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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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Dermatology

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Steatocystoma multiplex and Oligosymptomatic Pachyonychia congenita of the Jackson-Sertoli Type

Key Words
Steatocystoma multiplex
Pachyonychia congenita
Keratins

Abstract
A family with affected members, previously reported to carry an R94H mutation of keratin K17, and characterized by a variable and oligosymptomatic form of pachyonychia congenita of the Jackson-Sertoli type with steatocystoma multiplex, is described in detail.

Introduction
Pachyonychia congenita (MIM216700, MIM167210) and steatocystoma multiplex (MIM184500) are autosomal dominant disorders of keratinization [1-3]. Their concomitant inherited occurrence is known as pachyonychia congenita of the Jackson-Sertoli type [4] and transmitted by a single gene defect [3, 5].

Two forms of pachyonychia congenita are well characterized [4, 6]. The more frequent Jadassohn-Lewandowsky syndrome (pachyonychia congenita type I, MIM167200) is caused by mutations of keratins K6 and K16 resulting in thickened nails, oral leukokeratatoses, follicular keratoses, focal insuldbulged palmpplanar keratoderma and rare blistering [7, 8]. The rare Jackson-Sertoli syndrome (pachyonychia congenita type II, MIM167210) includes multiple epidermal cysts, thickened nails, focal insuldbulged palmpplanar keratoderma, dry or helicatated hair and neona
tal tead, is restricted to keratin K17 expressing tissues and is caused by mutations of the keratin K17 gene [8, 9].

Variable oligosymptomatic variants of the Jadassohn-Lewandowsky syndrome, such as focal insuldbulged palmpplanar keratoderma, are well documented [10, 11], however, similar variants of the Jackson-Sertoli syndrome are less characterized.

A family with 8 members affected by the Jackson-Sertoli syndrome is described. Three siblings were examined and exhibited a variable oligosymptomatic phenotype even though all carried the same keratin K17 mutation [9].

Case Reports
The pedigree of family ND is shown in figure 1. All affected individuals were anamnestically considered to suffer from steatocystoma multiplex and developed multiple sebaceous cysts at puberty. ND-3.2, aged 47, showed numerous large cysts on the back, groin and perineal areas (fig. 2A). ND-3.3, aged 42, and ND-3.4 (fig. 2D), aged 31, showed numerous small cysts on the neck, axillae, groin and submammary areas. Thickening of nails was absent in ND-3.2, restricted to thumbs in ND-3.3 and present on all fingers in ND-3.4 (fig. 2E). Nail changes anamnestically appeared only when ND-3.3, during adolescence, started a nervous tick with rubbing and flipping thumb nails and when ND-3.4, during childhood, started to bite fingernails. Nail changes were discrete and the affected finger nail plates had a thickness of about 1.5-3 mm in ND-3.3 and ND-3.4. Toenails were normal in all siblings. Insulated plantar and less severe palmar keratoderma was not noticed by the patients but more severe in ND-3.2 (fig. 2C) than in the sisters ND-3.3 and ND-3.4 (fig. 2F). Slight helcoidal hair was present in ND-3.2 but not noted subjectively (fig. 2B). Follicular keratoses or oral leukokeratoses were absent in all siblings. Neonatal or otherwise abnormal teeth were not noted. No other changes of tegument were noted. For a compilation of skin changes, see table 1.
Table 1. Clinical synopsis

<table>
<thead>
<tr>
<th></th>
<th>ND-3.2</th>
<th>ND-3.3</th>
<th>ND-3.4</th>
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<tbody>
<tr>
<td>Sebaceous cysts</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Number</td>
<td>+</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Size</td>
<td>2/20: +</td>
<td>10/20: (+)</td>
<td></td>
</tr>
<tr>
<td>Pachyonychia</td>
<td>+</td>
<td>(+)</td>
<td>(+)</td>
</tr>
<tr>
<td>Focal plantar keratoderma</td>
<td>(+)</td>
<td>(+)</td>
<td>(+)</td>
</tr>
<tr>
<td>Focal palmar keratoderma</td>
<td>(+)</td>
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<td>(+)</td>
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<tr>
<td>Helicocritica</td>
<td>-</td>
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<tr>
<td>Follicular keratosis</td>
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<tr>
<td>Leukokeratosis</td>
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<tr>
<td>Neonatal teeth</td>
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<td>Blistering</td>
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Fig. 2. Clinical findings in patients ND-3.2 (A–C) and ND-3.4 (D–F).

Discussion

The new nosological entity of keratin disorders now includes epidermolysis bullosa simplex (K5/K14), bullous congenital ichthyosiform erythroderma (K1/K10), ichthyosis bullosa (K2), pachyonychia congenita type 1 (K6/K16), pachyonychia congenita type II (K17), diffuse non-epidermolytic palmoplantar keratoderma (K1), diffuse epidermolytic palmoplantar keratoderma (K9), focal insidious non-epidermolytic palmoplantar keratoderma (K16), and white sponge nevus (K4/K13) (for ref. see 12, 13).

The recent insights into the molecular pathogenesis of keratin disorders have provided proof of old clinical and morphological concepts in some instances, e.g. the substantiated separation of bullous congenital ichthyosiform erythroderma of Brocq from ichthyosis bullosa of Siemens [14, 15] or diffuse palmoplantar keratodermas from insulated forms [11, 16, 28].

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17) which are caused by different gene defects. Other concepts were shaken in their nosological basis such as the thin and weak delineation of autosomal dominant ichthyosis exfoliativa from ichthyosis bullosa of Siemens [18–20], or Jadassohn-Lewandowski syndrome from focal insolated non-epidermolytic palmar-planter keratoderma [8, 11] which are caused by mutations of the same keratin genes.

By analogy, the nosological separation of the inherited form of steatocystoma multiplex from Jackson-Sertoli syndrome might be inadequate. The present cases charac-
terized by an R94H keratin 17 mutation [9] rather suggest that steatocystoma multiplex simply represents a monosymptomatic variant – and a diagnostic key symptom – of the Jackson-Sertoli syndrome. If the sister's ND-3.3 and ND-3.4 had not induced nail changes by continuous physical stress, their phenotype would have easily passed as steatocystoma multiplex. Future molecular analysis will resolve the issue whether an autosomal dominant form of steatocystoma multiplex without associated findings and without keratin 17 mutations truly exists.

Acknowledgments

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Key Words

Malignant at Cutaneous Pathogenesis Therapy

Introduction

Malignant scribed for t more as a 6 years later, g sizing its oft e ease mainly most part oc- mital cases i now, about 1 the literature

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