



Pachyonychia Congenita Project

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We hope that making available the relevant information on Pachyonychia Congenita will be a means of furthering research to find effective therapies and a cure for PC.

CASE STUDY

Vesna Petronic-Rosic, MD, MSc, Section Editor

Multiple Cystic Disease: *K17* Dysfunction?

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Our patient is a 29-year-old woman without any previous disease who presented with different kinds of lesions on her face, neck, and chest. She first noticed the lesions 10 years ago and, since that time, they have become more numerous. She has no affected relatives. On physical examination, she had multiple cystic lesions on her neck, chest, and vulva, which were between 0.3 cm and 1 cm and skin-colored or yellowish (Figure 1). She presented with small, white papules on her face measuring approximately 0.2 cm, localized on her forehead and cheeks. Some of these papules had a blueish appearance (Figure 2). She also presented clinically typical eruptive syringomas on her upper and lower eyelids and neck and multiple facial milia. Finally, a sacrococcygeal pilonidal cyst was diagnosed and surgically removed. Her nails and teeth were clinically normal. Biopsies of each kind of lesion were performed, with the following results: (1) neck cystic lesion: steatocystoma; (2) small, white facial papule: eccrine hidrocystoma; (3) blueish facial papule: apocrine hidrocystoma; and (4) small neck papule: syringoma (Figure 3). With these findings, our diagnosis was steatocystoma multiplex with multiple eccrine and apocrine hidrocystomas, eruptive syringomas, and sacrococcygeal pilonidal cyst. (*SKINmed*. 2013;11:301–303)

K₁₇ is a type I keratin with a complex pattern of expression. During development, the single-layered epithelial cells that express *K17* give rise to placodes, the precursors of ectoderm-derived appendages (hair, glands, nails, and teeth). After birth, its constitutive expression is restricted to hair follicles, nail matrix, and the myoepithelium surrounding secretory glandular cells.¹

The finding that links these two patterns of expression (embryologic and adult) is that *K17* is strongly inducible in epidermis following acute injury. During the epidermal repair process, expression of *K17* spreads distally from the edge of the wound and is maintained in keratinocytes that are migrating to the site. Follicular *K17* expressing keratinocytes greatly contribute to the process.¹ In addition, it has recently been studied that in the absence of epidermis, eccrine sweat glands can start wound repair possibly through myoepithelium *K17*-expressing cells.²

In pathological situations such as hyperproliferation or abnormal differentiation, *K17* expression is also increased. Psoriasis, inflammatory states, viral infections, and basal cell carcinoma are some examples.³ *K17* up-regulation seems to be a key fac-

tor in the activation, migration, and division of epithelium with important stromal interactions.

K17 mutations give rise to pachyonychia congenita type 2 (PC-2) and steatocystoma multiplex (SM), both autosomal-dominant disorders. Currently, 14 missense mutations have been identified that occur within the helix initiation motif.⁴ This sequence may be directly involved in keratin filaments assembly through end-to-end interactions; however, any phenotype can arise from the same mutation and, at the same time, these two diseases show highly heterogeneous clinical features. In SM, multiple steatocystomas develop around puberty. Milia and vellus hair cysts can also be present. Patients with PC-2 show hypertrophic nail dystrophy, focal keratoderma, follicular keratosis, teeth and hair abnormalities, and multiple cystic lesions of different kinds. These “follicular hybrid cysts” are highly heterogeneous and include steatocystomas, epidermal cysts, milia, vellus hair cysts, hidradenitis suppurativa–like cysts, and vulvar and scrotal cystomatosis.⁵

We can only speculate about the functional alterations of *K17* derived from its mutations. In SM and PC-2, *K17* structural function may be impeded giving room to hair shaft abnormalities and nail dystrophy, hyperkeratosis can contribute to infun-

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Figure 1. Multiple steatocystomas localized on the patient's neck.



Figure 2. Apocrine hidrocystoma (arrow).

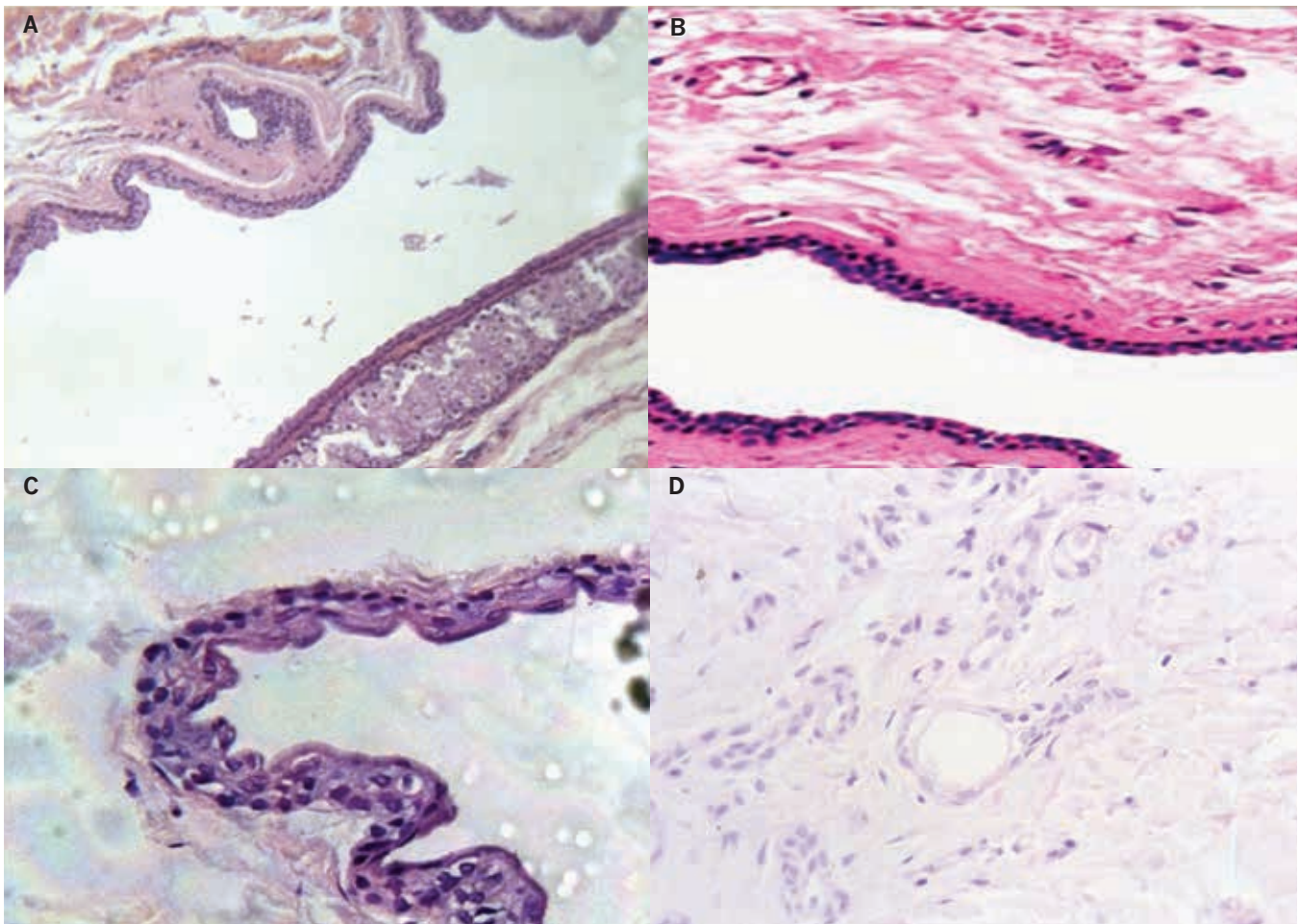


Figure 3. Histologic slides: (A) steatocystoma (hematoxylin-eosin stain, original magnification $\times 200$); (B) eccrine hidrocystoma (hematoxylin-eosin stain, original magnification $\times 200$); (C) apocrine hidrocystoma (hematoxylin-eosin stain, original magnification $\times 200$); (D) syringoma (hematoxylin-eosin stain, original magnification $\times 200$).

dibular occlusion and formation of retention cysts, and developmental alterations in appendage formation could be related to cystic, adenomatous, or hyperproliferative lesions.

CONCLUSIONS

Our patient presented with multiple steatocystomas and other lesions, most of them cysts derived both from eccrine and apocrine sweat glands, exhibiting a unique spectrum of clinical features. The presence of hydrocystomas exceeds a diagnosis of SM, and PC-2 would lack nail, teeth, or hair shaft alterations. We believe that a mutation in *K17* could explain this phenotype, which has not been previously reported in the literature.

REFERENCES

- 1 McGowan K, Coulombe PA. Onset of keratin 17 expression coincides with the definition of major epithelial lineages during skin development. *J Cell Biol.* 1998;143:469–486.
- 2 Miller S, Burke EM, Rader MD, Coulombe PA, Lavker RM. Re-epithelization of porcine skin wounds by the sweat apparatus. *J Invest Dermatol.* 1998;110:13–19.
- 3 Bianchi N, Depianto D, McGowan K, Gu C, Coulombe PA. Exploiting the keratin 17 gene promoter to visualize live cells in epithelial appendages of mice. *Mol Cell Biol.* 2005;25:7249–7259.
- 4 Se-Woong OH, Moon Young KIM, Jeong Sun LEE, Soo-Chan KIM. Keratin 17 mutation in pachyonychia congenita type 2 patient with early onset steatocystoma multiplex and Hutchinson-like tooth deformity. *J Dermatol.* 2006;33:161–164.
- 5 Covello SP, Smith FJ, Sillevs Simitt JH, et al. Keratin 17 mutations cause either steatocystoma multiplex or pachyonychia congenita type 2. *Br J Dermatol.* 1998;139:475–480.

