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Follicular Hybrid Cysts
An Expanded Spectrum

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Currently it is well established that each of the three parts of the hair follicle (infundibulum, isthmus, and the inferior portion) originates different types of cutaneous cysts. Thus, follicular cysts include infundibular, trichilemmal, and matrical cysts. Brownstein in 1983 described a mixed type of cutaneous cyst combining epidermoid, infundibular, and trichilemmal types of keratinization. We review and illustrate the different combinations of follicular hybrid cysts reported to date: infundibular and trichilemmal cyst, infundibular and pilomatrixoma cyst, trichilemmal and pilomatrixoma cyst, eruptive vellus hair cyst and steatocystoma, and eruptive vellus hair cyst and trichilemmal cyst. Therefore, the concept of hybrid cyst should not be restricted to those composed of infundibular and trichilemmal cysts, because any cyst arising from the various parts of the pilosebaceous unit can combine with others to form a large series of follicular hybrid cysts.

Key Words: Follicular cysts—Hybrid cysts.

Currently it is well established that each one of the three parts of the hair follicle (infundibulum, isthmus, and the inferior portion) originates different types of cutaneous cysts (Fig. 1). Thus, infundibular cysts include infundibular—epidermoid—cysts (1), milia (2), eruptive vellus hair cysts (EVHC) (3), and pigmented follicular cysts (4). Trichilemmal cysts derive from the isthmus of anagen hairs or from the sac surrounding catagen and telogen hairs (5). Steatocystoma is originated from sebaceous ducts (6). Pilomatrixoma is a neoplasm of the hair cystic.
the hair matrix cells (7), which sometimes show a cystic structure (8).

In 1983, Brownstein (9) described a mixed type of cutaneous cyst characterized by infundibular keratinization in the upper portion and trichilemmal keratinization in deeper areas, and he termed this "hybrid cyst." However, in addition to this, follicular cysts may include a wide spectrum of other hybrid cysts, characterized by a combination of different types of keratinization or by the presence of several follicular structures in the cyst wall. This article reviews the published cases of hybrid cysts of the pilosebaceous unit to demonstrate the diversity of that concept. We illustrate some of these combinations with our own material from the files of the Laboratory of Dermatopathology, Hospital Universitario San Carlos, Madrid, Spain. We are reviewing only follicular hybrid cysts, not the full spectrum of follicular cysts. We report our hybrid cysts and those hybrid cysts described in the liter-

**FIG. 2.** Hybrid cyst from infundibular and trichilemmal cysts. Note sharp transition from the infundibular to trichilemmal areas.

**FIG. 3.** Pseudohybrid cyst: (a) Trichilemmal cyst with foci of granular layer. (b) Close-up view showing trichilemmal keratinization.
FIG. 4. Cystic pilomatricoma with a pore-like connection with the overlying epidermis.

ature, but we make no mention of other follicular cysts (milium cysts, pigmented follicular cysts, dermoid cysts, warty diskroma, etc.) because we have not found any combination of them in our own material of follicular cysts, and hybrid cysts from these cysts have not been reported in the literature.

HYBRID CYST FROM INFUNDIBULAR AND TRICHELLOMALL CYSTS

This combination was described in the original report of hybrid cysts (9). These cysts combined infundibular keratinization in their upper portions and trichelomall keratinization in the remainder of the cyst wall. Connection between the cyst and the surface epidermis by a keratin-filled follicle pore was seen in some sections.

The report of these cysts originated controversy both with respect to their nomenclature (10) and to their first description (11). The histologic diagnosis of this hybrid cyst requires the existence of an abrupt transition from the infundibular to trichelomall areas (Fig. 2). The presence of scattered foci of granular layer in an otherwise typical trichelomall cysts is not unusual (Fig. 3), and without a sharp transition these cases should be considered pseudohybrid cysts (12).

HYBRID CYST FROM INFUNDIBULAR CYST AND PILOMATRICOMA

Infundibular keratinization may be found in the superficial connection of a cystic pilomatricoma with the overlying epidermis (Fig. 4). This feature has been described in the literature with variable names such as calcifying epithelioma of Malherbe of unusual histological type (13), cyst of "vanilla fudge" (14), or histologic variation of a pilomatricoma and in its connection to keratohyalin matrix. The typical feature of the hair matrix (Fig. 7) is the presence of hair shafts (15), but the typical cyst contents between laminated keratin in infundibular area and shadow cells in pilomatricoma-like area.

FIG. 5. Hybrid cyst from infundibular cyst and pilomatricoma. Note sharp transition in the cyst wall from infundibular to pilomatricoma-like areas as well as sharp delimitation in the cyst contents between laminated keratin in infundibular area and shadow cells in pilomatricoma-like area.

FIG. 6. Gardner’s syndrome: infundibular cyst with a column of shadow cells projecting into the cyst lumina. Note sharp delimitation between laminated and basophilic keratin of the infundibular cyst and shadow cells of the pilomatrixicoma-like column.

A true hybrid cyst from pilomatrixicoma and infundibular cyst is a single cyst with both types of keratinization in its wall, infundibular in the upper areas connected with epidermis surface and hair matrix-like cells in deeper zones of the cyst wall. The transition between both zones is also sharp (Fig. 5). This event should not be confused with the report of pilomatrixicoma associated with infundibular cyst (16), which consisted of the presence of a pilomatrixicoma adjacent to infundibular cyst as two different neighboring cysts. A combined infundibular cyst and pilomatrixicoma also should not be confused with the so-called perforating pilomatrixicoma (17–21). which consisted of masses of shadow and basophilic cells of pilomatrixicoma that are extruded from the upper dermis to the skin surface through a perforated epidermal channel.

A curious kind of hybrid cyst has been reported by Cooper and Fechner in patients with Gardner’s syndrome (22). These cysts were infundibular cysts, but in some areas of the cyst wall there were columns of shadow cells, similar to those of pilomatrixicoma, that projected into the lumina (Fig. 6). The cells, at the point of attachment of the columns to the cyst lining, were indistinguishable from the hair matrix-like, basophilic cells of pilomatrixicoma (Fig. 7). These features suggest that pilomatrixicoma-like changes in the cyst wall and into the lumina may be a characteristic of the infundibular cysts in patients with Gardner’s syndrome.

HYBRID CYST FROM TRICHILEMMAL CYST AND PILOMATRIXICOMA

There is only one article on pilomatrixicoma in association with a “pilar cyst” in the eyelid (23). The authors of this report speculated on the possible histogenesis of the tumor from the wall of the “pilar cyst.” This report, however, is lacking in detailed histological documentation. In any case, the existence of a combined trichilemmal and pilomatrixicoma cyst must be a very infrequent event. Trichi-
lemmal cysts are derived from the sac surrounding catagen and telogen hair. In these phases of the life cycle of the hair follicle, only a thin column of epithelial cells replaces the entire inferior segment of the follicle. Therefore, it is unlikely that pilomatricoma develops from these cells.

Another variant of hybrid cyst has been reported combining pilomatricoma and outer root sheath in the cyst wall (24). The lower part of the cyst wall was lined by basophilic cells that showed a gradual loss of nuclei and ultimately appeared as faintly eosinophilic, keratinized shadow cells. In contrast, the upper part of the cyst wall was composed of cells having clear cytoplasm, which contained periodic acid–Schiff-positive, diastase-digestive material. The peripheral layer of the clear cells showed a distinct palisade arrangement, and was surrounded by a homogeneous, eosinophilic hyaline layer. All these features in the upper part of the cyst wall closely resemble those of the middle or lower portion of outer root sheath.

HYBRID CYST FROM ERUPTIVE VELLUS HAIR CYST AND STEATOCYSTOMA

Differential diagnosis between EVHC and steatocystoma multiplex (SM) usually requires histopathologic examination, because there are clinical similarities between both entities. The histologic picture of EVHC (3) shows a small cyst in the middermis with a wall composed of several layers of squamous cells and a cavity containing laminated keratinous material and shafts of vellus hairs. On the other hand, histologic sections of SM show an empty cyst with a thin wall of stratified squamous epithelium and a prominent, acellular, hyalinized cuticle with undulating configuration recapitulating the sebaceous duct (25).

Nevertheless, Urbina et al. (26) have described a case of EVHC (Fig. 8a) in which serial sections showed two sebaceous-gland lobules within the cyst wall (Fig. 8b). Occasionally, clusters of hairs, mainly of lanugo size, could also be seen in steatocystomas (27–29). Recently, Sexton and Murdock (30) have reported a case of EVHC that histologically showed a cyst wall lined by squamous epithelium and a brightly eosinophilic, crenulated lining membrane, closely resembling the luminal cuticle of the steatocystoma. Serial sections of this cyst failed to reveal sebaceous glands within or immediately adjacent to the cyst wall. According to Brownstein's criteria (25), it is possible to make a diagnosis of steatocystoma if the characteristic hyaline luminal cuticle is present, even in absence of sebaceous cysts and sebaceous glands.

1. Level skin.
2. Epithelial cysts.
3. Ester cysts.
4. Mehr Cyst.

FIG. 8. Hybrid cyst from eruptive vellus hair cyst and steatocystoma. (a) This section shows an eruptive vellus hair cyst. Arrows indicate two vellus hair shafts. (b) Serial sections of the cyst demonstrated two sebaceous gland lobules within the cyst wall.

clinical sign, ologic pic
y in the eral layers of hair. The
 have described a patient with multiple papules on the forehead (31). Two biopsies were taken. The first biopsy showed features of EVHC. The second specimen was a typical steatocystoma. All these findings suggest that EVHC and SM are two related conditions, both representing nevoid malformations of the pilosebaceous duct junction; therefore, hybrid forms showing features of both are plausible. Similarly, Kamakiri et al. (32) described a case of EVHC in which the deep part of the cyst wall showed trichilemmal keratinization.

In conclusion, the concept of follicular hybrid cyst should not be restricted to those composed of infundibular and trichilemmal cysts. Practically, all of the cysts arising from the various parts of the pilosebaceous unit may occasionally combine to form a large variety of follicular hybrid cysts and, in addition to the combinations here reported, other possibilities of follicular hybrid cysts are plausible. Thus, in this article we are expanding the concept of follicular hybrid cysts to those follicular cysts that show distinctive, juxtaposed bimodal differentiation, with abrupt transition between them. This expanded concept will be useful in categorizing a large diversity of follicular cysts that have been described in the literature as well as other hybrid cysts that probably will be reported in the future.

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