

# Hereditary Basaloid Follicular Hamartoma Syndrome

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## GOAL

To understand basaloid follicular hamartoma syndrome (BFHS) to better manage patients with the condition

## OBJECTIVES

Upon completion of this activity, dermatologists and general practitioners should be able to:

1. Recognize the clinical presentation of BFHS.
2. Discuss the differential diagnosis of BFHS.
3. Explain the treatment options for BFHS.

**CME** Test on page 36.

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*Basaloid follicular hamartoma syndrome (BFHS) is a rare adnexal tumor genodermatosis. We present a case of hereditary BFHS and review the literature*

*concerning the clinical and histologic features of this entity.*

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**B**asaloid follicular hamartoma (BFH) is a benign adnexal tumor consisting of basaloid cells with follicular differentiation. BFH can occur as a solitary lesion, multiple lesions, or an autosomal dominant inherited syndrome—BFH syndrome (BFHS).<sup>1</sup> In patients with BFHS, adnexal tumors predominantly occur on the head, neck, and torso.



**Figure 1.** A patient with basaloid follicular hamartomas in a perioral distribution.

The syndrome often has coexisting hypotrichosis, hypohidrosis, and palmar/plantar pitting.<sup>1</sup> A familial presentation of BFHS with palmar pitting is discussed with a review of BFHS, including the differential diagnosis of palmar pitting.

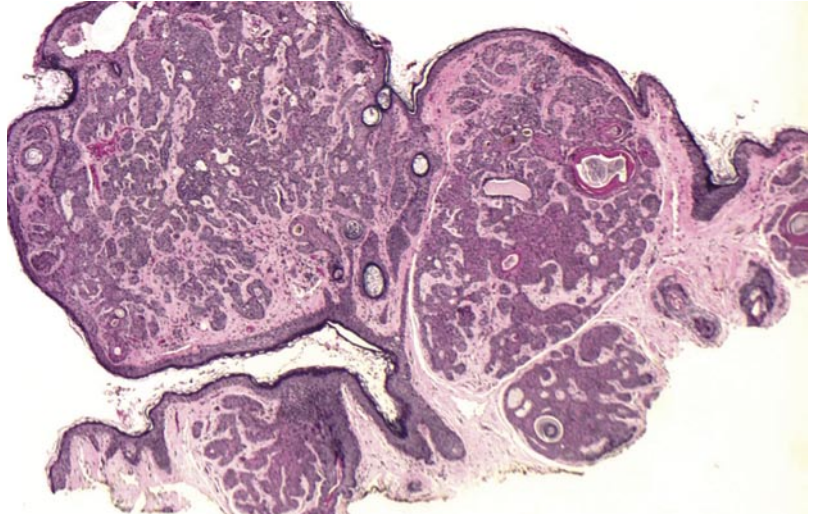
### Case Reports

A 67-year-old white woman presented to dermatology with a 20-year history of several lesions on her face that started as flesh-colored papules and progressively darkened. Most lesions were 3 to 6 mm and located symmetrically around the nose, mouth, chin, and eyes. The woman presented with her 39-year-old daughter, who had a 2-year history of similar lesions around her eyes, none in a perioral distribution. The women reported that when the mother's lesions first appeared, they had the same appearance as the daughter's lesions. The persistent lesions were otherwise asymptomatic. Review of systems for both the mother and daughter were negative for other cutaneous lesions and for systemic symptoms such as fever; weight loss; and cardiovascular, respiratory, gastrointestinal, and genitourinary symptoms. The mother's medical history was significant for hypertension, diabetes mellitus, hypothyroidism, and hypercholesterolemia. The daughter's medical history was significant only for diabetes mellitus.

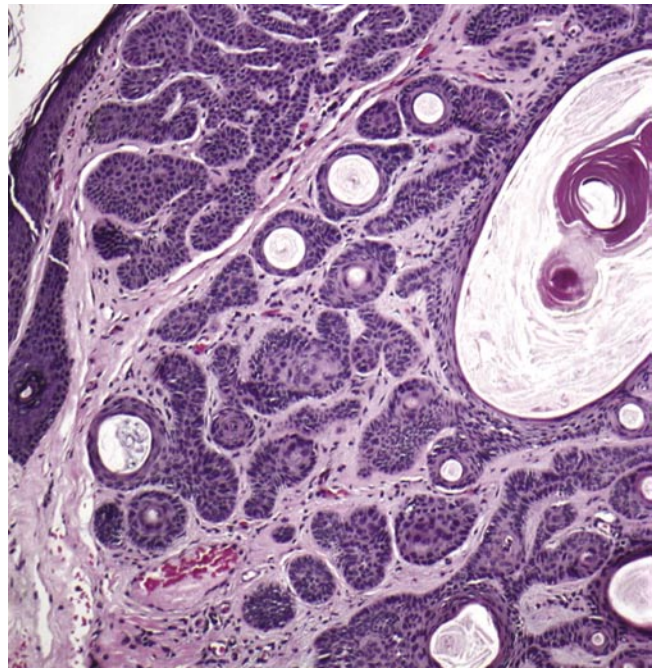


**Figure 2.** Palmar pits in the patient shown in Figure 1.

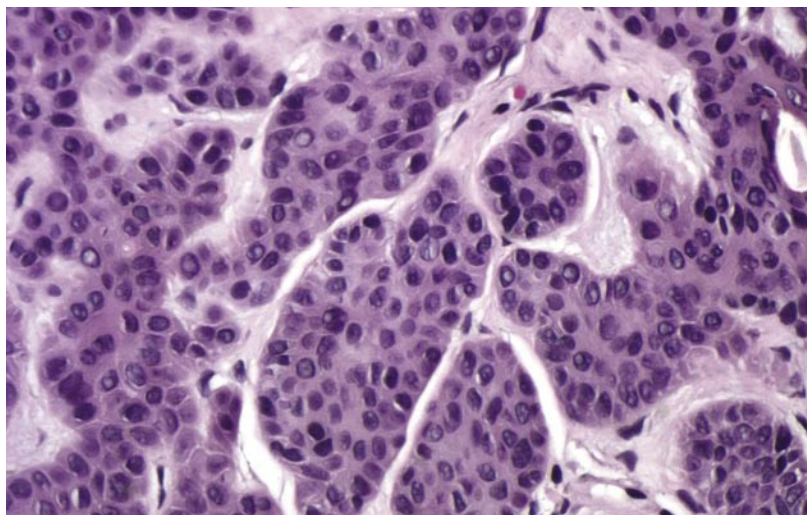
Results of a physical examination of the mother revealed hundreds of soft flesh-colored to hyperpigmented papules, most less than 6 mm in diameter. The papules coalesced in the perioral distribution (Figure 1). Results of a physical examination of the daughter revealed similar symmetric distribution of



**Figure 3.** A polypoid circumscribed lesion composed of anastomosing cords of basaloid cells with follicular differentiation (H&E, original magnification  $\times 4$ ).



**Figure 4.** Bland-appearing basaloid cells arranged in anastomosing and branching cords surrounded by a loose fibrous stroma. A few horn cysts appear among the basaloid cells (H&E, original magnification  $\times 10$ ).



**Figure 5.** No cellular atypia, atypical mitosis, or apoptotic figures are noted (H&E, original magnification  $\times 20$ ).

small (most 1–2 mm but all <6 mm in diameter) flesh-colored papules in bilateral nasolabial and periorbital areas. Symmetric palmar pitting was present in both women (Figure 2). The patients had no other clinical manifestations such as frontoparietal bossing, high arched palates, jaw cysts, short fourth metacarpals, ocular hypertelorism, or narrow sloping shoulders to suggest nevoid basal cell carcinoma syndrome (NBCCS). Histopathology results of both the mother and daughter revealed adnexal proliferation with follicular differentiation consistent with BFH (Figures 3–5).

### Comment

BFH is a rare benign adnexal tumor that exhibits protean clinical manifestations. Despite the polymorphic clinical presentations, lesions exhibit similar histologic appearance, with only small variations.<sup>1,2</sup> Lesions exist in both solitary and multiple forms.<sup>1,4</sup> Multiple forms generally exhibit autosomal dominant inheritance, while solitary forms usually are not inherited.<sup>3</sup> The solitary noninherited forms are more common than the multiple autosomal dominant inherited forms.<sup>3,5</sup>

Most reported solitary cases of BFH are in women, aged 20 to 88 years (median, 66 years; mean, 63 years).<sup>3</sup> Patients with multiple familial disease may exhibit associated systemic diseases, though systemic disease is less likely in patients with solitary lesions.<sup>2,3</sup> Systemic diseases that may be associated with BFHS include hypertension, cardiovascular disease, renal disease, obesity, carpal tunnel syndrome, and cancer of the breast and stomach.<sup>6</sup> Generalized lesions also have been associated with cystic fibrosis,<sup>7</sup> systemic lupus erythematosus,<sup>8</sup> and myasthenia gravis.<sup>9</sup>

BFHS lesions have a predilection for the face and scalp but also have been reported on the neck, axillae, shoulders, and pubic regions.<sup>4</sup> Wheeler et al<sup>6</sup> examined 18 members in one family and found that dominantly-inherited generalized BFHS exhibits variability of disease. The patients exhibited lesions that ranged from hundreds of pigmented papules with associated hypotrichosis and palmar/plantar pitting to minimal facial papules and a few milia involving only the face.<sup>6</sup> Most papules are 1 to 2 mm.<sup>3</sup> In mild forms, the lesions may go unnoticed or may be mistaken as normal.<sup>6</sup> Lesions also may be present at birth or may develop in early childhood.<sup>6,10-12</sup>

Findings on physical examination most commonly associated with BFHS include milialike papules, comedonal-like papules, hypotrichosis, hypohidrosis, and palmar/plantar pitting (Table).<sup>6</sup> Less common associated findings include atopic dermatitis, keratosis pilaris, lichen striatus, acrochordons, acanthosis

## Differential Diagnosis of Palmar Pitting

- Arsenical keratosis
- Basaloid follicular hamartoma syndrome
- Cowden disease
- Darier disease
- Keratosis punctata of palmar creases
- Nevoid basal cell carcinoma syndrome
- Pachyonychia congenital
- Palmoplantar warts
- Pitted keratolysis
- Porokeratosis punctata palmaris et plantaris
- Punctate palmoplantar keratoderma
- Reticulate acropigmentation of Kitamura

nigricans–like changes, dermatosis papulosa nigra, acne vulgaris, café au lait spots, punctate palmar keratosis, and steatocystoma multiplex.<sup>6</sup>

The differential diagnoses of multiple facial papules include angiofibromas (tuberous sclerosis), multiple trichilemmomas (Cowden disease), multiple trichoepitheliomas, multiple syringomas, steatocystoma multiplex, seborrheic keratosis, melanocytic nevi, sebaceous hyperplasia, and NBCCS or Gorlin syndrome.<sup>3</sup> NBCCS is believed to be caused by a lack of human homologue patched (PTCH) tumor suppressor gene function, whereas BFHS is reported to be caused by a decrease in PTCH function.<sup>13</sup> Girardi et al<sup>10</sup> suggested that familial BFHS possibly is a forme fruste of NBCCS (ie, since both entities involve the PTCH gene protein product or some member of its pathway).

Histologically, branching cords and thin strands of undifferentiated and anastomosing basaloid proliferations, which are surrounded by a loosely fibroblastic stroma, identify BFH.<sup>1</sup> This histologic pattern may be found in a wide spectrum of clinically nevoid presentations, and individual lesions may be indistinguishable from infundibulocystic basal cell carcinoma (BCC). Occasional peripheral pallisading, papillary mesenchymal bodies, and connections to the epidermis also have been described.<sup>1</sup>

BFH is categorized within the spectrum of basaloid epithelial neoplasms associated with dysregulation

of the PTCH signaling pathway.<sup>13</sup> However, in general, BFH lesions show less mitotic figures and necrosis when compared with BCC.<sup>6,13</sup> Immunohistochemistry results show CD34<sup>+</sup> stromal cells in peritumoral distribution, resembling trichoepithelioma and distinguishing the condition from BCC, which lacks CD34 expression.<sup>14</sup> Additional factors that distinguish BFH from BCC include BFH's low proliferative index (ie, low Ki-67) and lack of bcl-2 expression.<sup>13,14</sup>

BFHS is a rare entity. It is a mainly histologic diagnosis with varied clinical presentations.<sup>6</sup> Prognosis is good and treatment usually is cosmetic with shave, curette, or scissor methods most frequently reported.<sup>3</sup> Because of the benign nature of this follicular tumor, observation without treatment is an option. It is important to be able to recognize this disease to avoid overaggressive surgical management and to closely monitor for any new tumors that may develop in these lesions.<sup>1</sup> Monitoring and close follow-up of these lesions is necessary because some believe that familial BFHS is possibly a forme fruste of NBS. Any indications of malignant changes in these lesions (eg, nonhealing and bleeding lesions, biopsy suggestive of BCC or other skin cancer) warrant surgical therapy. If lesions do not indicate malignant change, however, they may be removed for cosmetic reasons, but aggressive surgery, such as Mohs micrographic surgery, may put the patient at risk for unnecessary infection and increased morbidity.<sup>1</sup>

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