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Case report

A case of pachyonychia congenita with unusual manifestations: an unusual type or a new syndrome?

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Conflicts of interest: None.

Abstract

A 30-year-old man presented with lesions on his oral mucosa and soles. There were no similar complaints in his family members. The dermatological examination revealed follicular hyperkeratosis on his trunk and upper extremities and flesh-colored, firm cystic lesions on his axillae. He had focal, painful, hyperkeratotic areas sited particularly on both his soles and palms. In addition to these, leukokeratosis and ulcerative areas on buccal, labial mucosa, tongue, and at corners of the mouth, and complete loss of teeth was observed. The proximal layering was revealed on all of his nails. The laboratory investigations produced normal results except the deficiency of immunoglobulin A. The psychiatric examination revealed mild mental retardation. Keratin gene (KRT6a, KRT6b, KRT16, and KRT17) mutations for pachyonychia congenita were negative. He got removable dental prosthesis because of inadequate alimentation. Squamous cell cancer developed on lower lip mucosa during follow-up. We present an individual who had different nail dystrophy, epidermal cysts, mental retardation, blepharitis, complete loss of teeth, and negative keratin gene mutations for pachyonychia congenita and developed squamous cell cancer on the oral leukokeratosis lesions. We think that the present case may be an unusual new type of pachyonychia congenita.

Introduction

Focal, areate or nummular, and linear or striate keratodermas have been distinguished. Focal keratodermas may be isolated or associated with other cutaneous or ectodermal findings. Pachyonychia congenita (PC) is a rare form of focal keratodermas, having characteristic nail findings. Focal palmoplantar keratoderma, leukokeratosis, and other ectodermal defects are variably expressed.[1–7] We present a case who had epidermal cysts, mental retardation, blepharitis, complete loss of teeth, and deficiency of IgA in addition to clinical features of PC, without the characteristic nail dystrophy and negative keratin gene mutations (KRT6a, KRT6b, KRT16, and KRT17) for PC. This case is similar to PC in terms of some clinical findings but is different because of different nail findings, development of squamous cell cancer (SCC), and negative keratin gene mutations.

Case

A 30-year-old man presented with severely painful callosities localized on soles since he was one year old. He also had hyperhidrosis and sometimes blisters on his feet. Oral mucosal lesions started 15 years ago and spread gradually. His parents were not relatives, and there were no similar complaints in his family members.

The physical examination revealed rough hairs, bilateral blepharitis, absence of teeth, and leukokeratosis on buccal and labial mucosa, tongue, and at the corners of the mouth (Fig. 1). There was follicular hyperkeratosis on

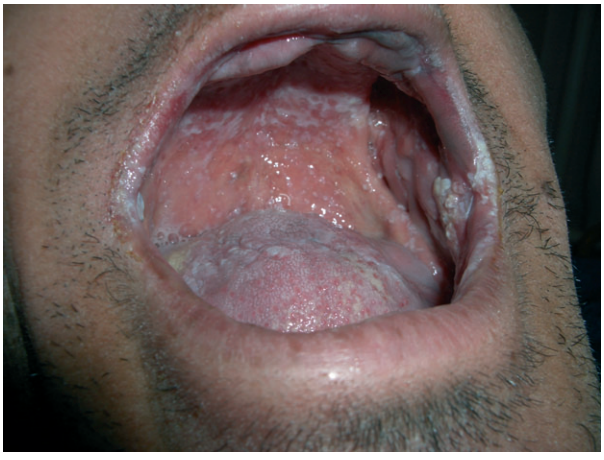

Figure 1 Leukokeratosis and ulcerative areas on buccal, labial mucosa, tongue, and at the corners of the mouth

the trunk and both arms, and flesh-colored, firm cystic lesions on his axillae (Figs. 2 and 3). The yellowish, well defined hyperkeratotic lesions were localized commonly at pressure sites on his soles. Hyperkeratotic lesions on plantar surfaces were extremely painful and restricted mobility. The hyperkeratosis of palms was less pronounced (Fig. 4). Nail dystrophy that showed proximal layering was observed on all of his nails, but it was most prominent on fingernails (Fig. 5).

Laboratory tests were in normal ranges except IgA deficiency. Serum tyrosine level was 1.27 mg/dl (normal, <3 mg/dl). The panoramic dental radiography showed no teeth other than two grained teeth, and dental bones were normal. Abdominal ultrasonography and esophagogastroduodenoscopy produced normal results. The cranial magnetic resonance imaging showed cortical atrophy and minimal dilatation of lateral and fourth ventricles of brain. Psychiatry consultation revealed slight mental retardation.

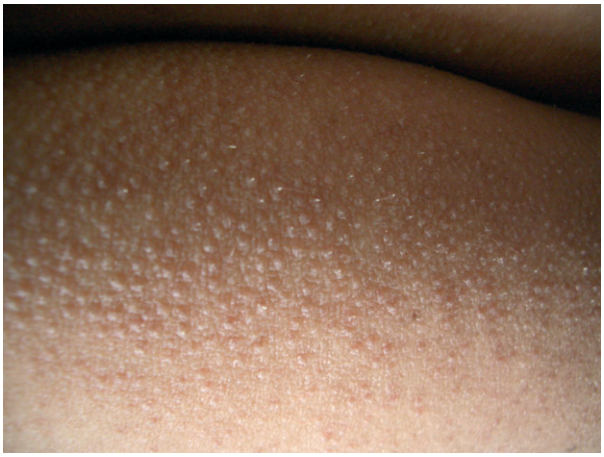

Figure 2 Follicular hyperkeratosis on the arm

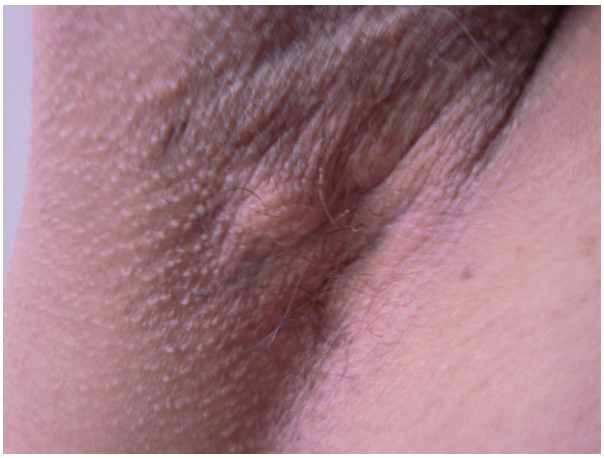

Figure 3 Epidermal cysts on the axilla

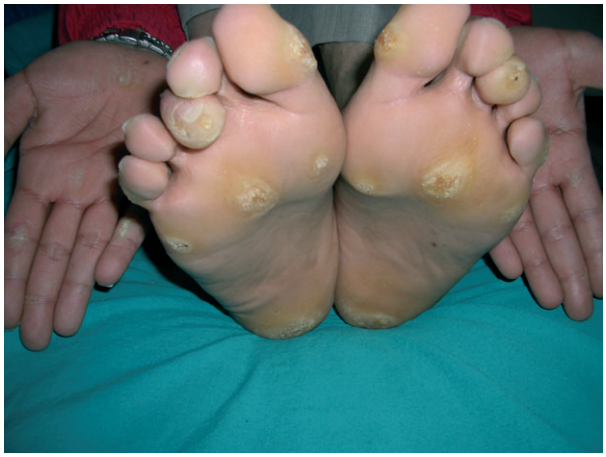

Figure 4 Focal hyperkeratosis over the palmoplantar pressure points

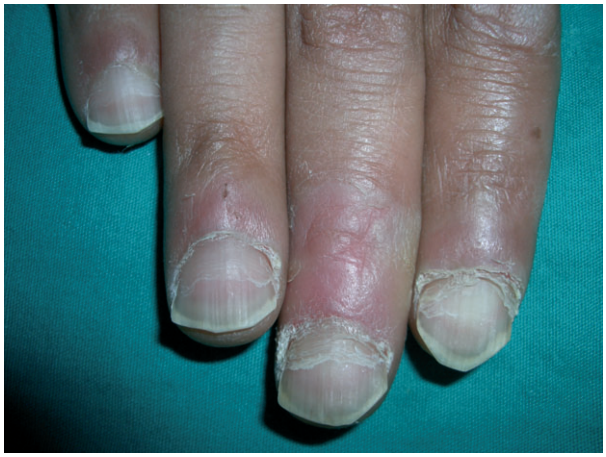

Figure 5 Dystrophy of fingernails

The histopathological examination of cystic lesions demonstrated epidermal cyst, and the lesions on the sole revealed compact hyperkeratosis, minimal papillomatosis, and hypergranulosis (Fig. 6a,b).

The genetic investigation for KRT6a, KRT6b, KRT16, and KRT17 mutations was performed, and the results were negative. Acitretin treatment (1 mg/kg per day) was started for painful palmoplantar hyperkeratosis. Although the pain of callosities dramatically regressed, therapy was discontinued because it caused severe headache.

The patient got a removable total dental prosthesis for oral rehabilitation, as his nutrition was poor because of lack of complete teeth. SCC developed on the lower lip mucosa one year after the prosthesis (Fig. 7). The SCC lesion was totally excised, and radiotherapy was then given. He has been followed up by otolaryngology.

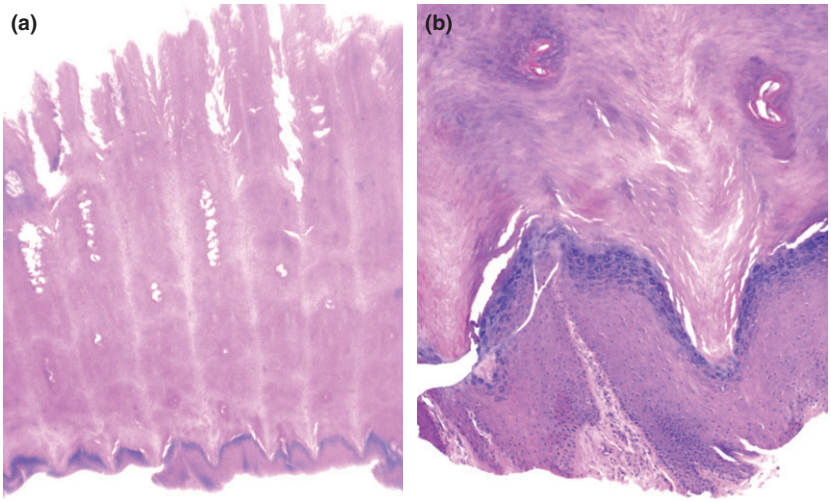

Figure 6 (a) Prominent hyperkeratosis and hypergranulosis (hematoxylin and eosin, ×10). (b) Prominent hyperkeratosis and hypergranulosis (hematoxylin and eosin, ×100)

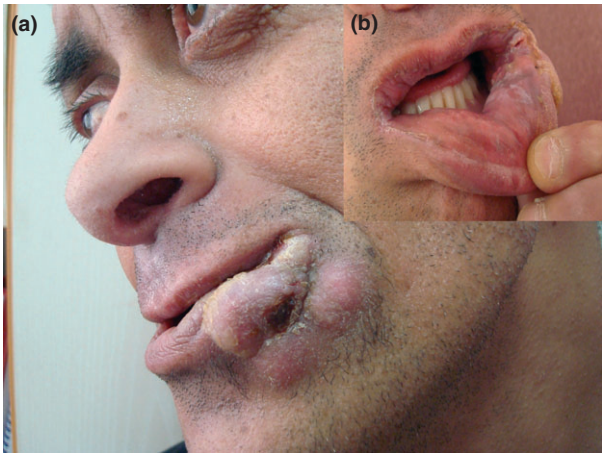

Figure 7 Squamous cell carcinoma on the lower lip (a), appearance of the lesions from mucosal surface (b)

Discussion

Focal palmoplantar keratoderma with associated features are found in Howel–Evans syndrome, Richner–Hanhart syndrome (tyrosinemia type 1), and PC.[1] The diagnosis of our case as PC was acceptable, because he had painful focal palmoplantar keratoderma, oral mucosal leukokeratosis, nail findings, follicular hyperkeratosis, firm cystic lesions, absence of teeth, and lack of corneal findings, although KRT6a, KRT6b, KRT16, and KRT17 mutations were negative.

PC is a rare group of genodermatosis usually inherited as an autosomal dominant trait. The characteristic finding of PC is typical nail dystrophy. These characteristic nail changes are prominent thickening of the nail bed, often with progressive distal elevation. The character of the nail changes and severity of the dystrophy are variable from patient to patient.[1,8,9] In our patient, we observed proximal layering of all the nails unlike characteristic thickened dystrophic nails of PC.

Two main subtypes of PC have been recognized, the Jadassohn–Lewandowsky (type 1) and Jackson–Lawler syndromes (type 2). Focal palmoplantar hyperkeratosis, follicular keratosis, and oral leukokeratosis are mostly associated with PC type 1. The bullae of palms and soles, fetal or neonatal dentition, and steatocystoma multiplex or epidermal cysts, angular cheilosis, corneal dyskeratosis and cataract, laryngeal lesions, hoarseness, mental retardation, hair anomalies, and alopecia can be less frequently observed in other forms of PC.[7] Our case had blepharitis, loss of teeth, and deficiency of serum IgA in addition to characteristic findings of PC type I.

Even though association of PC and low IgD and high IgM levels have been reported, IgA deficiency and PC have not been reported.[3] The IgA deficiency in our patient may be coincidental as it is a frequent finding in the general population. However, IgA deficiency may contribute to the development of oral lesions.

There is only one report of prosthetic devices in patients with PC in the literature. In this study, it has been reported that prosthetic rehabilitation was made with removable partial dentures for mucosal lesions. The authors have suggested that the oral rehabilitation of patients affected by PC should be directed to eliminate the possibility of chronic trauma to the oral mucosa.[10] In our case, one year after the prosthesis was made, the SCC developed on the oral mucosal leukokeratosis on the

lower lip. To the best of our knowledge, development of SCC on the oral mucosa has not been reported in PC previously. Moreover, it is agreed that the oral lesions do not evolve into SCC.[11] The present case is the first of PC that developed SCC on oral mucosal leukokeratosis. We think that dental prosthesis may contribute to developing SCC by causing chronic trauma.

Dominant-negative mutations in any of the four identified keratin genes (KRT6A, KRT6B, KRT16, or KRT17) cause PC.[6] However, it has been reported that some cases of PC may not show these keratin mutations.[12] The full coding sequences of K6a, K6b, K16, and K17 have been sequenced, and no mutation was identified in our patient. We therefore believe there may be other genes leading to a PC-like phenotype. Clinical diversity may be explained by different gene mutations.

The classification of inherited palmoplantar keratodermas is difficult because of its complexity. Tyrosinemia type 1, Howel–Evans syndrome, and focal palmoplantar and gingival hyperkeratosis were excluded clinically in our case. However, we could not exclude PC in this case because he had similar findings to PC, and we could not prove diagnosis of PC, as he did not have keratin gene mutations. We think that our case may be a new rare form of PC, which stems from different keratin gene mutation, or may be a new syndrome associated with focal palmoplantar keratoderma. In addition, this case is important because of development of SCC on oral mucosal leukokeratosis, and oral mucosal lesions must be followed closely, particularly if the patient has dental prosthesis.

Acknowledgments

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