaloid aggregates are surrounded by a prominent hyaline basement membrane. The folliculocentric basaloid proliferation has no keratin cysts, which is the most notable difference from BFH [16].

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The clinical significance of BFH is that it may be mistaken for BCC clinically and histologically, especially the IFBCC subtype. They must be differentiated carefully because BFH may be a benign tumor, and BCC is malignant. Excisional biopsy is a locally invasive tumor and rarely can metastasize. Moreover, about half of the patients who are diagnosed with BCC may develop new lesions within 5 years [18]. Avoiding sun exposure and regular skin screening are recommended for patients with BCC. On the other hand, BFH is clinically stable and limited in the superficial dermis. Surgical treatment is not usually needed except for cosmetic reasons or to exclude other skin tumors. We present a report of this rare skin tumor to emphasize its unique histopathological picture and benign nature. When multiple BFH lesions are present, clinicians should be aware that they may be associated with systemic diseases. BCC can rarely develop in BFH [19]. Biopsy should be done on rapidly growing lesions or lesions that exhibit a change in clinical appearance [10].

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