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15 March 2005

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The American Journal of Dermatopathology 19(3): 250–253, 1997

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Expression of Keratins (K10 and K17) in Steatocystoma Multiplex, Eruptive Vellus Hair Cysts, and Epidermoid and Trichilemmal Cysts

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We compared the patterns of keratin 10 (K10) and keratin 17 (K17) expression in epidermoid cysts, trichilemmal cysts, eruptive vellus hair cysts, and steatocystoma multiplex. Epidermoid cysts expressed K10 and eruptive vellus hair cysts expressed K17, whereas trichilemmal cysts and steatocystoma multiplex showed expression of both K10 and K17. Our findings support the opinion that eruptive vellus hair cysts, which stained negative for K10, and steatocystoma multiplex are distinct entities and not variants of one disorder.

Key Words: Keratin 10—Keratin 17—Steatocystoma multiplex—Eruptive vellus hair cyst—Trichilemmal cyst—Epidermoid cyst.

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Keratins form one of six classes of intermediate filaments and are the major part of the cytoskeleton of epithelial cells. According to their molecular characteristics, keratins can be further classified as subfamily I (type I, acid keratins) and subfamily II (type II, neutral/basic keratins) (1,2). In tissues, they are expressed as pairs containing one member from each subfamily, and the expression of the pair is determined by the state of differentiation and proliferation of the tissues (2).

Both keratin 10 (K10) and keratin 17 (K17) belong to type I keratins, but they show distinct tissue distributions. K10 is formed in the epidermis and the follicular infundibulum by suprabasal keratinocytes (1). It is also formed by luminal cells of the eccrine duct (3) as well as by cells of the sebaceous gland and duct (1,4). K17 is normally expressed in the outer root sheath of the lower portion of the hair follicle, in the sebaceous duct and gland (1,4), and in the myoepithelial cells of the eccrine gland. Luminal cells of the eccrine duct showed only a weak and variable reaction to K17 (3). K17 has also been reported to be expressed in psoriasis (5) as another marker of keratinocyte hyperproliferation, besides K6 and K16 (6). We undertook an immunohistochemical study to determine the expression of K10 and K17 in epidermoid cysts, trichilemmal cysts, eruptive vellus hair cysts, and steatocystoma multiplex.

MATERIALS AND METHODS

We studied 5 biopsy specimens of epidermoid cysts, 5 specimens of trichilemmal cysts, 7 specimens of steatocystoma biopsied from 5 cases of steatocystoma multiplex or simplex, and 2 biopsy specimens from 2 patients with eruptive vellus hair cysts.

The studies were performed on formalin-fixed, paraffin-embedded sections, which were deparaffinized and rehydrated in xylene and graded ethanol solutions. Before staining for K17, the sections on slides were boiled

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in 10 m*M* citrate buffer. After inactivation of endogenous peroxidase activity and preincubation with 1% bovine serum albumin/10% skim milk, the sections were incubated overnight with the following monoclonal antibodies (MoAbs): monoclonal mouse anti-human cytokeratin 10 (Dako-CK10, DE-K10; 1:50, DAKO A/S, Denmark) and monoclonal mouse anti-human cytokeratin 17 (Dako-CK17, E3; 1:10, DAKO A/S, Denmark). The slides were then developed with biotinylated goat anti-mouse immunoglobulin (Histofine, Nichirei, Tokyo, Japan) and streptavidin conjugated with horseradish peroxidase (Histofine), followed by visualization of the reaction by diaminobenzidine (DAB) solution, counterstaining with 1% methylgreen, and mounting with Entellan Neu (Merck). We considered negative immunoreactivity of the epidermis and the outer root sheath as a negative control for anti-human cytokeratin 17 and 10, respectively.

RESULTS

The results of immunostaining for K10 and K17 in our study, aimed particularly at possibly differentiating steatocystoma multiplex from eruptive vellus hair cysts by immunohistochemistry, were as follows. In eruptive vellus hair cysts, in contrast to the overlying epidermis, cells lining the cyst did not express K10 (Fig. 1A), but showed strong immunoreactivity for K17 (Fig. 1B). In steatocystoma multiplex and simplex, unlike in eruptive vellus hair cysts, expression of both K10 and K17 was demonstrated in the suprabasal cells lining the cyst, as shown in Fig. 2A and B. In trichilemmal cysts, the presence of K10 and K17 was also observed in suprabasal lining cells (Fig. 3A and B). In epidermoid cysts, K10 was expressed in the suprabasal compartment of the cyst wall (Fig. 4), whereas K17 showed no immunostaining (data not shown).

DISCUSSION

An epidermoid cyst originates in the follicular infundibulum as a result of proliferation, retention, and hyperkeratosis (7). In regions devoid of pilosebaceous follicles, such as palms and soles, it can arise from implantation of epidermal cells into the dermis subsequent to trauma (8,9). Histologically, the wall of an epidermoid cyst is composed of the stratified squamous epithelium containing a granular layer. Horny material arranged in laminated layers is found in the cyst lumen (10). Our study demonstrated the presence of K10 in the epidermoid cyst wall in exactly the same fashion as in the normal epidermis and the follicular infundibulum.

A trichilemmal cyst is a keratin-containing cyst (10), the wall of which is derived from the outer root sheath of the lower portion of the hair follicle between the hair bulb and the orifice of the sebaceous duct (7). Its epithelial lining shows abrupt keratinization without the

FIG. 1. Eruptive vellus hair cyst. Negative keratin 10 **(a)** and positive keratin 17 **(b)** immunohistochemical staining.

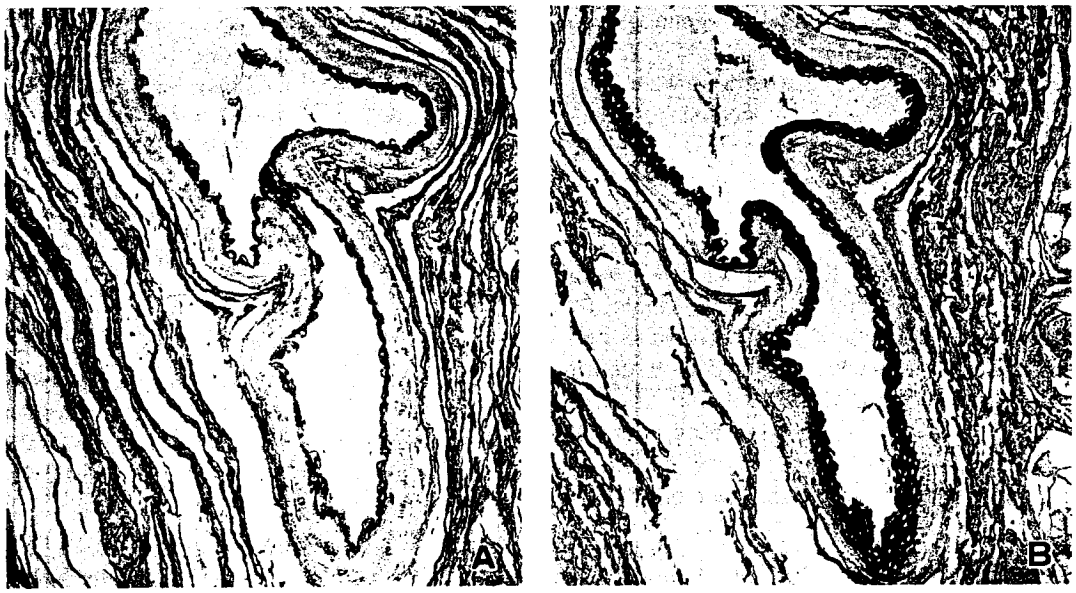

FIG. 2. Steatocystoma stained for keratin 10 **(a)** and keratin 17 **(b).**

presence of stratum granulosum (10). However, unlike the outer root sheath, the lining of a trichilemmal cyst stains positive with the serum raised against hair keratin extract (11). In our study, trichilemmal cysts showed reactivity not only for K17, normally expressed in the outer root sheath, but also for K10, which is not expressed in the lower hair follicle below the level of the sebaceous gland (1,4). Therefore, our findings further support those of Cotton et al. (11) indicating that pilar cysts show similarity but not antigenic identity with the outer root sheath of the hair follicle.

Steatocystoma multiplex (or simplex) is a cyst or, more precisely, a cystic hamartoma (12), lined by thin, wavy, sebaceous duct epithelium, containing sebaceous lobules of varying size as well as individual sebocytes. There is no granular layer. Steatocystoma is associated with a vellus hair follicle, the hairs of which may be trapped in the cyst cavity (13). Electron microscopy showed that steatocystoma multiplex has features similar to the sebaceous duct and sebaceous gland (13). The expression of K10 and K17, also expressed in the sebaceous duct and gland (1,4), confirms the origin of the lining of steatocystoma.

Eruptive vellus hair cysts are small cysts arising from the structures of vellus hair follicles. The pathogenesis is unknown (7). A possible pathogenetic mechanism has been proposed by Esterly et al. (14): An initially abnormal vellus hair follicle, with keratinous plugs at the follicular infundibulum, deflects vellus hair shafts to the deeper part of the follicle, resulting in its cystic dilatation

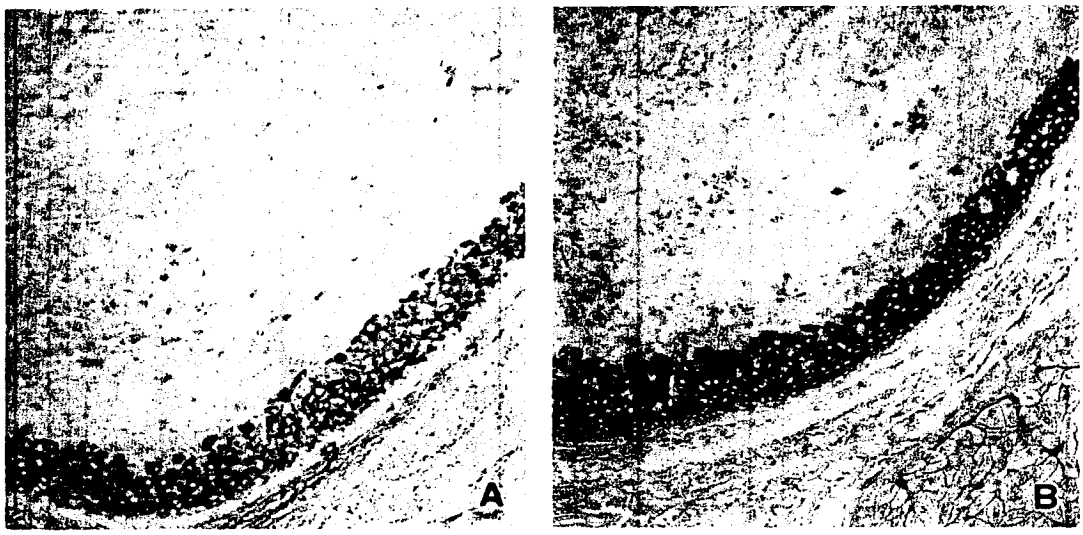

FIG. 3. Trichilemmal cyst. Staining for keratin 10 **(a)** and keratin 17 **(b).**

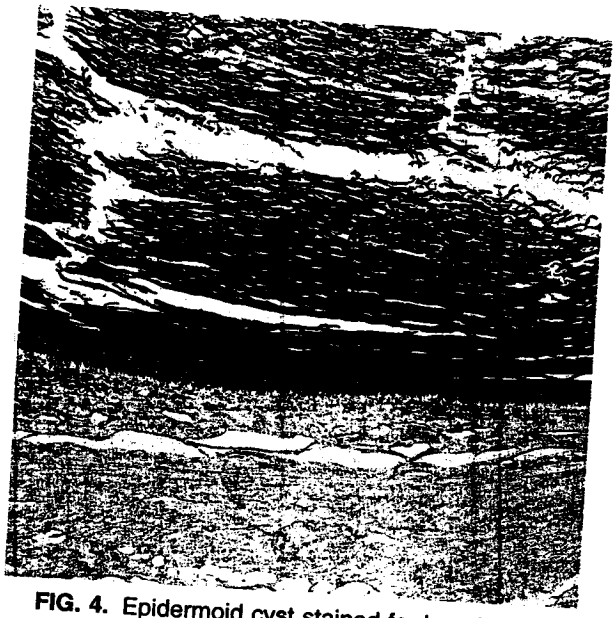

FIG. 4. Epidermoid cyst stained for keratin 10.

and gradual disruption of the continuity between proximal and distal follicle. Histologic examination shows a cyst localized in the mid-dermis and lined by stratified keratinizing epithelium. The lumen contains numerous small vellus hairs and keratinous material. A rudimentary hair follicle can be found in the cyst wall (7). Some eruptive vellus hair cysts were reported to be communicating with the surface (15), with others having vellus hairs emerging from folliclelike invaginations of the cyst wall (16). The walls of some eruptive vellus hair cysts were reported to be mixtures of epidermoid keratinization, as observed in the upper part of the follicular infundibulum, and trichilemmal keratinization of the lower part of the infundibulum and the follicular isthmus (17). We suggest that eruptive vellus hair cysts may originate in the lower infundibulum and the infundibular–isthmic junction of vellus hair follicles; their lining epithelia differentiate mainly in the direction of the infundibular epithelium, but unlike it, they do not express K10 but express K17 as the outer root sheath of the lower follicle.

The existence of overlapping conditions between steatocystoma multiplex and eruptive vellus hair cysts (18), as well as the existence of hybrid forms showing features of both steatocystoma multiplex and eruptive vellus hair cysts (19), has been suggested. However, other investigators interpreted these cystic conditions as steatocystomas (12).

Our findings indicate that K10, but not K17, is a useful marker for differentiating steatocystoma from eruptive vellus hair cysts and also support the opinion that eruptive vellus hair cysts and steatocystoma multiplex are distinct entities and not variants of one disorder, as suggested by some investigators (20,21). □

Acknowledgment: We thank Dr. Toshifumi Nakagawa, Department of Dermatology, Kagawa University Medical School, for providing us with the biopsy specimens of steatocystoma multiplex and eruptive vellus hair cyst.

REFERENCES

1. Moll I. Cytokeratine. Marker epithelialer Differenzierung. *Hautarzt* 1993;44:491–501.
2. Freedberg IM. Epidermal differentiation and keratinization. In: Fitzpatrick TB, Eisen AZ, Wolff K, et al., eds. *Dermatology in general medicine.* New York: McGraw-Hill, 1993:198–209.
3. Moll I, Moll R. Changes of expression of intermediate filament proteins during ontogenesis of eccrine sweat glands. *J Invest Dermatol* 1992;98:777–85.
4. Hughes BR, Morris C, Cunliffe WJ, Leigh IM. Keratin expression in pilosebaceous epithelia in truncal skin of acne patients. *Br J Dermatol* 1996;134:247–56.
5. Leigh IM, Navsaria H, Purkis PE, et al. Keratins (K16 and K17) as markers of keratinocyte hyperproliferation in psoriasis in vivo and in vitro. *Br J Dermatol* 1995;133:501–11.
6. Weiss RA, Eichner R, Sun TT. Monoclonal antibody analysis of keratin expression in epidermal disease: a 48-kD and a 56-kD keratin as molecular markers for hyperproliferative keratinocytes. *J Cell Biol* 1984;98:1397.
7. Braun-Falco O, Plewig G, Wolff HH. *Dermatologie und Venerologie.* Berlin: Springer-Verlag, 1995.
8. Leonforte JF. Palmoplantare Epidermiszyste. *Hautarzt* 1978;29: 657–8.
9. Fisher BK, Macpherson M. Epidermoid cyst of the sole. *J Am Acad Dermatol* 1986;15:1127–9.
10. Ho WCY, McLean DI. Benign epithelial tumors. In: Fitzpatrick TB, Eisen AZ, Wolff K, et al., eds. *Dermatology in general medicine.* New York: McGraw-Hill, 1993:855–72.
11. Cotton DWK, Kirkham N, Young BJJ. Immunoperoxidase anti-keratin staining of epidermal and pilar cysts. *Br J Dermatol* 1984; 111:63–8.
12. Steffen C, Ackerman AB. *Neoplasms with sebaceous differentiation.* Philadelphia: Lea & Febiger, 1994.
13. Plewig G, Wolff HH, Braun-Falco O. Steatocystoma multiplex: anatomic reevaluation, electron microscopy, and autoradiography. *Arch Dermatol Res* 1982;272:363–80.
14. Esterly NB, Fretzin DF, Pinkus H. Eruptive vellus hair cysts. *Arch Dermatol* 1977;113:500–3.
15. Piepkorn MW, Clark L, Lombardi DL. A kindred with congenital vellus hair cysts. *J Am Acad Dermatol* 1981;5:661–5.
16. Lee S, Kim JG. Eruptive vellus hair cyst. Clinical and histological findings. *Arch Dermatol* 1979;115:744–6.
17. Kumakiri M, Takashima I, Iju M, et al. Eruptive vellus hair cysts—a facial variant. *J Am Acad Dermatol* 1982;7:461–7.
18. Sexton M, Murdock DK. Eruptive vellus hair cysts. A follicular cyst of the sebaceous duct (sometimes). *Am J Dermatopathol* 1989;11:364–8.
19. Reguena L, Sanches-Yuz E. Follicular hybrid cysts: an expanded spectrum. *Am J Dermatopathol* 1991;13:228–33.
20. Kiene P, Hauschild A, Christophers E. Eruptive vellus hair cysts and steatocystoma multiplex. Variants of one entity? *Br J Dermatol* 1996;134:365–7.
21. Ohtake N, Kubota Y, Takayama O, et al. Relationship between steatocystoma multiplex and eruptive vellus hair cysts. *J Am Acad Dermatol* 1992;26:876–8.