

# Bulboma: A Benign Keratosis With Differentiation Toward the Lower Segment of the Hair Follicle

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**Abstract:** Bulboma is an appellation proposed to designate a distinctive solitary keratosis exhibiting differentiation toward the bulb of the lower segment of the hair follicle. Bulboma is composed of a papillated proliferation of epithelial cells beneath which is a broad front of interconnected follicular papillae. Overlying these coalescing follicular papillae are follicular germinative cells ascending into matrical cells and supramatrical cells. Cells demonstrating differentiation toward Huxley's and Henle's layer of the inner root sheath at the level of the bulb are present including strikingly bright eosinophilic trichohyalin granules and the blue-grey corneocytes of the stem. There is overlying hypergranulosis and orthokeratosis. The clinical and histopathological findings in 4 cases of bulboma, a rare, benign solitary keratosis are presented.

**Key Words:** lower segment of follicle, follicular bulb, follicular stem, bulboma, panfolliculoma

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## INTRODUCTION

A unique keratosis with follicular differentiation has been sporadically documented under the appellation “epidermal panfolliculoma.”<sup>1–3</sup> However, these lesions are markedly distinct from panfolliculoma; predominantly exhibiting differentiation toward the bulb but not the upper stem, isthmus, or infundibulum of the hair follicle. Bulboma is an appellation proposed to denominate a benign acanthoma exhibiting differentiation toward all elements of the bulb of the lower segment of the hair follicle, namely the follicular papilla, hair germinative cells, the matrix, and the supramatrical zone, up to the keratogenous zone and the inner root sheath at the level of the bulb and lower stem. Findings are novel, specifically: (1) a broad and focally papillated proliferation of fibrocytes with associated delicate fibrillary bundles of collagen in the papillary dermis, resembling a coalescing collection of contiguous follicular papillae, above which lies an exoendophytic proliferation of epithelial cells characterized by

(2) follicular germinative cells (3) matrical cells enveloping the subjacent follicular papillae, beneath (4) supramatrical cells and (5) cells exhibiting differentiation toward the inner root sheath elements of the bulb and lower stem. This report serves to document 4 cases, collected over the course of 22 years, of bulboma, a distinctive solitary keratosis exhibiting differentiation toward the bulb of the lower segment of the hair follicle.

## MATERIALS AND METHODS

Four cases of bulboma were collected from the private office laboratory of 2 community based outpatient dermatology practices. Clinical information including age, sex, site, and clinical differential diagnosis were obtained from the requisition form submitted by the clinician and the patient's medical records. Each specimen was fixed in 10% buffered formalin, embedded in paraffin, sectioned between 5 and 6  $\mu\text{m}$ , and stained with hematoxylin and eosin in the routine manner.

## RESULTS

### Case Reports and Histopathologic Findings

#### Case 1

A 52-year-old man phototype II presented with a solitary, slightly scaly papule measuring 9 mm on the medial aspect of the left leg. The clinical diagnosis was “hypertrophic actinic keratosis.” In 21 years follow-up, there has been no evidence of recurrence or metastasis.

#### Case 2

A 62-year-old woman phototype II presented with a solitary papule measuring 3 mm on the left thigh. The clinical diagnosis was “keratosis.” In 12 years follow-up, there has been no evidence of recurrence or metastasis.

#### Case 3

A 69-year-old woman phototype II presented with a solitary scaly papule measuring 5 mm on the left thigh. The clinical impression was “squamous cell carcinoma.” On 9-year follow-up, the patient has not had a recurrence or metastasis of the lesion.

#### Case 4

A 58-year-old man phototype II presented with a solitary papule measuring 5 mm on the left thigh. The clinical differential diagnosis was “seborrheic keratosis versus

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The authors declare no conflicts of interest.

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squamous cell carcinoma.” In 8 years follow-up, the lesion has not recurred or progressed.

### Histopathology

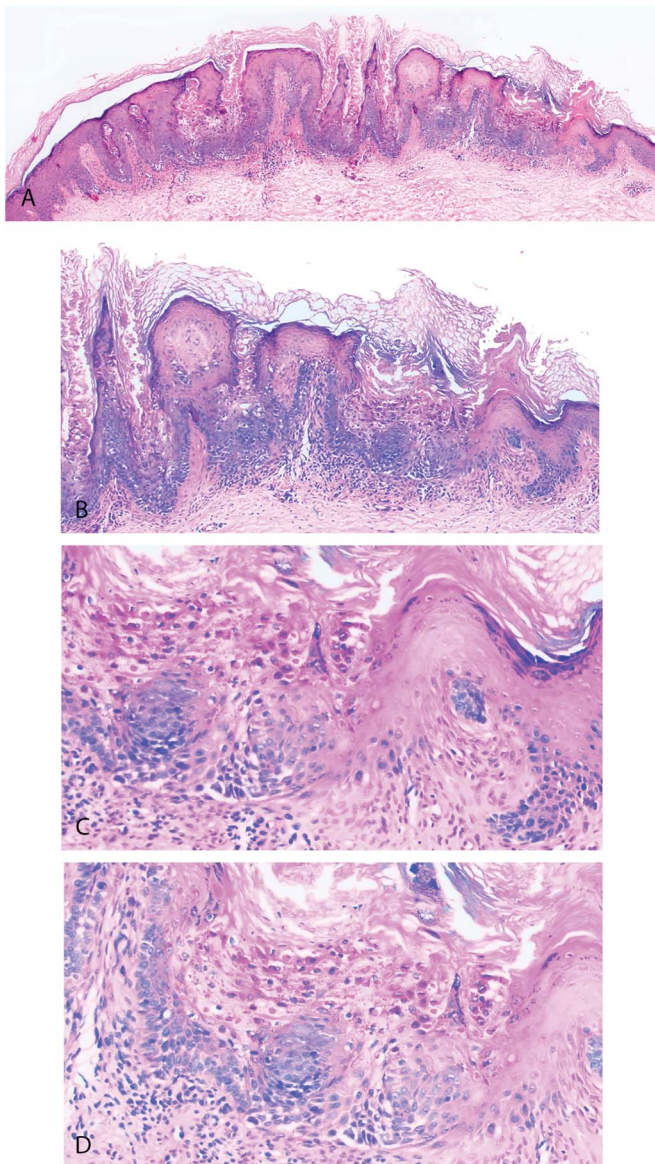
Findings were similar in all 4 cases (Figs. 1–4): superficial, papillated proliferations of epithelial cells, subtended by a broad, continuous front of interconnected follicular papillae, composed of delicate, fibrillary bundles of collagen with minimal associated mucin, and numerous, plump

fibrocytes, irregularly-arranged within the superficial papillary dermis. Overlying and enveloping follicular papillae were follicular germinative cells ascending into matrical cells with supramatrical cells, superiorly. Mitotic figures were readily apparent within matrical cells. Cells exhibiting differentiation toward Huxley’s and Henle’s layers of the inner root sheath at the level of the bulb, viz., vividly eosinophilic trichohyalin granules, along with the lower stem’s compactly arranged, blue-gray corneocytes, were identified. There was hypergranulosis, along with overlying basket-weave orthokeratosis. Case 4 exhibited an ulcer, probably secondary to excoriation, with overlying purulent crust.

### DISCUSSION

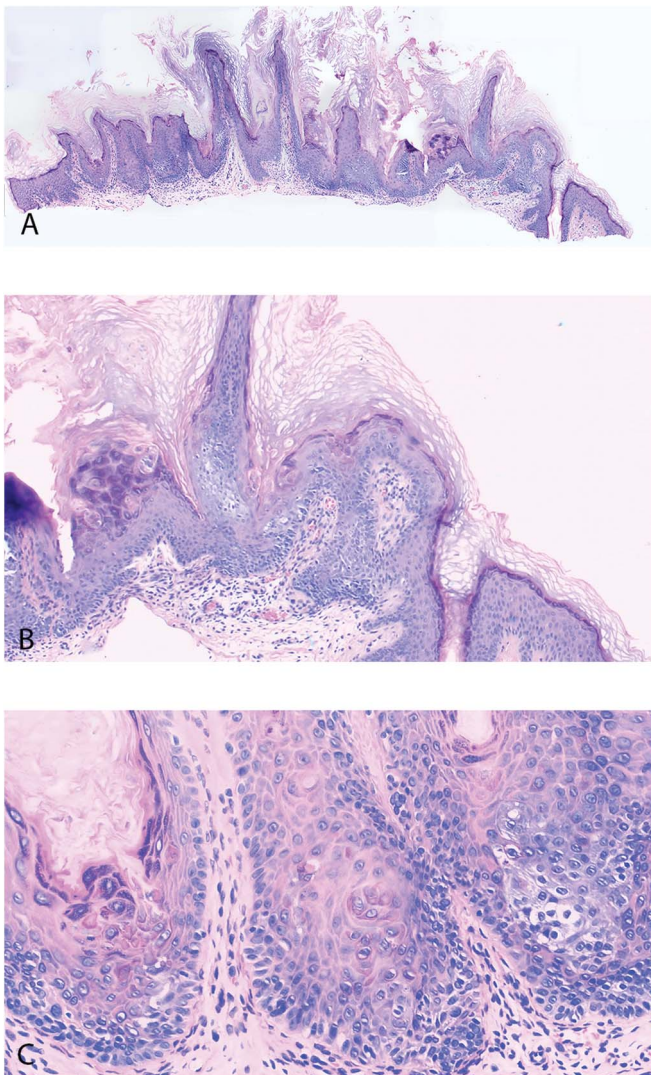
The hair follicle is composed of a lower segment and an upper segment. The upper segment is divided into the infundibulum, superiorly, and the isthmus, inferiorly. The lower segment of the follicle is made up of the stem, superiorly, and the bulb, inferiorly; the latter undergoes characteristic cyclical changes. Ascending superiorly, the bulb is made up of 4 regions: follicular germinative cells, the matrix, the supramatrical zone, and the keratogenous zone. Follicular germinative cells are uniform columnar cells arranged in a palisade as is seen in the follicular germ in fetal development or at the periphery of a follicular bulb during early anagen. Trichoblastoma, and its small nodular variant, trichoepithelioma are benign neoplasms composed predominantly of follicular germinative cells and basal cell carcinoma is a malignant neoplasm of follicular germinative cells. Up to the stem, the matrix is comprised of crowded epithelial cells that are large and round, have little cytoplasm, are relatively hematoxylinophilic, and exhibit numerous mitotic figures. Matrical cells differentiate in 2 directions, namely, toward what eventually becomes the keratogenous zone and hair shaft, and toward the inner root sheath. Matrical epithelium is seen in such neoplasms as pilomatricoma, pan-folliculoma, matricoma, and matrical carcinoma. The matrix and the base of the supramatrical zone surround the follicular papilla. The supramatrical zone represents the region of the bulb above the matrix, composed of rounder epithelial cells, with abundant cytoplasm, imparting paler staining. Supramatrical epithelium is seen in pilomatricoma and matricoma. The keratogenous zone, located superior to the supramatrical zone, is characterized by elongated nuclei in parallel array, that, as they ascend, become the cornified cells of the hair shaft. Keratogeneous zone changes are seen within the aberrant follicular elements of a trichofolliculoma.

Five cases first documented as “benign keratosis with a spectrum of follicular differentiation”<sup>1</sup> appear similar to those described herein. Subsequently 2 more cases were reported and the novel designation “epidermal panfolliculoma” was proposed.<sup>2</sup> One additional case was then reported.<sup>3</sup> Although all, including the present 4 cases, appear to be the same entity, the designation “epidermal panfolliculoma” is inaccurate, because specific changes of the upper segment of the hair follicle, the isthmus and infundibulum, are not identified. In particular, isthmic differentiation, as evidenced by cells with abundant, pale-to-brightly-eosinophilic



**FIGURE 1.** A, An exophytic papillated proliferation of epithelial cells is present within the epidermis. Differentiation at the level of the isthmus and infundibulum are not present. B, Confluent follicular bulbs and papillae with overlying abundant trichohyalin. C, Follicular germinative, matrical and supramatrical cells with overlying inner root sheath differentiation, at the level of the lower stem, evidenced by brightly eosinophilic trichohyalin granules. D, Bulb and papillae with overlying brightly eosinophilic trichohyalin.





**FIGURE 2.** A, Follicular papillae surrounded by matrical cells of the bulb with overlying papillated epithelial hyperplasia within the epidermis. Cells of the outer root sheath at the stem are absent and there are no infundibular horn pseudocysts present. B, Bulb and papillae. Above the matrical cells are supramatrical epithelial cells which are larger, rounder and contain more cytoplasm than matrical cells. C, Follicular germinative cells, matrical cells of the bulb with mitotic figures, supramatrical cells, and abundant trichohyalin.

cytoplasm, some exhibiting apoptosis (as seen within the isthmus during catagen) is not apparent. Although basket-weave orthokeratosis and hypergranulosis are present, such changes are not specific to the infundibulum, and are better interpreted, here, as epidermal. More specifically infundibular features as in the original case of panfolliculoma,<sup>4</sup> namely, infundibular horn pseudocysts and tunnels were also absent in the cases reported here, and in the prior publications.<sup>1–3,5</sup>

The appellation bulboma is proposed for this unique benign keratosis because the primary histologic changes are differentiation toward all components of the bulb of the hair follicle, namely, the follicular papilla, follicular germinative

cells, matrix, and the supramatrical zone, up to the keratogenous zone, including inner root sheath at the level of the bulb and lower stem. Bulboma represents the first benign epithelial proliferation within the epidermis described with matrical differentiation. It is distinct from other neoplasms exhibiting matrical components, that is, pilomatricoma, matricoma, matrical carcinoma, and trichofolliculoma.

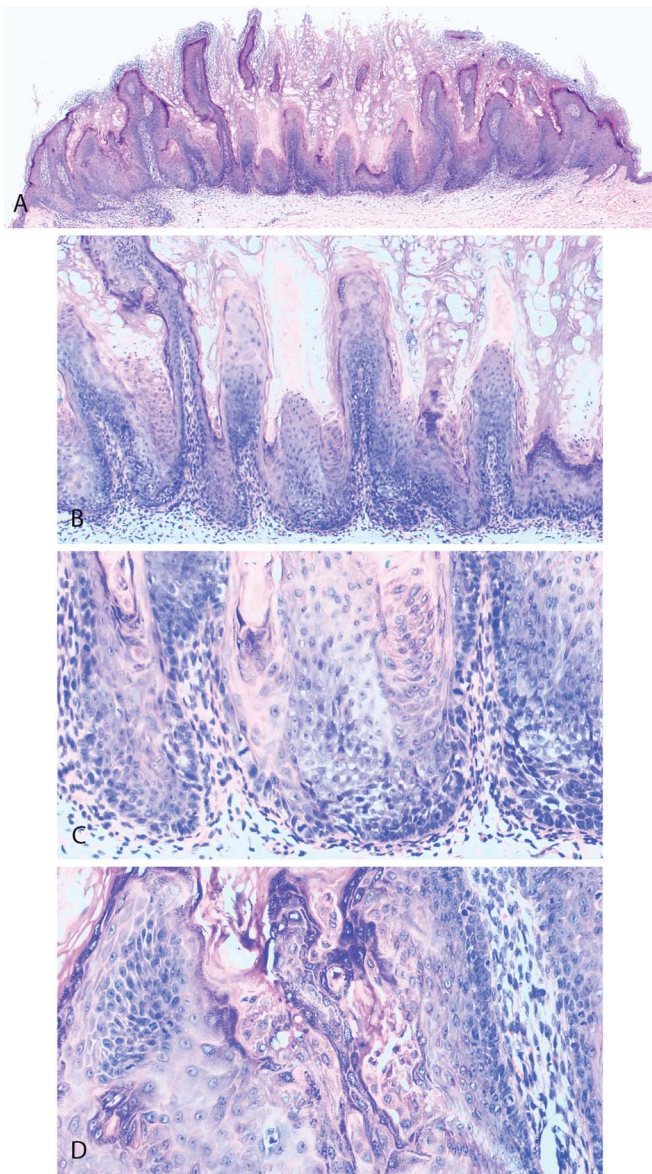
It is also distinct from the neoplasm first described by Ackerman as pan-folliculoma.<sup>4</sup> That neoplasm is a benign intradermal proliferation with differentiation toward *all* elements of the follicle, namely the bulb, stem, isthmus and infundibulum, does *not* show any changes within the overlying epidermis, and does not arise there, either. Shan and Guo<sup>5</sup> document 19 cases of panfolliculoma which they classify into 3 subtypes: 3 of nodular panfolliculoma, 7 of cystic panfolliculoma and 9 of superficial panfolliculoma. Of those, only superficial panfolliculoma is defined as involving the epidermis and/or superficial dermis, and as having changes similar to those termed “epidermal panfolliculoma” by Harris.<sup>2</sup> However, the cases described as superficial panfolliculoma also do not appear to display differentiation toward the upper segment of the hair follicle, namely, specific changes of the isthmus or infundibulum.

So-called “epidermal panfolliculoma”<sup>2,3</sup> does arise *within* the epidermis, but is follicular, not epidermal, does not extend into the dermis, as pan-folliculoma *sensu* Ackerman does, and lacks isthmic and specific infundibular differentiation. Thus, “epidermal panfolliculoma” is neither epidermal, nor an in situ lesion of panfolliculoma, either. The appellation bulboma is proposed for these unique lesions.

There are both mesenchymal and epithelial elements of hair bulb present in bulboma. The base of the lesion is composed of follicular bulbs with subjacent confluent follicular papillae and follicular germinative cells, with matrical and supramatrical cells present, as are cells displaying inner root sheath differentiation with formation of trichohyalin granules. However, there is no hair shaft formation, as would be seen above Adamson’s Fringe from the stem or higher, further emphasizing the absence of upper segment elements. Therefore, this lesion does not show elements of all levels of the follicle, and is not truly pan-follicular.

The differential diagnosis includes an epidermolytic acanthoma. Normal inner root sheath is composed of a cuticle, Huxley’s layer, and Henle’s layer, and exhibits a distinctive pattern of cornification at the level of the bulb characterized by eosinophilic trichohyalin granules within Huxley’s and Henle’s layer. As these cells ascend to the level of the stem, they convert to densely-packed blue gray corneocytes devoid of trichohyalin granules. Bulboma shows similar inner root sheath differentiation at the level of the bulb with formation of trichohyalin granules. The differentiation toward inner root sheath in bulboma with the formation of abundant trichohyaline granules is similar to that seen in epidermolytic hyperkeratosis and epidermolytic acanthomas. However, epidermolytic acanthoma does not show the other elements of follicular bulb and papillae, present in bulboma. Changes within epidermolytic hyperkeratosis are solely confined to the spinous and granular layers. In addition, epidermolytic hyperkeratosis and epidermolytic acanthoma are characterized by both an increase in trichohyalin

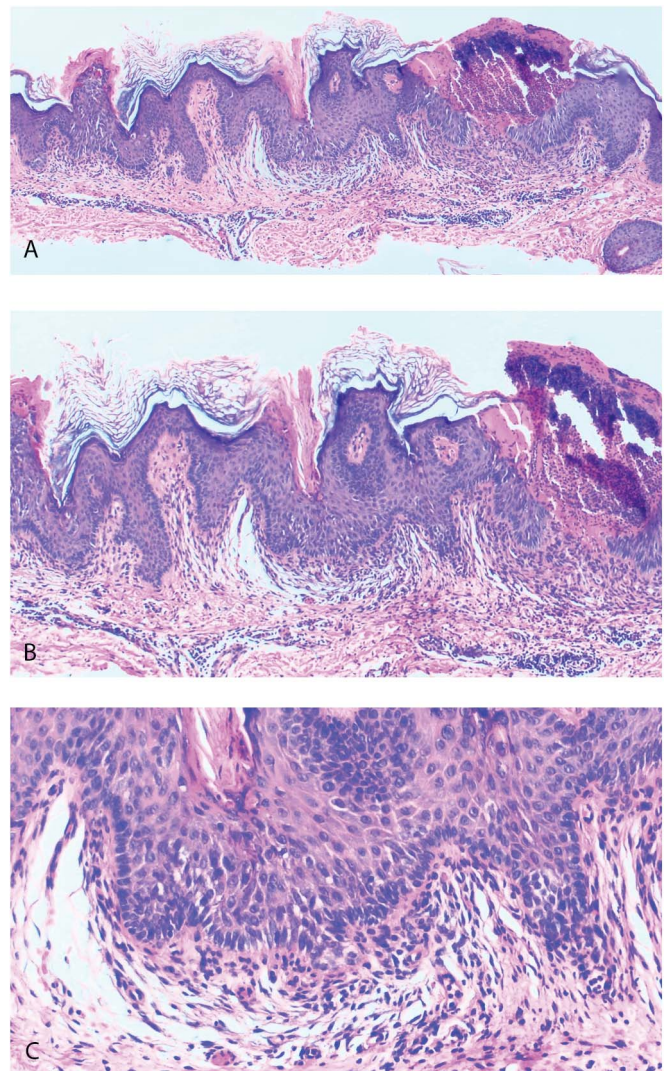




**FIGURE 3.** A, Merging follicular papillae beneath coalescing follicular bulbs with overlying papillated epithelium. B, Contiguous collections of bundles of collagen, with an associated proliferation of fibrocytes, mimicking follicular papillae, beneath follicular bulbs. No evidence of differentiation toward the upper segment of the follicle is identified. C, Follicular germinative cells, matrical cells with numerous mitotic figures, and supramatrical cells forming the bulb, with trichohyalin of the inner root sheath at the level of the stem, above. D, Eosinophilic trichohyalin with blue-gray corneocytes of the inner root sheath at the level of the stem, above.

and keratohyalin granules, whereas bulboma only has an increase in trichohyalin, with a normal granular zone.

Within the embryo, the follicular papilla induces development of the follicle. Subsequently, the papilla serves to induce the changes in the lower segment of the follicle that constitute the anagen, catagen, and telogen stages of the cycling follicle. As an acquired lesion, bulboma probably represents a benign



**FIGURE 4.** A, Papillated epidermal hyperplasia with confluent proliferation of follicular bulbs and papillae, ulcerated. B, Papillae, surrounded by follicular germinative cells, matrical cells, beneath supramatrical cells. C, Inner root sheath differentiation of Huxley's and Henle's layers at the level of the stem, characterized by bright red trichohyalin granules, above matrical and supramatrical cells.

neoplasm differentiating toward the lower segment of the anagen follicle and not a hamartoma or malformation.

In summary, bulboma represents a distinct, benign keratosis, differentiating toward all elements of the hair bulb, including follicular papilla, matrix, supramatrical zone, and inner root sheath (the latter at the levels of the bulb and lower stem). The changes are striking and distinct and should not be confused with pan-folliculoma. On long term follow-up of the 4 patients in this series, bulboma demonstrated completely benign behavior, without any evidence of persistence, recurrence, or progression.

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