Solitary Basaloid Follicular Hamartoma: A Report of Two Cases

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ABSTRACT Basaloid follicular hamartoma (BFH) is rare benign follicular malformation that is often clinically misdiagnosed. Patients with BFH demonstrate a variety of clinical manifestations and associated abnormalities. BFH may be a familial, congenital, or acquired condition with localized or generalized distribution. Several clinical variants of generalized BFH are known, and they can be associated with a diverse spectrum of abnormalities. Herein, we report two cases of solitary BFH in pediatric patients, both documented dermoscopically.

KEY WORDS: basaloid follicular hamartoma, adexal lesion, dermoscopy

INTRODUCTION

Basaloid follicular hamartoma (BFH) is a benign follicular malformation that is often clinically misdiagnosed. Although classified as a relatively rare hamartoma, BFH is probably underreported due to variable clinical presentation that may lead to diagnostic difficulties. BFH may be a congenital, familial, or acquired condition. Several clinical variants of BFH have been described, including the localized (solitary and multiple lesions) and generalized forms, with the latter being mostly associated with systemic syndromes and various diseases such as myasthenia gravis, systemic lupus erythematosus, cystic fibrosis and alopecia (1-7). Herein we report two cases of solitary BFH in pediatric patients.

CASE REPORTS

Case 1

A 16-year-old boy with a history of autism spectrum disorder was admitted to our department for consultation due to a harmless dermal nevus on his face. According to his mother, his past medical and family history was unremarkable. During the total body skin examination, a small slightly pigmented papule was observed on his lower back (Figure 1, A). A dermoscopic examination of the lesion highlighted the presence of blue-gray dots and globules over the brownish background with a linear irregular vessel (Figure 1, B). An excisional biopsy was performed with a presumptive diagnosis of basal cell carcinoma (BCC). A histopathological examination revealed

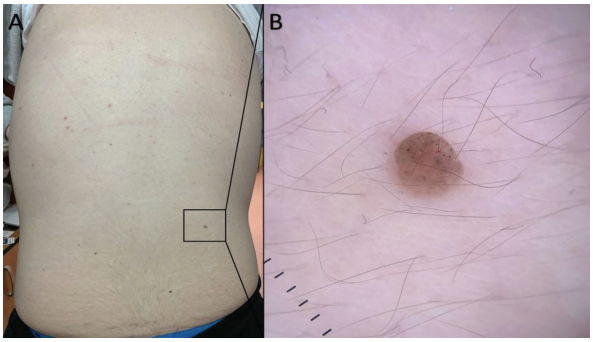

Figure 1. Clinical and dermoscopic features of BFH in a boy. (A) Solitary papule on the right lumbar region. (B) Multiple blow globules and linear vessels observed on dermoscopy.

numerous cords and strands of basaloid cells arranged in a radial and anastomosing pattern over the scant fibrous stroma (Figure 1, A). Basaloid cells showed subtle peripheral palisading without nuclear pleomorphism and mitotic activity and without the presence of cell necrosis (Figure 2, B). Additionally, immunohistochemistry revealed positivity of peripheral basaloid cells for Bcl-2 (Figure 2, C) as well as CD34 and CD10 stromal cells positivity (Figure 2, D, E). Overall, those features were consistent with a diagnosis of BFH.

Case 2

A 6-year-old girl presented with a 10-month history of an asymptomatic, skin-colored papule located on the right nasolabial fold (Figure 3, A) that gradually increased in size over time. During a dermoscopy assessment, linear irregular vessels were observed on the whitish-pinkish background (Figure 3, B). Based on the clinical and dermoscopic features alone, suspicion of skin adnexal neoplasm was considered. An excisional biopsy was performed, and the histopathological examination revealed the presence of cords and strands of bland-looking basaloid cells with a branching and anastomosing pattern in the superficial dermis (Figure 4, A). Immunohistochemical stains for Bcl-2, CD34, and CD10 were obtained, showing Bcl-2 positivity in peripheral neoplastic cells (Figure 4, B) and positive staining for both CD34 and CD10 in stromal cells (Figure 4, C, D). Based on the histopathological and immunohistochemical features, diagnosis of BFH was established.

DISCUSSION

Originally described in 1969 by Browen *et al.*, and later named by Mehregan and Baker in 1985, BFH is a rarely encountered follicular malformation with diverse clinical presentations (8,9). According to genetic studies, the development of BFH involves a mutation in the patched homologue (PTCH) gene located on the chromosome band 9q23, a tumor suppressor gene also implicated in the pathogenesis of basal cell nevus syndrome (BCNS) (10,11). Namely, the PTCH gene product acts as a part of the receptor for the sonic hedgehog (SHH) protein, which has a fundamental role in numerous processes during embryonic development. The PTCH protein forms a receptor complex with a transmembral signaling protein known as SMO (smoothened). In the absence of SHH protein, PTCH receptor prevents the transduction of the downstream signal through the inactivation of SMO. In contrast, when SHH binds to PTCH receptor,

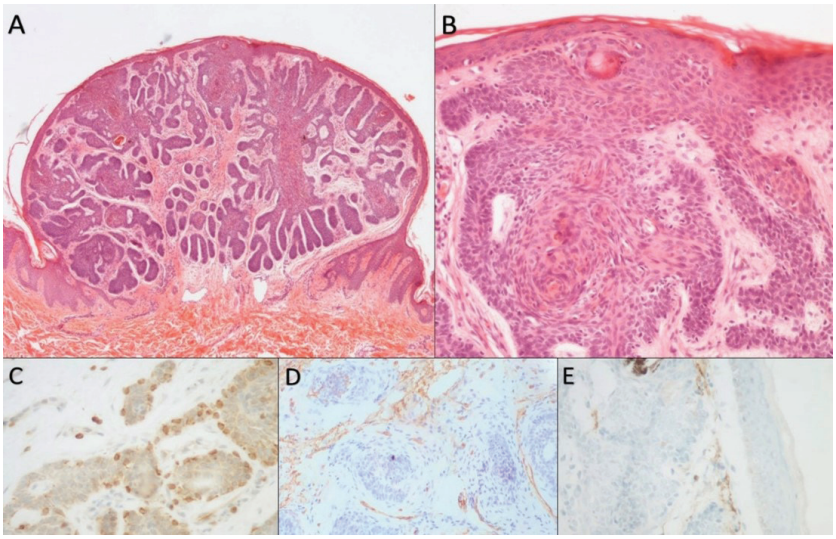

Figure 2. Histopathological and immunohistochemical features of BFH. (A) Cords and strands of basaloid cells arranged in a radial and anastomosing pattern (hematoxylin and eosin ×4). (B) Basaloid cells with subtle peripheral palisading without nuclear pleomorphism and mitotic activity and without the presence of cell necrosis (hematoxylin and eosin ×10). (C) BCL2 positivity in peripheral basaloid cells. (D and E) CD 34 and CD 10 positivity in stromal cells.

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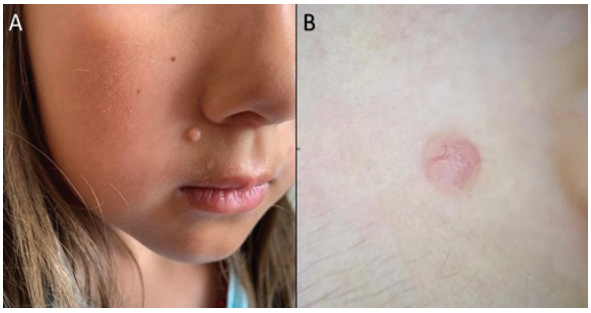

Figure 3. Clinical and dermoscopic features of BFH in a girl. (A) Solitary nonpigmented papule on the right nasolabial fold. (B) Linear irregular vessels over the whitish-pinkish background observed on dermoscopy.

it releases the inhibition of SMO, which in turn leads to the upregulation of hedgehog target genes by transcription factors in the Gli family (10,11). Activation of this signaling pathway may lead to increased cell proliferation, resulting in abnormal growth and lesion formation (3,10,11).

Patients with BFH demonstrate a variety of clinical manifestations and associated abnormalities. BFH may be a familial, congenital, or acquired condition with localized or generalized distribution. In the context of localized disease, BFH may be present as a solitary lesion or display a linear and/or unilateral arrangement of multiple lesions (1-6). Most described cases of localized BFH were situated on the scalp and face, although other locations including the trunk and extremities are also possible. Clinically, lesions usually appear as a skin-colored-to-brown papule, plaque, or patches of alopecia in the case of scalp involvement (1-8). Contrary to localized forms, generalized BFH is commonly associated with a diverse spectrum of abnormalities. Several clinical variants of generalized BFH have been recognized, including the following: a sporadic form of multiple BFHs without a systemic disease; an acquired form associated with alopecia and autoimmune diseases including myasthenia gravis and systemic lupus erythematosus; a familial form with autosomal dominant inheritance without or with associated abnormalities including multiple milia, comedo-like lesions, hypotrichosis, hypohidrosis, and palmar and/or plantar pits (also known as generalized BFH syndrome); and finally a congenital form of multiple BFHs associated with alopecia and cystic fibrosis (3-7). Additionally, BFH may occur in association with genodermatoses such as Bazex-Dupre-Christol syndrome, BCNS, and Happle-Tinschert syndrome (unilateral and segmental BFHs occurring along Blaschko lines) (1-7).

Depending on the clinical presentation alone, a broad list of differential diagnosis should be considered. Dermal melanocytic nevi, BCC, trichoepithelioma, trichilemmoma, sebaceus hyperplasia, seborrheic keratosis, syringoma, acrochordons, and angiofibroma should be ruled out in case of solitary BFH. Linear BFH may be misdiagnosed as linear epidermal nevus, linear lichen striatus, and linear morphea, while generalized BFH may mimic BCNS, tuberous sclerosis, Cowden syndrome, Rombo syndrome, and multiple trichoepitheliomas (1,11).

From the histopathological perspective, BFH is composed of radial and anastomosing cords and

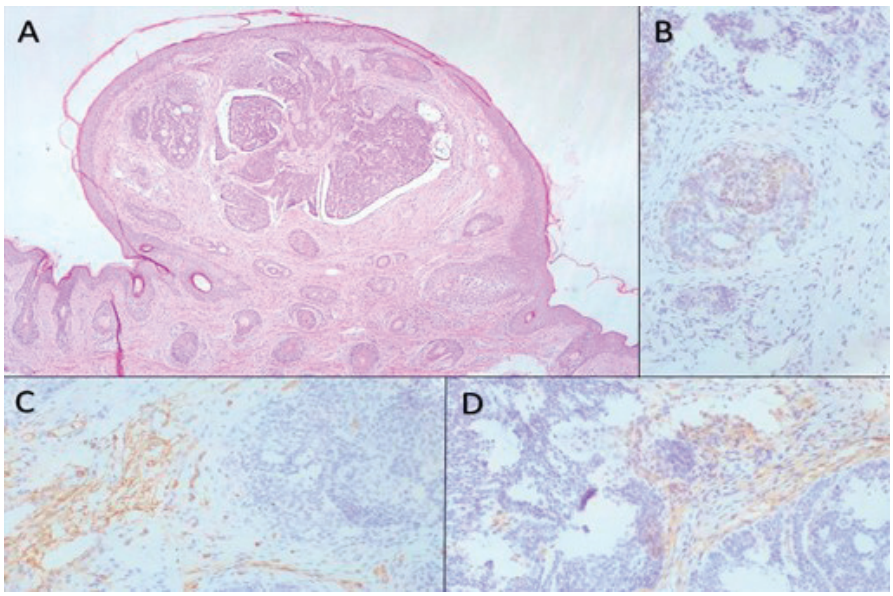

Figure 4. Histopathological and immunohistochemical features of BFH. (A) cords and strands of basaloid cells arranged in a radial and anastomosing pattern with subtle peripheral clefting (hematoxylin and eosin ×4). (B) BCL2 positivity in peripheral basaloid cells. (C and D) CD 34 and CD 10 positivity in stromal cells.

strands of basaloid cells which display an epithelial attachment and/or arise from follicles. The basaloid cells are typified by bland morphology without pleomorphic nuclei and absent or occasional cell necrosis and mitotic activity. If the presence of peripheral palisading is observed, it should be focal and lacking in the degree typically seen in BCC. Other than those observations, keratin cysts may be observed inside basaloid cords. BFH lesions are superficial and only appear where normal hair follicles are present. Therefore, the interfollicular and deeper reticular dermis are not affected. Surrounding stroma is scant and consists of eosinophilic compact collagen and a small number of fibrocytes. While minimal retraction clefts between neoplastic tissue and stroma is occasionally reported in BFH, this feature is typical for BCC or trichoepithelioma. As for immunohistochemistry, BFH has a low proliferative rate, which can be demonstrated with Ki-67 expression in a small number of cells. Bcl-2 positivity may be observed in the outermost basaloid cells of BFH, while CD34 and CD10 are both expressed within stromal cells (11,12).

Histopathologically, lesions that should be differentiated from BFH include BCC, trichoepithelioma, and folliculocentric basaloid proliferation. The differential diagnosis between BFH and BCC may be challenging given the overlapping features of cords and stands of basaloid cells in both lesions. However, basaloid cells in BCC present increased mitotic activity, single cell necrosis, as well as pronounced palisading and clefting. Furthermore, the neoplastic basaloid nests of BCC tend to involve the interfollicular dermis and destroy pre-existing hair follicles. BCC has been reported to display a higher Ki67 mitotic index, prominent Bcl-2 staining, and a lack of expression of CD34 in stromal cells. Abundant stroma with numerous fibrocytes, prominent keratin cyst formation, and the presence of papillary mesenchymal bodies in trichoepithelioma allow a straightforward differentiation from BFH. A folliculocentric basaloid proliferation is a reactive proliferation of mantle epithelium that occurs in the skin adjacent to BCC. Histopathological features that favor the diagnosis of folliculocentric basaloid proliferation over BFH include: a vertically oriented basaloid proliferation with a surrounding prominent basement membrane and absence of both keratin cysts and direct epidermal attachment (11-12).

Although the histopathological findings are consistent in all clinical variants of BFH, the dermoscopic appearance of this rare hamartoma is quite variable (13-18). Namely, reports on the dermoscopic features of BFH are scarce and limited to a few case reports. Mauleon *et al.* were the first ones to report dermoscopy of BFH which displayed an unspecific structureless blue pattern (1). Other reported dermoscopic features of BFH include a structureless brown pattern (15), a papillomatous and cobblestone pattern with brown-black globules, dots and comedo-like openings, and blue-gray and brown globules over a pinkish background with linear irregular vessels (13,18). Recently, Besagni *et al.* reported the cases three pediatric patients with BCNS with multiple BCCs and BFHs, presenting dermoscopic features of blue-gray globules and nests within both types of lesions and typical arborizing vessels in BCCs (18). They highlighted the vascular pattern as a possible dermoscopic clue when differentiating between those lesions (18). However, this vascular pattern was present in both of our cases and could thus support that observation.

CONCLUSION

We reported two cases of solitary BFH in pediatric patients, the incidence of which is probably higher than what is reported in the current literature, given the overlapping clinical, histological, and dermoscopic features of other benign and malignant lesions, particularly BCC. BFH should be considered in the differential diagnosis of solitary lesions in the pediatric population.

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