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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.

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Familial pachyonychia congenita with steatocystoma multiplex and multiple abcesses of the scalp due to the p.Asn92Ser mutation in keratin 17

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Pachyonychia congenita (PC) is a rare genodermatosis transmitted as an autosomal dominant trait, caused by mutations in the differentiation-specific keratin genes *KRT6a* (52%), *KRT6b* (3%), *KRT16* (28%) or *KRT17* (17%) which are expressed in the nails, skin, oral mucosa, larynx, hair and teeth.[1] Approximately 1000 patients with PC have been identified, of which 400 have been confirmed genetically. Two sub-types have been classically described: PC-1 (Jadassohn-Lewandowsky type, OMIM#167200), caused by *KRT6a* or *KRT16* mutations, with predominant oral leucokeratosis and palmoplantar keratoderma, and PC-2 (Jackson-Lawler type, OMIM#167210) resulting from *KRT6b* or *KRT17* mutations, with neonatal teeth, pili torti and multiple cysts.[2,3] The presence of multiple sebaceous cysts (steatocystoma multiplex (SM)) at puberty has been proposed to differentiate PC-2 from PC-1[2,3], but it is now recognized that there is a considerable overlap between the two classical sub-types of PC, and a new classification based on the mutated keratin gene has now been proposed (PC-6a, PC-6b, PC-16 and PC-17).[4,5]

A 12-year-old girl presented with a painful inflammatory plaque on her scalp recently appeared without any fever. She had a previous history of microcysts on her face and multiple unsuccessful treatments for suspected fungal infection of fingernails and toenails. She had neonatal teeth. Her mother had multiple steatocystomas on her face and trunk (Fig. 1a), focal plantar

keratoderma (Fig. 1b), normal nails and a history of neonatal teeth. She had no history of abcesses. Clinical examination of the scalp of the proband showed multiple suppurative, well-circumscribed, alopecic and cicatricial plaques on her vertex (Fig. 2a) and rough hair. She had multiple microcysts on her face predominant on the forehead (Fig. 2b), sebaceous cysts in the armpits, ophryogenes type keratosis pilaris of the eyebrows, pachyonychia of all finger and toenails (Fig. 2c) and keratosis pilaris on both thighs. She had no palmoplantar keratoderma. Histology of the scalp revealed a cystic formation with an empty content, lined with a thin eosinophilic epithelial lining highly suggestive of a sebaceous cyst (Fig. 2d). A non perifollicular polymorphic inflammatory granuloma, rich in neutrophils, lymphocytes and plasmocytes, was seen in the deep dermis, Fungal examination was negative and bacteriological cultures yielded occasional colonies of *Staphylococcus aureus*. Microscopic examination of the hair-shaft showed normal thickness, a longitudinal fissure giving a flat appearance, in places triangular, suggestive of pseudo-pilitorti. Genetic analysis of the proband and her mother identified a heterozygous c.275A>G (p.Asn92Ser) mutation in the *KRT17* gene, a frequent mutation reported in PC-17. [4]

The final diagnosis in our patient was suppurative sebocystomatosis of the scalp complicating PC-17. The scalp lesion responded quickly and favourably to drainage and oral antibiotherapy. A cicatricial alopecia persisted after 1 year. Inflammatory episodes of the axillary cysts also occurred.

Considerable heterogeneity in clinical severity and disease expression has been reported in PC. The p.Asn92Ser missense mutation is the most frequent mutation (37%) reported in PC-17, with phenotypic variability reported mainly between families. [4,7] To date, affected members from families with this mutation showed similar clinical features or minor differences in the age at onset, severity of symptoms, and the presence or absence of cysts.[6-8] Our case illustrates the remarkable intra-familial phenotypic variability of PC due to the same *KRT17* mutation.[9] Indeed, while the proband

has multiple cysts, marked pachyonychia of all nails, with no palmoplantar keratoderma, her mother has multiple sebocystomatosis, plantar keratoderma with no pachyonychia. Such variability is likely to be under the influence of modifier genes and environmental factors such as traumas which could aggravate keratoderma[4].

Steatocystoma multiplex (SM, OMIM #184500) is a rare disorder characterised by multiple sebaceous cysts or steatocystomas, with an oily liquid or compact and caseous content, that occur at puberty. SM is inherited in an autosomal dominant manner and is also caused by *KRT17* mutations. The p.Asn92Ser missense mutation has been identified in patients with SM without nail changes in some families, or in patients with PC-17 in other families.[10] The most frequent localisations of SM are the pre-thoracic and axillary regions, the face, the back and the buttocks, whereas the scalp is less often affected. In one-third of cases, these cysts are complicated by inflammatory suppurative episodes leaving permanent scars. These episodes are difficult to distinguish from hidradenitis suppurativa (HS). However, cysts in SM appear first and stay un-inflamed in most cases, whereas in HS they usually form after a flare during the healing process. Their histopathology is also different. Finally, suppurative episodes of SM on the scalp can also mimic dissecting cellulitis, but the association of dissecting cellulitis with PC-17 has not been reported to our knowledge.

In conclusion, although SM is a common manifestation of PC-17, suppurative complication of the scalp is extremely rare in this condition. The considerable intra-familial variability in the disease phenotype associated with the common p.Asn92Ser *KRT17* mutation suggests the implication of additional factors.

Figures legends

Figure 1. Clinical features of the mother

(a) multiple steatocystomas of the face predominating on the forehead. **(b)** focal plantar keratoderma of the heel.

Figure 2. Clinical features of the proband

(a) alopecic and cicatricial plaques of the vertex. **(b)** microcysts of the forehead. **(c)** pachyonychia of fingernails. **(d)** histology of a scalp lesion showing an empty cyst delineated by a corrugated cyst wall consisting of a squamous epithelium with an eosinophylic lining with no granular

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