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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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Steatocystoma multiplex: keratin 17 – the key player?

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MADAM, Steatocystoma multiplex (SM) is a rare disorder of the pilosebaceous unit characterized by the eruption of numerous sebum-containing dermal cysts. Most cases are sporadic; however, familial cases with autosomal dominant inheritance have also been described.[1] The aetiopathogenesis of SM remains elusive but there are several hypotheses to explain its cause, such as it originating from sebaceous retention cysts, or representing a naevoid malformation of the pilosebaceous duct. Surgical removal and decapitation of the cyst surface are the most frequently applied therapeutic options. Mutations in the keratin 17 (K17) gene (*KRT17*) have been repeatedly reported for familial cases of SM. K17 is a type I keratin expressed in a number of epidermal appendages, such as the nail bed, hair follicles and sebaceous glands. Here, we present a family comprising five affected individuals with SM with remarkably varying severity.

The index patient is a 46-year-old patient who presented in our clinic with an inflamed and painful tumour on his left cheek (Fig. 1a). The patient reported that similar lesions had occurred in the past, leading to numerous consultations with surgeons and dermatologists. Upon further examination, hundreds of dermal to subcutaneous nodules distributed all over the patient's body were found, with an accentuation on the upper trunk (Fig. 1b). The patient's history revealed that only a few lesions had been present since birth, and the majority appeared during adolescence. The skin lesions were yellowish to skin-coloured nodules lacking a central pore (Fig. 1a). The patient's family history revealed that his mother, his older brother and his two children were similarly affected with various severity (Fig. 2b), whereas the index patient showed the most extensive presentation compared with his older brother and his mother (Fig. 1c,d). No nail changes were found among the affected individuals.

Ultrasound examination revealed the characteristic morphology of a cyst. Histopathology showed the picture of a thin-walled cyst, filled with trichilemmal horn and homogeneous

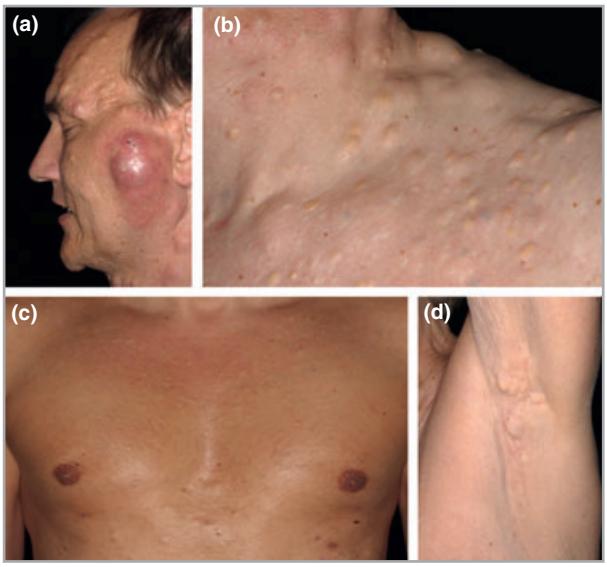

Fig 1. Clinical phenotype: (a) dermal to subcutaneous painful tumour on the left cheek of the index patient and (b) multiple yellowish to grey nodules in the upper trunk and shoulder region. (c) Multiple, scattered small yellowish to grey nodules on the trunk of the index patient's brother. (d) Yellowish indolent nodules and tumours in the axillary region of the index patient's mother.

sebum. The lining of the cyst was composed of a stratified squamous epithelium consisting of few cell layers, lacking a granular layer. In addition, numerous sebaceous glands in or adjacent to the cyst wall were present (Fig. 2a). Based on these findings the diagnosis of SM was made.

After informed consent was obtained, blood samples were taken from the index patient and three affected family members. DNA was extracted from peripheral blood leucocytes using standard methods. Polymerase chain reaction was performed on DNA samples of the affected family members and on a nonrelated control person using standard conditions with primer pairs covering exon 1 of the *KRT17* gene.

Sequencing analysis of the index patient revealed the heterozygous missense mutation c.280C>T in exon 1 of *KRT17* (Fig. 2c). We confirmed cosegregation in all affected patients. The mutation c.280C>T, which leads to the amino acid exchange p.R94C, was previously reported in other families with SM and pachyonychia congenita (PC) type 2 (PC-2).[2]

The clinical diagnosis of SM is usually straightforward. However, the index patient's severe manifestation compared with the other family members gave indication to genetic analysis. Sequencing analysis confirmed the clinical diagnosis in the family and revealed a heterozygous missense mutation in exon 1 of *KRT17*. This and other mutations in *KRT17* have been described not only in patients with SM, but also in those with PC-2. PC-2 comprises a group of autosomal dominantly inherited diseases characterized by hypertrophic nail dystrophy and varying features of ectodermal dysplasia.[2] Notably, no signs of PC and no nail changes were found among the family members described in this study.

The question of whether SM is a variant of PC-2 or whether both diseases represent two distinct entities is still unanswered, although patients with the c.280C>T mutation were reported to develop exclusively either clinical features of PC or SM.[2] In general, the mutations found in SM are localized in the same gene regions of *KRT17* or are even the same as those for PC-2.[3–5] This observation has been explained by the existence of further factors, such as distinct modifier genes influencing the course of the disease.[3] To date, no specific

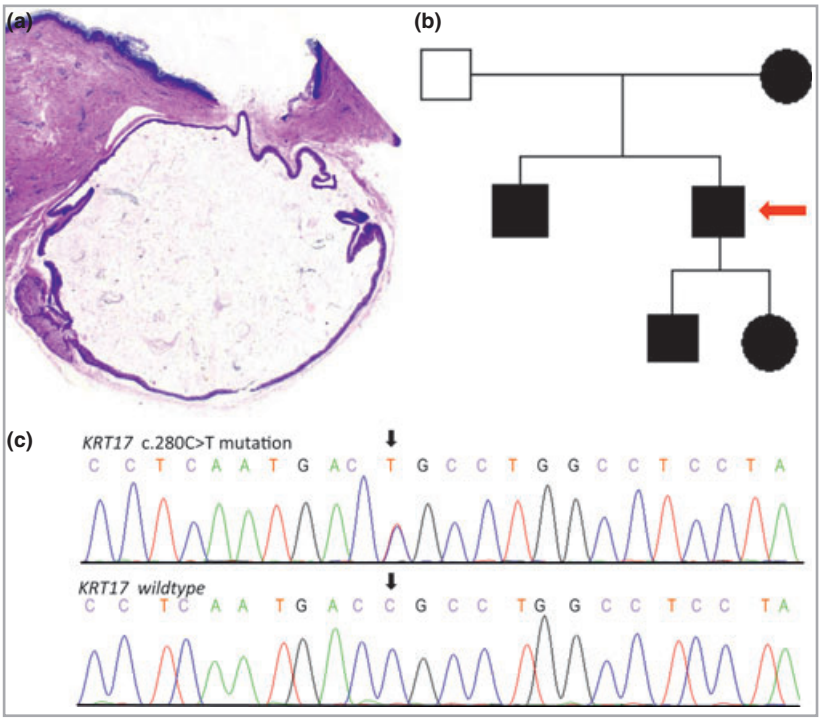

Fig 2. (a) Histopathology reveals a cystic structure, filled with trichilemmal horn and homogeneous sebum. The lining of the cyst is composed of stratified squamous epithelium consisting of few cell layers, lacking a granular layer. Numerous sebaceous glands in or adjacent to the cyst wall are present. (b) Pedigree of the family. The arrow indicates the index person. Blackened symbols, affected individuals; circle, female; square, male. (c) Sequencing analysis reveals a heterozygous c.280C>T transition in exon 1 of *KRT17* in the index patient compared with a wild-type *KRT17* sequence.

accessory genes have been identified in PC-2 or SM families, leading to the distinct phenotypes. Further investigation is needed to evaluate additional environmental and/or genetic factors besides K17 mutations to understand better the pathogenesis of SM and PC.

In summary, we identified a known mutation in the *KRT17* gene in a family with SM. However, we have demonstrated a broad range of expression in a single pedigree and herewith expand the spectrum of clinical manifestations of SM.

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Acknowledging island pedicle flaps for the repair of defects of the medial canthus

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Madam, I read with great interest the recent article published in this Journal by Skaria regarding the utility of island pedicle flaps (IPF) for the aesthetic single-stage reconstruction of surgical defects of the medial canthus.[1] The author very eruditely discusses the design, execution and excellent cosmetic results that may be achieved when performing this repair in a difficult location. Although I agree with the author that this repair option is not commonly discussed in 'textbooks', it should be noted that a large series regarding the utility of an IPF in medial canthal defects was recently published in the reconstructive literature.[2]

The option of an IPF repair in the medial canthus is attractive due to the inherent efficiency of tissue dissection, a reduction in the chances of inducing suboptimal canthal webbing and enabling the principles of cosmetic subunit repair to be respected. I, like the author, elevate IPFs using a bilevelled tissue dissection technique, resulting in an obliquely orientated pedicle which allows a wide range of flap movement compared with 'conventional' IPF pedicles. It should be recognized, however, that this technique of tissue dissection was first promulgated by Chan[3] in the reconstructive literature in the 1980s, more than 15 years before the author's publication in the dermatology literature.[4]

In the medial canthus, I have also found that creating a rotating[5] or lenticular[6] IPF is not only invaluable in reducing the chances of canthal webbing but also that the rotational element enables larger defects to be closed with a single flap as opposed to two opposing IPFs. This rotational element also enables the flap to be pexed (if so required) to the periosteum of the upper nasal sidewall; however, in my experience, for smaller IPFs such as those presented, a pexing suture may compromise the vascularity of the flap and thus may be avoided if the flap is advanced slightly beyond the most distal point of the defect and then the straight limb of the 'Y' sutured first, enabling the flap to be 'supported' in place.

The IPF is a very attractive single-stage repair for defects of the medial canthus and I commend the author for raising its profile in the dermatology literature.

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