Folliculosebaceous Cystic Hamartoma With Spindle Cell Lipoma-Like Stromal Features

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Abstract: Folliculosebaceous cystic hamartoma is a distinctive cutaneous hamartoma composed of follicular, sebaceous, and mesenchymal components. The lesions are most commonly found on the face and scalp of young adults, with approximately 30% occurring in the nasal or paranasal regions of the face. The clinical differential diagnoses are extensive and include epidermoid cyst, dermal nevus, soft fibroma, and adnexal tumors including sebaceous neoplasms. Here, the authors present a case of a 24-year-old man who presented for evaluation of an asymptomatic growth on the nose, which had slowly enlarged over 9 years. On examination, there was a 0.6 cm dome-shaped flesh-colored papule on the nasal bridge. The clinical differential included dermatofibroma versus intradermal nevus. A shave biopsy was performed, and histological examination of the sections showed a proliferation of multiple enlarged and irregular-appearing sebaceous glands attached to a cystic follicular structure. The associated dermal mesenchymal component consisted of numerous mature-appearing adipocytes associated with a fibromyxoid stroma, prominent collections of mucin, and bundles of ropey collagen resembling a spindle cell lipoma. This combination of a folliculosebaceous cystic hamartoma with a spindle cell lipoma-like mesenchymal proliferation is unusual and has not been previously reported.

Key Words: folliculosebaceous cystic hamartoma, spindle cell lipoma, stroma, sebaceous trichofolliculoma, CD34, nestin

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INTRODUCTION

Folliculosebaceous cystic hamartoma (FSCH) classically consists of a central infundibular cyst with radiating sebaceous structures and a variable surrounding mesenchymal component.[1] The lesions often present as an asymptomatic flesh-colored papule most commonly found on the scalp and nasal region of the face of young adults. Reported locations of the lesion also include the groin and trunk, rarely including the extremities. With the exception of rare reported cases of giant FSCH lesions, most are small in size and rarely progress to greater than 2.0 cm.[1,2] FSCH is rarely diagnosed clinically because of its indistinct clinical features. Thus, the clinical differential diagnoses are often extensive, and the final diagnosis is made through review of pathology. There are multiple pathological variants of FSCH, with neural, vascular, and melanocytic components have been reported. We believe this case to represent a unique variant of FSCH with spindle cell lipoma-like features, which has yet to be reported.

REPORT OF A CASE

A 24-year-old man was seen for evaluation of an asymptomatic growth on his nose, which had reportedly slowly enlarged over 9 years. On examination, there was a 0.6 cm dome-shaped flesh-colored papule on his nasal bridge (Fig. 1). The clinical differential diagnosis included dermatofibroma versus intradermal nevus, and a shave biopsy was performed. Histological examination showed a proliferation of multiple enlarged and irregular-appearing sebaceous glands attached to several cystically dilated follicular structures, findings consistent with a FSCH (Figs. 2A, B). The associated dermal mesenchymal component consisted of numerous mature-appearing adipocytes associated with a fibromyxoid stroma, $CD34^+$ spindle cells, and bundles of ropey collagen, findings mimicking a spindle cell lipoma (Figs. 2C, D). The stromal spindle cells surrounding the adipocytes and sebaceous structures were found to be nestin positive (Fig. 2E).

DISCUSSION

Clinically, FSCH often presents as a single asymptomatic, skin-colored, exophytic nodule with a rubbery to firm consistency.[1,3] It rarely presents as a red nodule or dome-shaped tumor commonly seen in hamartomas.[1] In the largest study of FSCH by Ansai et al,[1] 153 cases were reviewed, revealing that lesions are most frequently found on the face and scalp and rarely exceed 2.0 cm in size. Those exceeding the average size upwards of 2.0 cm were found in unusual locations, including the forearm, sacral area, and scrotum.[1,2,4,5] Although once thought to be an extremely rare clinical finding most commonly found in Eastern Asian populations, recent studies suggest a higher frequency that also extends to European populations. The indistinct clinical presentation of FSCH is similar to that of many other lesions in the differential diagnosis, including epidermal cysts, melanocytic nevi, soft fibromas, sebaceous hyperplasia, basal cell carcinoma, or benign soft-tissue neoplasms.[1,3]

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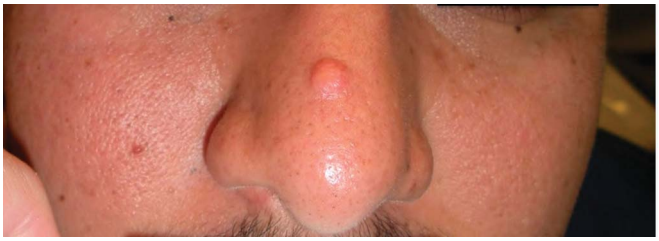

FIGURE 1. Clinical presentation consists of a 0.6 cm dome-shaped flesh-colored papule on the nasal bridge.

Classic histopathologic characteristics of FSCH lesions include follicular, sebaceous, and mesenchymal elements, often presenting as sebaceous structures arising from a central infundibular cyst confined to the dermis.[3] Mesenchymal changes, represented by fibrillary bundles of collagen with proliferating adipocytes and increased number of capillaries and small venules, are commonly found throughout the stroma.[3,6] Clefts between the epithelial component and the adjacent dermis are present.[3] Immature adipocytes with spindle- or starry-shaped nuclei and lipid droplets have been seen in the stroma of lesions, often neighboring the sebaceous structures.[6] These histopathologic findings of FSCH have remained essentially unchanged since its initial description by Kimura et al in 1991.[7]

Multiple histopathologic differential diagnoses for our present lesion could be considered, including fibrofolliculoma, nevus lipomatosus cutaneous superficialis with folliculosebaceous cystic hamartoma features, FSCH with a neural component, and FSCH with perifollicular mucinosis. Although fibrofolliculoma may show a cystically dilated follicular structure, it often contains keratinous material, and there are multiple thin epithelial cords, lacking the fully developed sebocytes and mucinous stroma of our lesion.[8] Unlike FSCH, nevus lipomatosus cutaneous superficialis lesions are composed entirely of mature fat cells, and lack spindled cells and ropey collagen, as well as epithelial structures.[9] FSCH with a neural component should show evidence of neural differentiation and most likely present with nerve

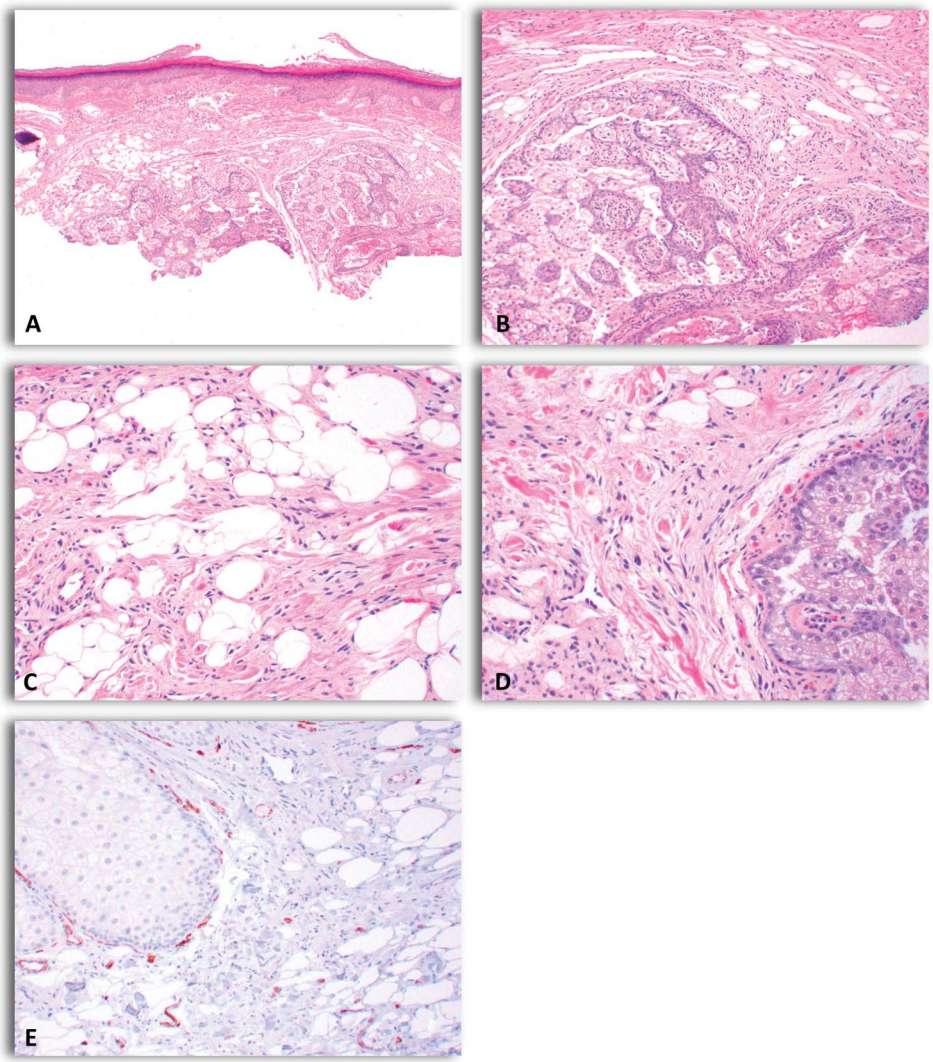

FIGURE 2. Histopathology: A and B, Proliferation of enlarged irregular sebaceous glands. C and D, Mature adipocytes, bland spindle cells, and bundles of ropey collagen mimicking spindle cell lipoma, E, Nestin-positive stromal spindle cells surrounding adipocytes and sebaceous structures.

bundles underlying the tumor.[10,11] In addition, both FSCH with a neural component and FSCH with perifollicular mucinosis lack the adipocytes, ropey collagen, and spindled cells found in the myxoid stroma that are present in our lesion.[10–12]

Two immunohistochemical studies have examined the histogenesis of FSCH. Using antibodies directed against p63, CD10, CD34, Factor XIIIa, androgen, and alpha-estrogen receptor, Suarez-Peñaranda et al[3] reported that the immunohistochemical profile of the epithelial component of FSCH closely resembled that of normal sebaceous glands. Expression of p63 has been found in sebaceous carcinomas but is absent in normal mature sebocytes, suggesting its use as a diagnostic marker for epidermal or adnexal tumors in the skin.[3] The strength of p63 staining was highest in the basal and suprabasal cells of the epithelial units and was inversely related to the maturation of sebaceous cells.[3] CD10 expression has been associated with mature sebocytes and components of normal skin and hair follicles.[13] Thus, its absence in the stroma of FSCH lesions suggests that it is of hamartomatous nature rather than of sebaceous derivation.[6] To distinguish FSCH from basal cell carcinoma, CD34 staining was used as an indication of maturity of the FSCH cells.[6]

A different study by Misago et al[6] reported that the epithelial component of the lesions was characterized by activated and proliferating CK-15–positive stem cells showing sebaceous differentiation. The basal cells of the infundibulosebaceous structures in FSCH were CK-15 positive, yet CK-19 negative, suggesting the lack of differentiation towards the epidermis.

The histogenesis of the mesenchymal component of FSCH is uncertain. The stromal adipocytes were previously thought to be the result of metaplasia. However, Misago et al[6] proposed that the adipocytes originate from nestin-positive multipotent stem cells. They demonstrated that in some lesions of FSCH, the expression of nestin was upregulated in sebaceous duct structures in occasional association with nestin-positive spindle cells in the stroma surrounding the adipocytes. Preadipocytes, characterized by S100 positivity, were also identified in proximity to the sebaceous structures, suggesting lipogenesis. Nestin-positive multipotent stem cells normally found in the connective tissue sheath of human hair follicles have demonstrated the capability to differentiate into adipocytes, Schwann cells, smooth muscle cells, melanocytes, endothelial cells, and chondrocytes.[13,14] The wide variety of possible differentiated forms of the stem cells suggests their involvement in the multiple variations of FSCH recorded. Nestin-positive stem cells may therefore underlie the unique presentation of spindle cell lipoma-like FSCH, as well as other reported variants including FSCH with nevus lipomatosus, FSCH with melanocytic nevus, FSCH with a neural component, and FSCH with vascular-mesenchymal overgrowth.[4,10,11,15,16]

A relationship between FSCH and sebaceous trichofolliculoma (TF) has been suggested by multiple investigators, implying that FSCH is a late-stage TF.[1] However, the 2 can be differentiated by the mesenchymal changes seen in FSCH, which are absent in TF. Interestingly, TF also lacks the upregulation of nestin found in the stroma of FSCH.[3] This lack of nestin may account for the absence of stromal variation in TF lesions.[6] In addition, the relatively minor follicular differentiation of FSCH differs from the presentation of TF, in which numerous terminal hairs and vellus hairs extend from the cystically dilated infundibular wall.[1,3] Furthermore, the congenital cases of FSCH argue against its relationship to TF.[17]

Although once considered exceedingly rare, FSCH lesions are increasing in reported frequency and variation. Here, we present a new variant of FSCH, which shows spindle cell lipoma-like features; this combination of a folliculosebaceous lesion associated with a mesenchymal proliferation resembling spindle cell lipoma has not been previously reported. Similar to other variants of FSCH, the mesenchymal elements of the lesion are nestin positive, further supporting the hypothesis of nestin-positive multipotent stem cells as the origin for stromal variants of FSCH. Our case contributes to the expanding variations of FSCH recorded and to elucidating the histogenesis of the mesenchymal components of FSCH.

REFERENCES

1. Ansai SI, Kimura T, Kawana S. A clinicopathologic study of folliculosebaceous cystic hamartoma. *Am J Dermatopathol.* 2010;32:815–820.
2. Zheng LQ, Han XC. Giant folliculosebaceous cystic hamartoma on the right forearm. *J Dermatol.* 2011;38:1208–1210.
3. Suarez-Peñaranda JM, Vieites B, Ramírez-Santos A, et al. Clinicopathological and immnuohistochemical findings in a series of folliculosebaceous cystic hamartoma. *J Cutan Pathol.* 2009;26:251–256.
4. Brasanac D, Boricic I. Giant nevus lipomatosus superficialis with multiple folliculosebaceous cystic hamartomas and dermoid cysts. *J Eur Acad Dermatol Venereol.* 2005;19:84–86.
5. Brücher JJ, Franke I, Ulrich J, et al. Giant genital variant of folliculosebaceous cystic hamartoma: successful management by CO2 laser and acitretin therapy. *Br J Dermatol.* 2007;157:833–835.
6. Misago N, Kimura T, Toda S, et al. A revaluation of folliculosebaceous cystic hamartoma: the histopathological and immunohistochemical features. *Am J Dermatopathol.* 2010;32:154–161.
7. Kimura T, Miyazawa H, Aoyagi T, et al. Folliculosebaceous cystic hamartoma. A distinctive malformation of the skin. *Am J Dermatopathol.* 1991;13:213–220.
8. Cho E, Lee JD, Cho SH. A solitary fibrofolliculoma on the concha of the ear. *Int J Dermatol.* 2012;51:616–617.
9. Bancalari E, Martínez-Sánchez D, Tardío JC. Nevus lipomatosus superficialis with a folliculosebaceous component: report of 2 cases. *Patholog Res Int.* 2011:105973.
10. Toyoda M, Morohashi M. Folliculosebaceous cystic hamartoma with a neural component: an immunohistochemical study. *J Dermatol.* 1997;24:451–457.
11. Donati P, Balus L. Folliculosebaceous cystic hamartoma. Reported case with a neural component. *Am J Dermatopathol.* 1993;15:277–279.
12. Aloi F, Tomasini C, Pippione M. Folliculosebaceous cystic hamartoma with perifollicular mucinosis. *Am J Dermatopathol.* 1996;18:58–62.
13. Yada K, Kashima K, Daa T, et al. Expression of CD10 in basal cell carcinoma. *Am J Dermatopathol.* 2004;26:463–471.
14. Jahoda CAB, Whitehouse J, Reynolds AJ, et al. Hair follicle dermal cells differentiate into adipogenic and osteogenic lineages. *Exp Dermatol.* 2003;12:849–859.
15. Fogt F, Tahan SR. Cutaneous hamartoma of adnexa and mesenchyme. A variant of folliculosebaceous cystic hamartoma with vascular-mesenchymal overgrowth. *Am J Dermatopathol.* 1993;15:73–76.
16. Kang H, Kim SE, Park K, et al. Nevus lipomatosus cutaneous superficialis with folliculosebaceous cystic hamartoma. *J Am Acad Dermatol.* 2007;56(2 suppl):S55–S57.
17. Noh S, Kwon JE, Lee KG, et al. Folliculosebaceous cystic hamartoma in a patient with neurofibromatosis Type I. *Ann Dermatol.* 2011;23:S185–S187.