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QUIZ SECTION

Palmoplantar Hyperkeratoses and Hypopigmentation: A Quiz

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A 17-year-old German girl presented with painless hyperkeratoses of the palms and soles of the feet, which had been noted immediately after birth, and which had been unsuccessfully treated, as viral warts. Her medical and family histories were unremarkable. Physical examination revealed pink-yellowish papulous hyperkeratoses, sized 2–10 mm, on both soles (Fig. 1A), and fewer similar lesions on the palms with no involvement of the dorsal sides. Moreover, irregular-shaped hypopigmented macules, up to 2 cm in diameter, were noted on the upper and lower extremities, sparing the hands, feet, face and trunk (Fig. 1B). According to the girl's mother, these "white spots" had also been present since birth. The rest of her skin, hair, teeth, nails and mucous membranes appeared normal. Skin biopsy specimens were taken from a plantar lesion for light microscopy (Fig. 2) and ultrastructural analysis.

What is your diagnosis? See next page for answer.

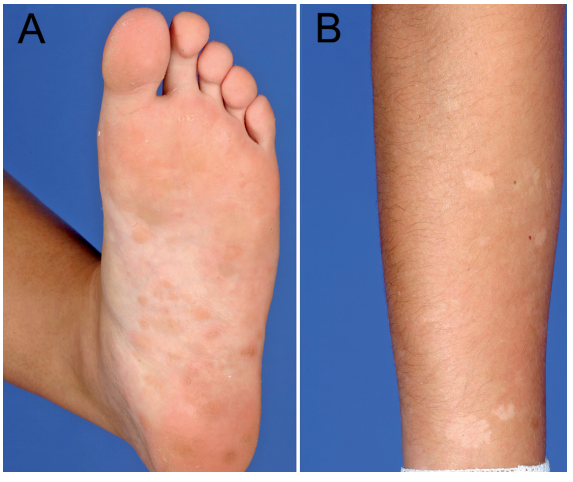

Fig. 1. (A) Papulous hyperkeratoses, up to 1 cm in diameter, on the soles. (B) Irregular-shaped hypopigmentations on the forearm.

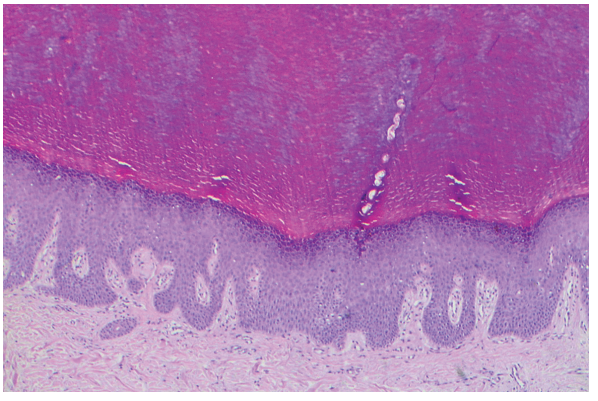

Fig. 2. Haematoxylin eosin-stained skin biopsy specimen from a hyperkeratotic papule, showing massive orthohyperkeratosis, acanthosis and a broad granular layer. Magnification: ×20.

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ANSWERS TO QUIZ

Palmoplantar Hyperkeratoses and Hypopigmentation: Comment

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Diagnosis: **Cole disease**

Fig. 2 shows acanthosis with a broad granular layer, massive orthohyperkeratosis and a sparse perivascular inflammatory infiltrate in the upper dermis. There were no signs of epidermolytic hyperkeratosis, cytolysis, vacuolization, elastorrhexis or parakeratosis, and no cornoid lamellae. In glutaraldehyde-fixed specimens analysed by electron microscopy, tonofilaments, keratinosomes and keratohyalin appeared normal and no horny lamellae inclusions were noted (not shown). These findings were compatible with hereditary punctate palmoplantar keratosis, but were non-specific. The combination with congenital guttate hypopigmentation led to the diagnosis of Cole disease.

Cole disease is an extremely rare autosomal dominant genodermatosis characterized by co-occurrence of punctate palmoplantar keratoderma with guttate hypopigmentation. The molecular defect underlying Cole disease has not yet been identified. The first family was described by Cole in 1976 (1). Subsequently, one additional family and one single case have been published (2, 3). In previous reports, palmoplantar lesions and hypopigmentations were either present at birth or developed in early infancy until 3 years of age (1–3). Hypopigmentations are typically irregular in shape and often limited to the extremities (2, 3), but the young adult described by Cole additionally exhibited guttate hypopigmentations on the trunk, and small islands of normal pigmentation within hypopigmented macules (1). Histology of hypopigmented areas shows normal melanocyte density and regular amounts of melanosomes within melanocytes, but decreased melanin and melanosomes within keratinocytes, suggesting defective melanosome transport (2).

Differential diagnosis of localized de- or hypopigmentation in childhood includes vitiligo, piebaldism, Waardenburg syndrome, Tietze's syndrome, ash-leaf macules in tuberous sclerosis, and hypomelanosis of Ito, but none of these disorders is associated with palmoplantar hyperkeratoses (4). Punctate palmoplantar keratoderma is a feature of Buschke-Fischer-Brauer disease, focal acral hyperkeratosis, acrokeratoelastoidosis and punctate porokeratosis, which, however, manifest later in life (5). The last two are distinguishable by characteristic histological features, i.e. cornoid lamellae and parakeratosis or disorganized elastic fibres. Co-occurrence of guttate hypopigmentation and palmoplantar hyperkeratosis may be found in Darier's disease and in epidermolysis bullosa simplex with mottled pigmentation (6, 7), but do not fit with the presented case.

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