Letter to the Editor

Dear *Cutis*®:

I propose that Lee et al, the authors of "Hereditary Basaloid Follicular Hamartoma Syndrome" (*Cutis*. 2006;78:42-46), reconsider their diagnosis in favor of nevoid basal cell carcinoma syndrome (NBCS), especially in the context of their own statement to the effect that "familial BFHS [basaloid follicular hamartoma syndrome] possibly is a forme fruste of NBCS." The countless brown papules on the face in Figure 1, the palmar pits in Figure 2, and the histopathologic findings stereotypical of infundibulocystic basal cell carcinoma (BCC) in Figure 3 surely compute to a diagnosis of a syndrome but one that in the skin consists of BCCs rather than basaloid follicular hamartomas. In brief, the captions originally published with the figures do not convey that every patient with innumerable infundibulocystic BCCs has NBCS.[1]

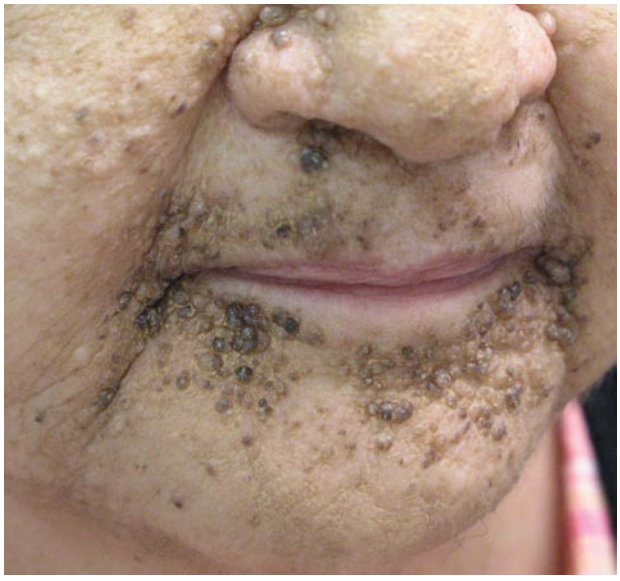

Figure 1. A patient with basaloid follicular hamartomas in a perioral distribution. Reprinted with permission from *Cutis.* 2006;78:42-46. ©2006, Quadrant HealthCom, Inc.

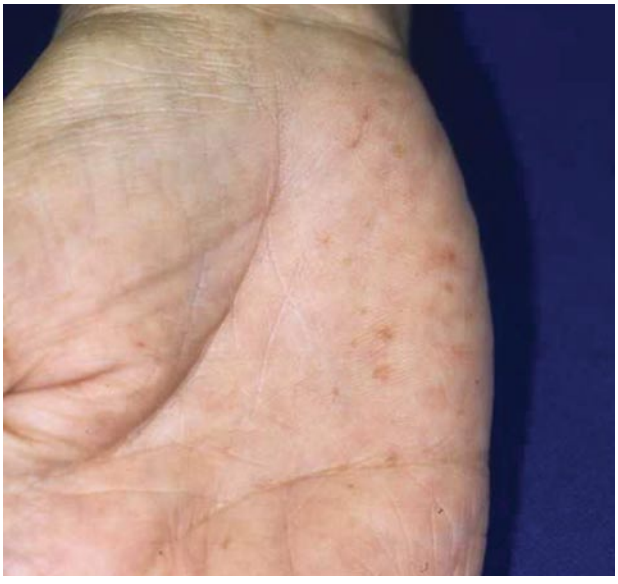

Figure 2. Palmar pits in the patient shown in Figure 1. Reprinted with permission from *Cutis.* 2006;78:42-46. ©2006, Quadrant HealthCom, Inc.

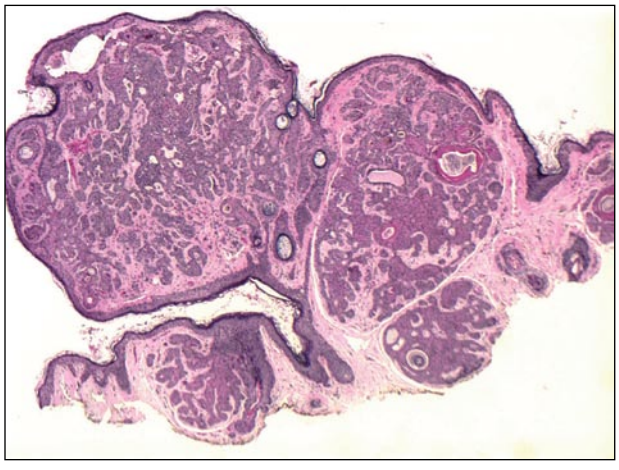

Figure 3. A polypoid circumscribed lesion composed of anastomosing cords of basaloid cells with follicular differentiation (H&E, original magnification ×4). Reprinted with permission from *Cutis.* 2006;78:42-46. ©2006, Quadrant HealthCom, Inc.

Sincerely,
A. Bernard Ackerman, MD
New York, New York

The author reports no conflict of interest.

REFERENCE

1. Ackerman AB, Reddy VB, Soyer HP. *Neoplasms With Follicular Differentiation*. 2nd ed. New York, NY: Ardor Scribendi; 2001.

Author Response

We appreciate Dr. Ackerman's comments, and with his recent letter to the editor concerning academic dermatology,[1] we will engage in an "interplay of ideas" consisting of both dermatopathologic and clinical perspectives on why the syndrome aspects of basaloid follicular hamartomas (BFHs), infundibulocystic basal cell carcinomas (BCCs), and BCCs are not the same entities.

Dermatopathologically, one is always tempted to classify BFHs as BCCs. However, as pointed out in most of the standard dermatopathology texts, BFH is composed of folliculocentric strands and cords of blue cells that do not possess a high grade of nuclear pleomorphism, and usually does not possess the strikingly fibrous stroma of BCCs that is focally myxoid.[2] In addition, with BFH one does not observe numerous mitotic and apoptotic figures as seen in BCCs. Also, molecular studies suggest that the human homologue patched (PTCH) signaling pathway might be altered in BFH; however, the level of dysregulation is lower than in patients with nevoid BCC syndrome (NBCS).[3]

Clinically, hereditary or generalized BFH syndrome (BFHS), multiple hereditary infundibulocystic BCCs (MHIBCCs), and NBCS can be distinguished based on several varying characteristics (Table).

In our article, to give a balanced review of the literature, we did mention that some authors believe

Syndrome Review

	Basaloid Follicular Hamartoma Syndrome[4-6]	Multiple Hereditary Infundibulocystic Basal Cell Carcinoma[5,7]	Nevoid Basal Cell Carcinoma Syndrome[5,6,8]
Inheritance	AD	AD	AD
Gene	Decreased PTCH signaling pathway	Normal PTCH signaling pathway	Lack of PTCH signaling pathway
Skin morphology	Papules	Papules	Papules, plaques, nodules
Basal cell carcinoma–like appearance	No	Yes	Yes
Aggressive nature	No	No	Yes
Distribution favors head and neck	Yes	Yes	No
Palmar pitting	Yes	No	Yes
Bone disease	No	No	Yes
Ocular disease	No	No	Yes
Systemic diseases	Yes (autoimmunity)	No	No
Systemic neoplasia	No significant association (breast and stomach CA, chondrosarcoma reported)	No significant association	Significant association (medulloblastoma, fibromas)

*AD indicates autosomal dominant; PTCH, human homologue patched; CA, cancer.

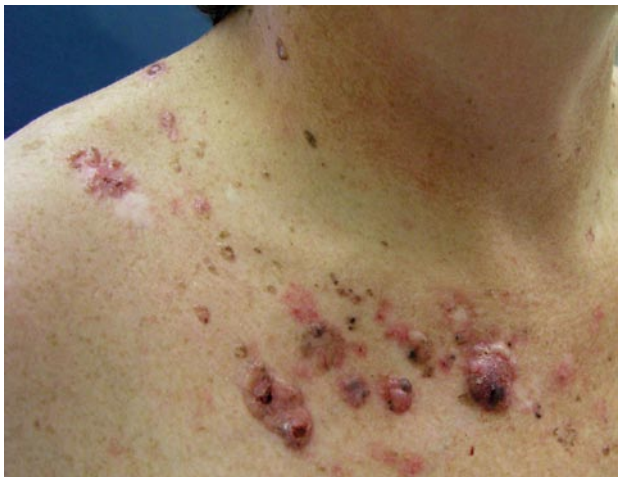

Figure 4. Typical lesions of nevoid basal cell carcinoma syndrome.

these syndromes are the same. Some patients with NBCS have been reported to have BFH intermixed among BCCs.[9] However, side-by-side comparisons do not support this premonition.[4-8] BFHS acts and looks different than MHIBCC and NBCS (Figures 1 and 4). In fact, MHIBCC also is different from NBCS.[5,7] Furthermore, medulloblastomas, rare tumors associated with NBCS, have not been reported in BFHS or MHIBCC.[8] Finally, BFHS lesions are benign and do not require extensive surgical procedures as is routine for patients with NBCS.[4]

Although, in general, dermatology and dermatopathology would benefit from reevaluation and consolidation of some entities, we feel that hamartomas such as BFH should not be classified with malignant neoplasms such as BCC; rather, if consolidation would need to be performed, one should classify all of the hair follicle–derived hamartomas together. In conclusion, to say the patient we presented had NBCS is incorrect, even withstanding dermatopathologic controversies. We do agree with Crawford and Kobayashi[5] in that these syndromes may share characteristics of abnormalities in the same signaling pathway but with resultant variations in extent and severity of each.

Sincerely,
Drazen M. Jukic, MD
Joseph C. English III, MD
Pittsburgh, Pennsylvania

The authors report no conflict of interest.

REFERENCES

1. Ackerman AB. Academic? [letter]. *J Am Acad Dermatol*. 2006;55:542.
2. Brownstein MH. Basaloid follicular hamartoma: solitary and multiple types. *J Am Acad Dermatol*. 1992;27(2 pt 1):237-240.
3. Jih OM, Shapiro M, James WD, et al. Familial basaloid follicular hamartoma: lesional characterization and review of the literature. *Am J Dermatopathol*. 2003;25:130-137.
4. Lee PL, Lourduraj LT, Palko MJ III, et al. Hereditary basaloid follicular hamartoma syndrome. *Cutis*. 2006;78:42-46.
5. Crawford KM, Kobayashi T. Nevoid basal cell carcinoma syndrome or multiple hereditary infundibulocystic basal cell syndrome. *J Am Acad Dermatol*. 2004;51:989-995.
6. Lee DA, Grossman ME, Schneiderman P, et al. Genetics of skin appendage neoplasms and related syndromes. *J Med Genet*. 2005;42:811-819.
7. Requena L, Farina MC, Robledo M, et al. Multiple hereditary infundibulocystic basal cell carcinomas: a genodermatosis different from nevoid basal cell carcinoma syndrome. *Arch Dermatol*. 1999;135:1227-1235.
8. James WD, Berger TG, Elston DM. Epidermal nevi, neoplasms and cysts. In: James WD, Berger TG, Elston DM, eds. *Andrews' Diseases of the Skin: Clinical Dermatology*. 10th ed. Canada: Saunders Elsevier; 2006:633-684.
9. Oseroff AR, Shih S, Frawley NP, et al. Treatment of diffuse basal cell carcinomas and basaloid follicular hamartoma in nevoid basal cell carcinoma syndrome by wide-area 5 aminolevulinic acid photodynamic therapy. *Arch Dermatol*. 2005;141:60-67.