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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 REPORT

Pachyonychia congenita tarda

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SUMMARY

A 42-year-old man presented with painful toenails which were overcurved transversely and onycholytic. Examination revealed that all toenails, the thumbs and index fingers were similarly affected. In addition, he had a small area of leukokeratosis in the mouth, epidermal cysts of the scrotal skin and a small area of hyperkeratosis on the ulnar borders of his hands. His characteristic nail changes began in the great toenails at the age of 20 years. After renal transplantation at age 59, the other nails changed and he developed the features described above. His sister has overcurvature of the fifth toenails. A diagnosis of pachyonychia congenita tarda was made. His case is compared with 14 other reported cases of this rare syndrome.

Key words: epidermal cysts, immunosuppression, keratin 17, nails, oral leukokeratosis, palmar hyperkeratosis, renal transplant recipient, scrotum.

INTRODUCTION

Pachyonychia congenita refers to a group of rare disorders characterized by transverse overcurvature and onycholyosis of the nails developing in infancy. The condition is separated into types by the presence of associated features; different keratin abnormalities have been described in the two main types. Pachyonychia congenita tarda is a rare form in which nail changes develop in the second or third decade.1 We describe a 42-year-old man with this condition which was exacerbated after renal transplantation.

CASE REPORT

A 42-year-old man presented with abnormal painful toenails. Four years earlier he had a renal transplant for treatment of end-stage renal failure due to vesico-ureteric reflux. His medications were azathioprine, cyclosporin, prazosin, amlodipine, calcitriol and metoprolol.

He gave a history of being aware of an abnormality of his fifth toenails from infancy. From the age of 20 years his great toenails became thickened and lifted distally, overcurved transversely and painful. He had one nail surgically removed but it later grew back unchanged. After his renal transplant in 1995, he developed similar changes in the rest of his toenails and also those of his thumbs and index fingers. He also developed epithelial cysts in the skin of his scrotum and these continued to slowly increase in number. After his transplant he also developed bilateral palmar thickenings of the buccal mucosa. He said that his eyebrows became bushy and required constant trimming, his scalp hair grew thicker and the hairs on his legs became curlier, changes he attributed to therapy with cyclosporin. He described a minor abnormality of the skin of the ulnar border of his hands. At this site he developed small tumours which discharged a thick, whitish material leaving a firm lump in the skin. He was unaware of a history of natal teeth, hyperhidrosis, blisters, hoarseness or corneal dystrophy. He complained of pain in his toenails, especially if wearing shoes or walking. He worked as a truck driver and wore boots to work.

He said that his 56-year-old sister had some transverse overcurvature of her fifth toenails. She had no cutaneous cysts. Neither parent is said to have any abnormalities but none of his family members was available for examination.

Examination of the patient showed wedge-shaped nails with transverse overcurvature, discolouration, distal onycholyosis and subungual hyperkeratosis of the nails of all toes, thumbs and index fingers (Figs. 1–5). Under the left great toenail distally there appeared to be a fibroma. Slight pressure on the toenails caused pain. He had numerous epidermal cysts on the base of the penis and scrotum. There was a focal keratoderma of less than 1 cm² on the ulnar borders of both hands. In his mouth was a small area (approximately 1 cm²) of leukokeratosis on the buccal mucosa near the commissures (Fig. 4). His hair was woolly and his eyebrows were bushy. Clinical features not present included hyperkeratoses of the soles, elbows or knees; follicular hyperkeratoses; blisters; hyperhidrosis; hoarse voice; and corneal dystrophy. Investigations included subungual scrapings and nail clippings from the great toe, fourth toe and thumbnails. Microscopy and culture for fungi were negative on all specimens. Swabs from the buccal mucosa grew normal bacterial flora and Candida albicans. A punch biopsy of the ulnar border of the hand showed hyperkeratosis consistent with the biopsy site, focal compact parakeratosis and a small keratin granuloma. Biopsy of a scrotal lesion showed an epidermal cyst. X-ray of hands and feet did not demonstrate any bony
Figure 1  Toenails showing overcurvature, subungual hyperkeratosis and fibroma, and onycholysis.

Figure 2  Thumb- and fingernails showing similar changes of pachyonychia congenita.

Figure 3  Lateral view of changes in the index fingernail.

Figure 4  Leukokeratosis of the buccal mucosa.

Table 1  Summary of reported features of pachyonychia congenita tarda

<table>
<thead>
<tr>
<th>Ref. no.</th>
<th>Sex</th>
<th>Age onset (years)</th>
<th>PPKD</th>
<th>Leukokeratosis</th>
<th>Cutaneous cysts</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>15</td>
<td>R palm, Soles</td>
<td>Mild, buccal</td>
<td>Absent</td>
</tr>
<tr>
<td>1</td>
<td>F</td>
<td>Teenage</td>
<td>Soles</td>
<td>Tongue, buccal</td>
<td>Scalp</td>
</tr>
<tr>
<td>1</td>
<td>M</td>
<td>Teenage</td>
<td>Mild, Soles</td>
<td>Tongue, buccal</td>
<td>n.d.</td>
</tr>
<tr>
<td>1</td>
<td>F</td>
<td>Teenage</td>
<td>Absent</td>
<td>Mild</td>
<td>n.d.</td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>59</td>
<td>Palms, Soles</td>
<td>n.d.</td>
<td>n.d.</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>44</td>
<td>Warty palms, Soles</td>
<td>n.d.</td>
<td>n.d.</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>20s</td>
<td>Absent</td>
<td>n.d.</td>
<td>n.d.</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>50s</td>
<td>Absent</td>
<td>n.d.</td>
<td>n.d.</td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td>20</td>
<td>Thick, Soles</td>
<td>Scrotal Tongue</td>
<td>Absent</td>
</tr>
<tr>
<td>8</td>
<td>M</td>
<td>10</td>
<td>1st palm, Soles</td>
<td>n.d.</td>
<td>Hundreds</td>
</tr>
<tr>
<td>9</td>
<td>M</td>
<td>12</td>
<td>Palms, Soles</td>
<td>Tongue, buccal</td>
<td>Absent</td>
</tr>
<tr>
<td>12</td>
<td>M</td>
<td>15</td>
<td>Palms, Soles</td>
<td>n.d.</td>
<td>n.d.</td>
</tr>
<tr>
<td>Present</td>
<td>M</td>
<td>20</td>
<td>Mild, palm</td>
<td>Buccal</td>
<td>Scrotal cysts</td>
</tr>
</tbody>
</table>

PPKD, Palmoplantar keratoderma; absent, author specifies absence of this feature; n.d., no details reported on this feature; R, right; 1, left; M, male; F, female; present, present study.
abnormality of the digits to account for the tumour underneath the anterior border of his left great toenail.

Subsequent treatment with oral nystatin had no effect on the oral leukokeratosis. A repeat swab following treatment was not performed. He was referred for surgical removal of the great toenails and nail matrix ablation.

**DISCUSSION**

The term pachyonychia congenita (PC) refers to a group of rare disorders usually inherited as an autosomal dominant trait. There have been approximately 250 reports of this syndrome in the literature. There is a number of classifications of this disease and that proposed by Shonfeld is widely accepted. The characteristic nail changes of transverse overcurvature, distal onycholysis, subungual hyperkeratosis and variable discoloration are a common feature of all types. Type 1 (Jadassohn–Lewandowsky, PC-1) also consists of hyperkeratosis of palms, soles, knees and elbows, follicular hyperkeratosis and oral leukokeratosis. Occasionally, blister formation, hoarse voice due to laryngeal involvement, and hyperhidrosis occur. In type 2 (Jackson–Lawler, PC-2) the palmar planar keratoderma and oral changes are less marked or absent. In addition, a history of natal teeth and the development of epidermal cysts or sebostomas are found. Type 3 (Schafer–Brunauer, PC-3) has the features of PC-1 and also leukokeratosis of the cornea. A fourth form in which the typical nail changes began in the second and third decades of life has been described as pachyonychia congenita tarda. Other authors have since reported similar cases.

There have been reported cases which do not fit this classification clearly. A Moroccan family has been described with early onset nail changes in the absence of other associated features.

Our case demonstrates the typical nail changes developing in the third decade of life and progressing after renal transplantation. The reported early onset abnormality of the fifth toenails seemed minor and may have been irrelevant. The epidermal cysts on the soles were more localized than those usually reported in PC-2. Similarly, the oral leukokeratosis and palmar hyperkeratosis were minor features but consistent with PC-2. The significance of the palmar keratin cyst is uncertain. The changes in his scalp and eyebrow hair may have been due to therapy with cyclosporin which regularly causes hypertrichosis. His X-rays were normal but bone erosions have been reported in association with PC tarda.

A literature search revealed 14 reported cases of the tarda variety (Table 1). Some of these cases could be classified as PC-1 and others as PC-2. The commonest features were nail changes and palmpoplantar keratoderma. The nail changes were reported to affect all fingers and toes, unlike our case where there was sparing of some fingers. There was a great variation in the degree of palmpoplantar hyperkeratosis in different cases with some cases showing diffuse warty thickening of the palms and soles and others describing more focal and asymmetrical keratoderma. This heterogeneity of expression of associated hyperkeratoses is a feature of both classical and late onset pachyonychia congenita. In only two cases were cutaneous cysts noted. In one patient, the scalp was diffusely affected, and in the other there were hundreds of epidermal and vellous hair cysts distributed over the entire skin. In one report, two brothers developed whitening of the toenails (one of them at age 12 years), rather than the typical thickening and onycholysis. These authors refer to a report in the German literature in which pachyonychia was absent in three of 93 cases of pachyonychia congenita reviewed.

Although our patient reported minor abnormalities of his fifth toenails from infancy, the characteristic nail changes developed in later life and so he should be classified as one of the tarda group. Some reported cases of the PC tarda variety showed associated features from infancy, but it is the development of the characteristic nail changes in the second or third decades of life instead of in infancy that defines this tarda variety. Activation of the mutant allele may, thus, be a progressive event or some environmental or immunologic factor may be relevant. In our patient, most of the changes occurred when the patient was immunosuppressed in order to prevent renal transplant rejection. Thus, immune surveillance may be an important factor in gene expression. Candida albicans infection superimposed on leukokeratosis of the tongue in association with a defect of immune response to C. albicans has been reported with PC. Our patient, similarly, grew C. albicans on culture of his oral lesions but did not respond to antifungal treatment with oral nystatin. This may have been due to his immunosuppression; however, the area of leukokeratosis was fixed in size and not suggestive of oral candidiasis as it appears in an immunosuppressed patient.

Treatment is with keratolytics and emollients for the hyperkeratotic changes. Oral retinoids have been reported to alleviate the palmoplantar keratoderma, subungual hyperkeratosis, and the keratotic patches on the knees and in the mouth. Surgical treatment involves nail removal and various techniques to ablate the nail matrix.

**REFERENCES**