PACHYONYCHIA CONGENITA TYPE I WITH SEVERE ORAL LEUKOKERATOSIS

Zuhal Kirzioglu [1], *Yildirim Erdogan* [2]*

1. Prof. Süleyman Demirel University, Faculty of Dentistry, Department of Pediatric Dentistry Isparta/TURKEY.
2. Assist. Prof. Pamukkale University, Faculty of Dentistry, Department of Pediatric Dentistry, Denizli/TURKEY.

Abstract

Pachyonychia Congenita (PC) is a rare autosomal dominant keratin disorder that affects a number of ectodermal structures including the nails and palmoplantar skin, and often involves the oral mucosa, tongue, larynx, teeth and hair. Clinical features are usually present at birth or early infancy. There are two main subtypes of PC. Fingernail thickening and oral keratosis are more common and severe in PC-1 and cystic lesions, hair abnormalities, natal teeth and pili torti are more common in PC-2. We report the case of a 6-year-old boy with PC-1 presenting with severe and painful oral leukokeratosis and extensive caries.

Review (J Int Dent Med Res 2012; 5: (2), pp. 88-93)

Keywords: Pachyonychia congenita, oral manifestations, oral leukokeratosis.

Received date: 15 July 2015 **Accept date:** 04 August 2015

Introduction

Pachyonychia Congenita (PC) is an uncommon autosomal dominant keratin disorder that typically affects a number of ectodermal structures including the nails and palmoplantar skin, and often involves the oral mucosa, tongue, larynx, teeth and hair[1-3]. Clinical features are usually present at birth or early infancy [4]. It is estimated that there are 1000–10,000 cases of PC worldwide[5]. It was first described by German dermatologists Josef Jadassohn and Felix Lewandowsky in 1906, who identified a 15-year-old girl with unusual keratinization of the skin and the tongue, and extremely thickened nails of the fingers and toes[6]. At present, the disorder is known as Pachyonychia Congenita Type 1 (PC-1) or Jadassohn–Lewandowsky Syndrome. Another subtype, PC-2 (Jackson-Lawler Syndrome), was described in 1951, and the ratio of PC-1/PC-2 is approximately 3 [7, 8]. Patients with PC-2 tend to have cystic lesions (steatocystoma multiplex, pilosebaceous cysts, and vellus hair cysts), hair abnormalities, natal teeth and pili torti, but fingernail thickening and oral keratosis are more common and severe in PC-1 [3, 6, 9]. However, genotyping has shown that the degree of oral leukokeratosis and nail thickening can be quite variable in both PC-1 and PC-2, and pilosebaceous cysts can be seen in both types [1, 4].

The genetic basis of PC was identified in 1995 by McLean et al. [10], who discovered the first mutations in keratin genes *KRT16* and *KRT17* [11, 12]. Keratin disorders are caused by a mutation in any one of four genes: *KRT6A*, *KRT6B*, *KRT16*, and *KRT17.* These genes encode keratin proteins K6a, K6b, K16, and K17, respectively. Traditionally, mutations in *KRT6A* and *KRT16* are associated with PC-1 and mutations in *KRT6B* and *KRT17* are associated with PC-2 [2, 13].

Most PC patients have oral manifestations, which are more commonly associated with PC-1. Oral leukokeratosis is frequently seen on the tongue and buccal surfaces and is approximately three times more frequent in PC-1 than in PC-2. The gingival surfaces are rarely involved[14]. These oral findings often present soon after birth and may be the earliest signs of PC[14,15]. There are also some varieties, abnormalities and pathologies associated with the dentition and periodontium

Corresponding author:
Dr. Yıldırım ERDOĞAN
Pamukkale University, Faculty of Dentistry, Department of Pediatric Dentistry
20160, Pamukkale Municipalty, Denizli / TURKEY
Tel: 90 258 296 42 04,
Fax: 90 258 296 17 63
E-mail: yldrmerdogan@hotmail.com

such as natal/neonatal teeth, early multiple tooth development and eruption, early primary tooth loss, and mucosal hyperplasia in dental papillae, which relate strongly to the PC-2 phenotype [1].

This paper reports the case of a patient with PC-1, presenting with severe and extended oral leukokeratosis, but no dental variation or anomalies.

Case Report

A 6-year-old boy was referred to the Clinic of Pediatric Dentistry, Dentistry Faculty of Süleyman Demirel University (Isparta, Turkey) for mucosal pain and dental caries (Fig. 1).

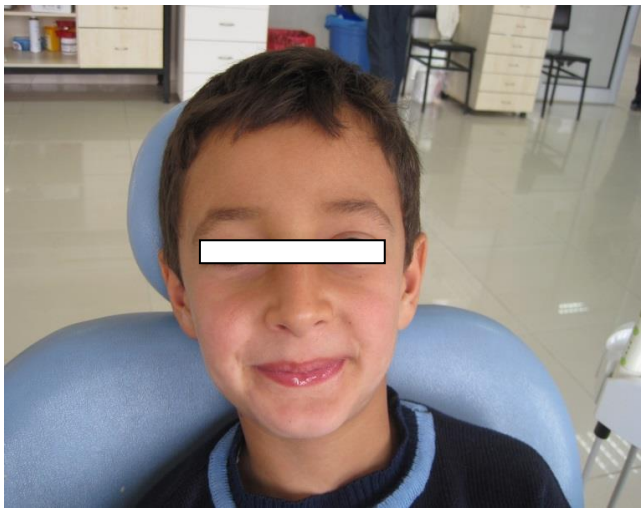

Figure 1. 6 year-old Pachyonychia Congenita type I patient.

A signed informed consent form was received from the parents prior to clinical and radiographical examination. The patient had been diagnosed with PC-1 by the Medical Faculty of Süleyman Demirel University when he was an infant. Hoarseness, nail abnormalities, and white patches in the mouth were seen in first year of life. At the time of presentation at our clinic, the patient was using an oral aromatic retinoid, Acitretin, and a urea-based cream for the symptomatic treatment of the keratinization disorder. No family history of PC was identified. An extraoral examination revealed hyperkeratosis and thickening of all fingernails (Fig. 2) and toenails (Fig. 3), palmoplantar keratoderma (Fig. 4 and 5), and keratotic follicular spikes on the elbow (Fig. 6), and knees (Fig. 7).

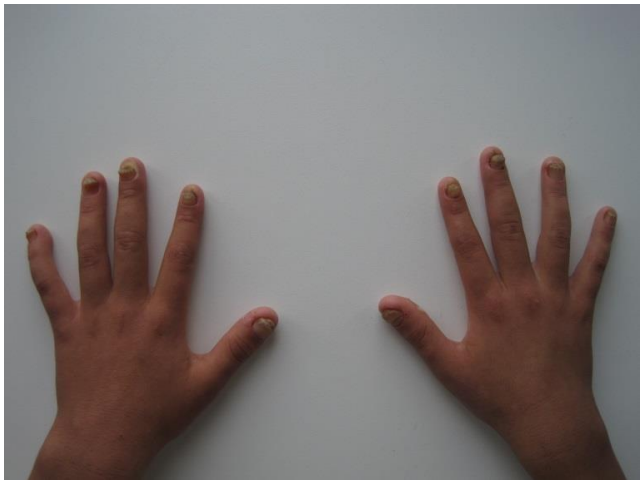

Figure 2. Hyperkeratosis and thickening of fingernails.

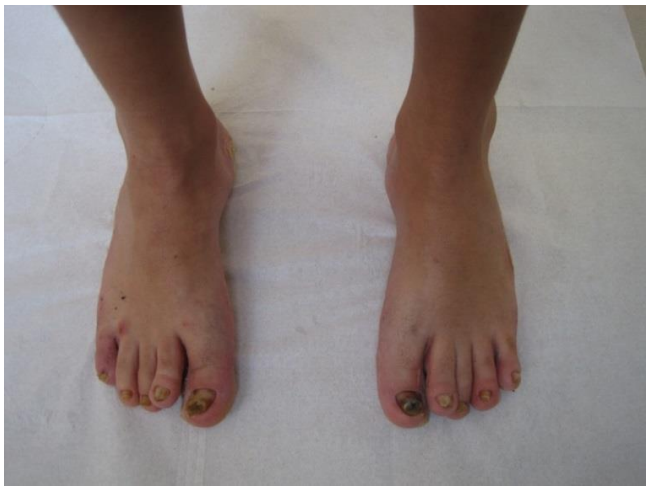

Figure 3. Hyperkeratosis and thickening of toenails.

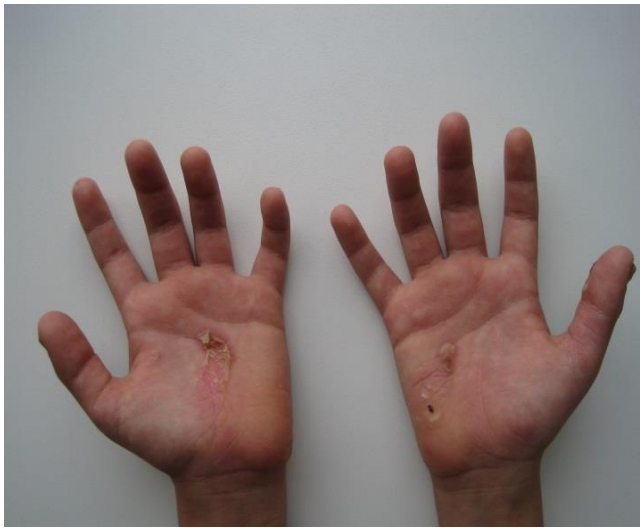

Figure 4. Palmoplantar keratoderma.

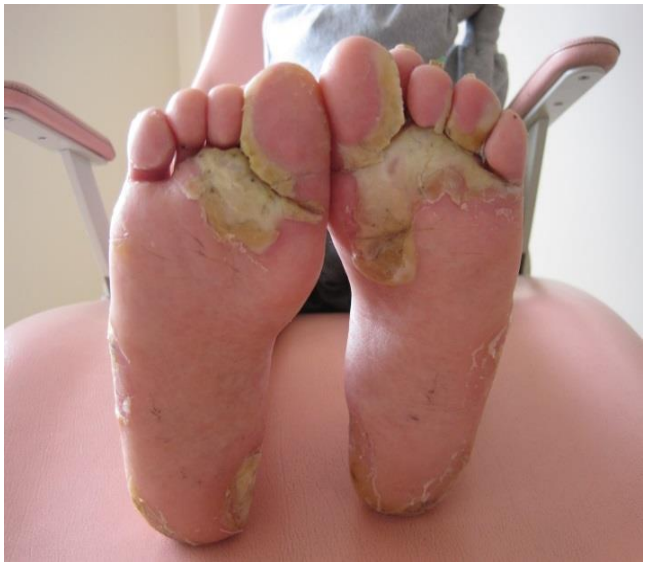

Figure 5. Palmoplantar keratoderma.

The patient had difficulty walking and standing due to pain from the palmoplantar keratoderma, and hence used a wheelchair. An intraoral examination revealed white keratotic plaques on the tongue (Fig. 8), lingual frenulum (Fig. 9), lower lip, gingiva and gingival margins (particularly the labial attached gingiva on the anterior teeth) (Fig. 10), buccal mucosa (Fig. 11), floor of the mouth (Fig. 12), hard and soft palate, eruption areas of permanent maxillary first molar teeth and maxillary tuberosity (Fig. 13).

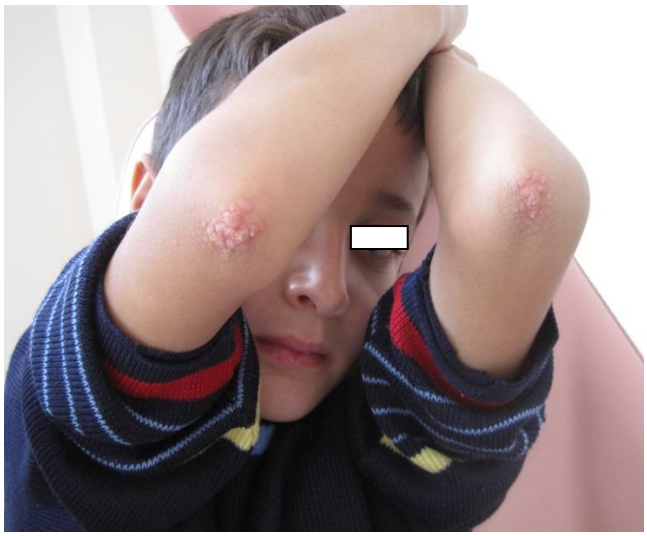

Figure 6. Keratotic follicular spikes on the elbow.

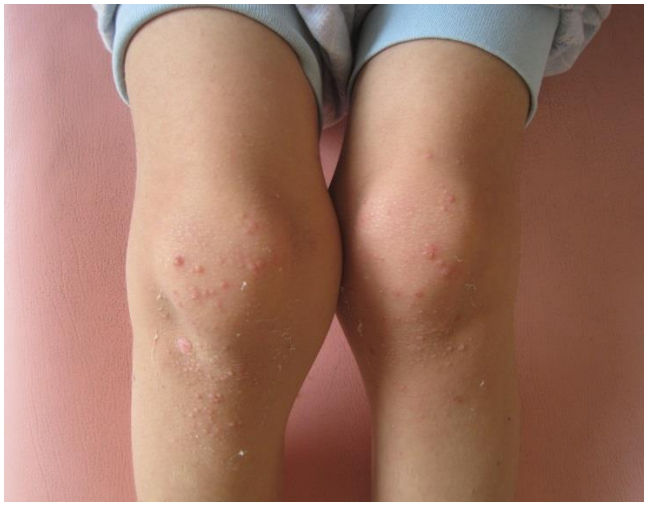

Figure 7. Keratotic follicular spikes on the knees.

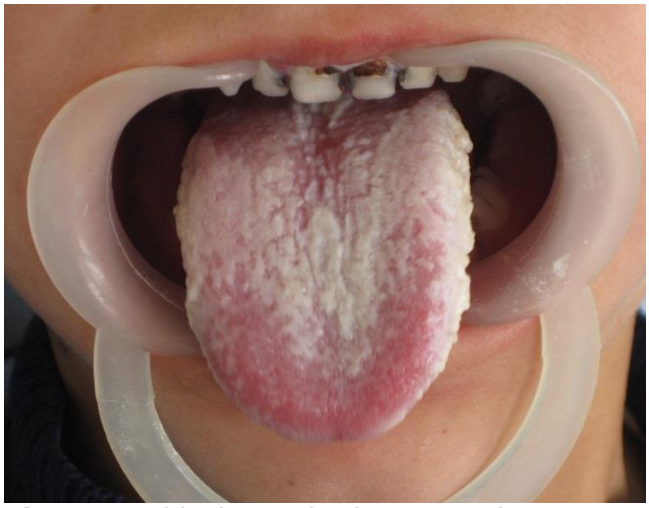

Figure 8. White keratotic plaques on the tongue.

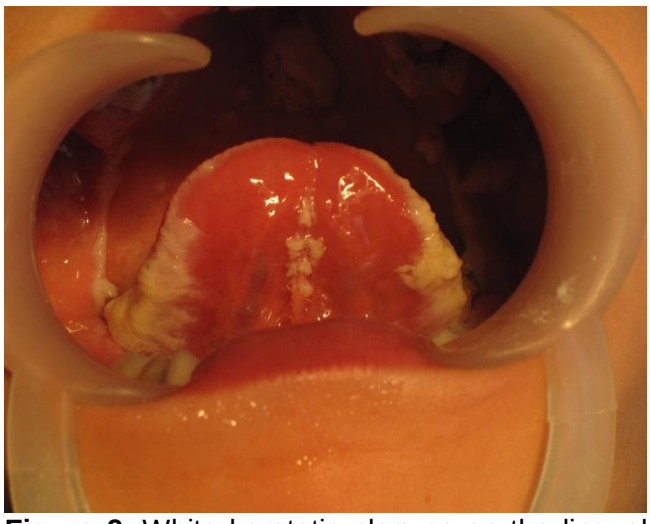

Figure 9. White keratotic plaques on the lingual frenulum.

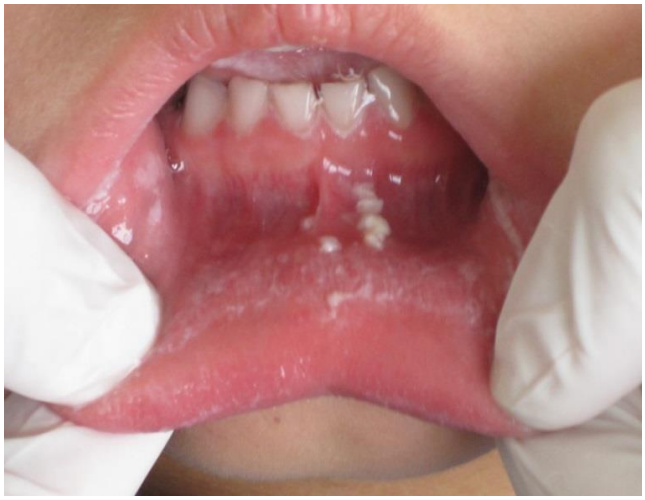

Figure 10. White keratotic plaques on the lower lip, gingiva and gingival margins.

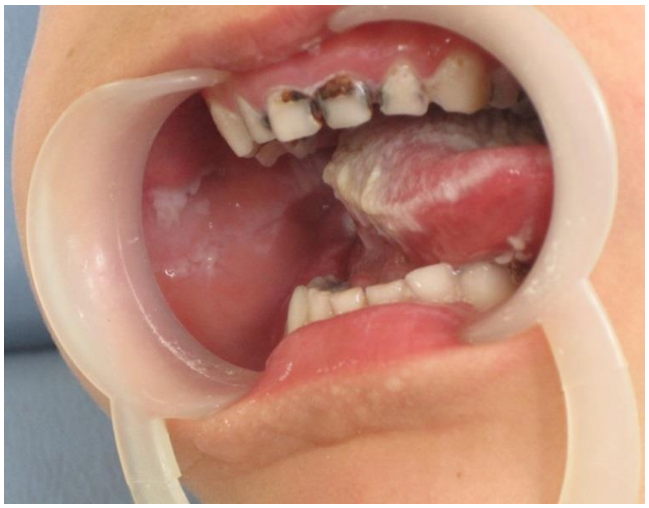

Figure 11. White keratotic plaques on the buccal mucosa.

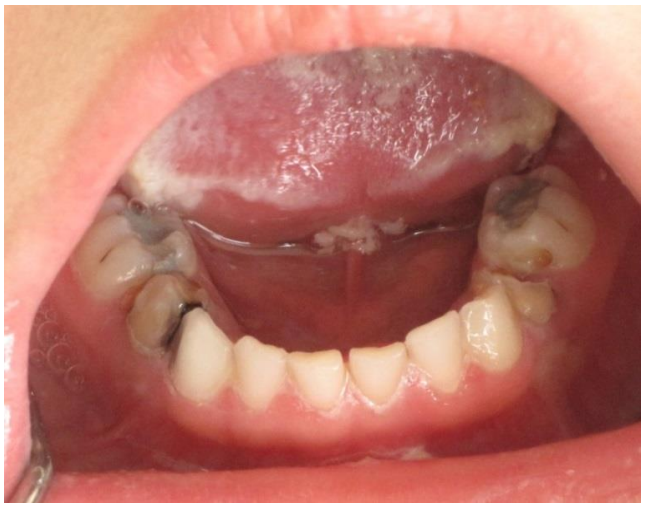

Figure 12. White keratotic plaques on the floor of the mouth.

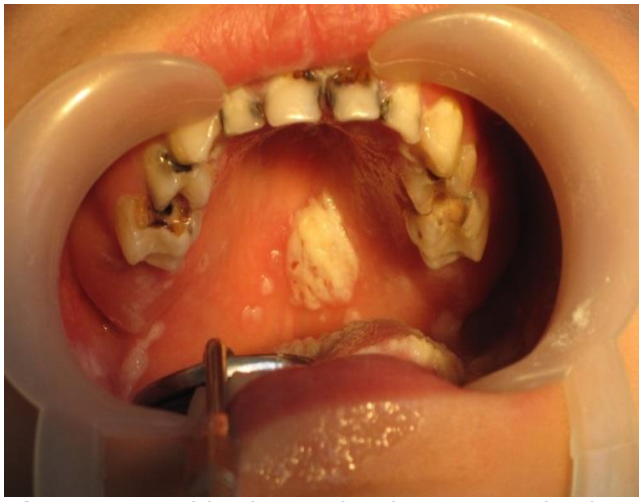

Figure 13. White keratotic plaques on the hard and soft palate, eruption areas of permanent maxillary first teeth and maxillary tuberosity.

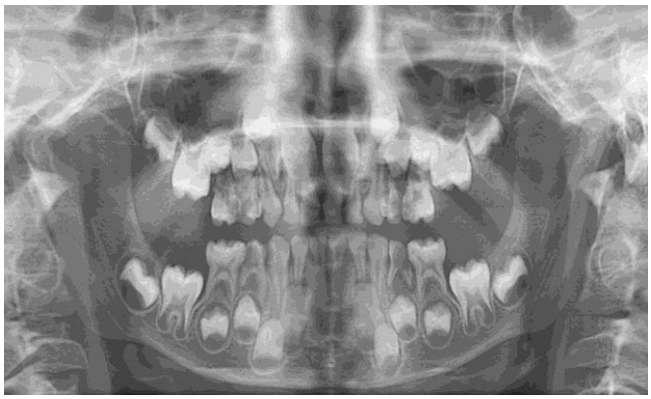

Figure 14. Panoromic radiograph of patient.

The oral lesions were painful during feeding and were sensitive to touch. Dentinal caries were present in all of the primary maxillary teeth, mandibular canines, and mandibular first molars. Amalgam restorations were present on the primary mandibular second molar teeth. Radiographic examination showed extensive caries around the primary first molars, with extensive alveolar bone resorption (Fig. 14). Dens invaginatus was identified on unerupted permanent maxillary central incisors. There were no number or position anomalies of the permanent teeth. The treatment plan for the patient consisted of extraction of primary first molar teeth, filling of carious teeth conservatively or endodontically, and placement of space maintainers. Frequent gentle brushing with a toothbrush was recommended as vigorous brushing could cause trauma to the mucosa and keratosis.

Discussion

We discuss a rare case of PC-1 with severe oral leukokeratosis. This autosomal dominant disorder was diagnosed on the basis of clinical findings when the patient was 1 year old. According to the literature, 83% of the cases are diagnosed during the first year of life, and 29-46% of cases report a negative family history [1]. In this case, the parents were clinically unaffected.

The most common clinical feature in PC is hypertrophic nail dystrophy in association with painful palmoplantar keratoderma, which progresses with age [8, 16]. Nail changes include transverse overcurvature, distal onycholysis, subungual hyperkeratosis, and variable discolouration [17]. Other common findings are oral leukokeratosis (67%), follicular keratosis (53%) and cysts (64%) [8]. PC-1 and PC-2 can be distinguished clinically as oral leukokeratosis occurs in PC-1, and steatocystomas/pilosebaceous cysts, vellus hair cysts, hair abnormalities (alopecia, pili torti) and natal/neonatal teeth occur in PC-2, usually [1]. Also, hoarseness due to laryngeal involvement is generally associated with PC-1 [17].

Clinically, oral leukokeratosis can mimic the symptoms of oral candidiasis, white sponge nevus, hairy tongue, and leukoplakia [15]. PC must be diagnosed by the presence of other signs. In rare cases, oral candidiasis occurs concomitantly with leukokeratosis in immunocompromised patients [18].

The features of PC-1 are found in a variety of autosomal dominant keratodermas that have oral lesions [19], such as focal palmoplantar and gingival keratosis, focal non-epidermolytic palmoplantar keratoderma with oral-genital-follicular lesions, and focal palmoplantar keratoderma associated with esophageal cancer. These all involve focal and pressure-related palmoplantar hyperkeratosis and oral hyperkeratosis. In focal palmoplantar and gingival keratosis, lesions appear in the attached gingiva. Palmoplantar keratodermas exhibit oral lesions in the buccal mucosa, palate and occasionally the gingiva. Hyperkeratotic lesions are more commonly seen in oral regions and the tongue is characteristically affected with buccal mucosa in PC-1. This case describes severe hyperkeratotic plaques in different regions on the oral mucosa and tongue. Additionally, in focal palmoplantar keratoderma associated with esophageal cancer and focal non-epidermolytic palmoplantar keratoderma with oral-genital-follicular lesions, nails are usually normal[8].

With the exception of the previously described keratodermas, there are a number of differential diagnoses for PC-1. Hyperkeratotic nail thickening is seen in onychomycosis, similar to PC, but fungal infection does not affect all nails in early infancy [8, 20].

Clouston syndrome, a rare autosomal dominant genetic disorder, is characterized by the major triad of features: nail dystrophy, generalized hypotrichosis, and palmoplantar hyperkeratosis. This is similar to PC; however, alopecia is a common feature of Clouston syndrome, which is not typically seen in PC [21]. Dyskeratosis Congenita is a rare inherited fatal disorder that mimics the skin, nail and oral features of PC. Unlike PC, progressive bone marrow failure is one of the most well-known symptoms of Dyskeratosis Congenita and the primary cause of mortality [22].

As yet, there is no effective and specific treatment for PC [23]. The treatment of manifestations focuses primarily on nail grooming and management of pain due to palmoplantar keratoderma. Treatment options fall into four broad categories: non-invasive (mechanical removal of keratin), invasive (electrofulguration, deep curettage, excision), chemical (urea, propylene glycol) and pharmacological (systemic retinoids) [24].

The treatment of oral lesions is based on providing good oral hygiene and reducing tenderness. Angular cheilitis and fissures can be treated with heavy moisturizers. Regular and gentle brushing with a toothbrush is recommended. Brushing of the tongue could have a beneficial effect on reducing leukoplakia. In neonates, using bottles that have a free-flowing nipple and topical anesthetics can support feeding. No effective methods are available for the treatment of oral leukokeratosis [24].

Conclusion

PC is a disorder that negatively affects the quality of life of patients due to problems in movement and aesthetics. Oral treatment plans must take into consideration the mostly painful and sensitive presentation of oral leukokeratosis,

as well as the difficulty of maintaining good oral hygiene and regular dental visits for these patients.

Declaration of Interest

The authors report no conflict of interest and the article is not funded or supported by any research grant.

References

1. Leachman SA, Kaspar RL, Fleckman P, et al. Clinical and pathological features of pachyonychia congenita. *J Investig Dermatol Symp Proc.* 2005;10(1):3-17.
2. McLean WH, Hansen CD, Eliason MJ, Smith FJ. The phenotypic and molecular genetic features of pachyonychia congenita. *J Invest Dermatol.* 2011;131(5):1015-1017.
3. Gonul M, Cevirgen Cemil B, Keseroglu HO, Kaya Akis H. New described dermatological disorders. *Biomed Res Int.* 2014;2014:616973.
4. Haber RM, Drummond D. Pachyonychia congenita with laryngeal obstruction. *Pediatr Dermatol.* 2011;28(4):429-432.
5. Kaspar RL. Challenges in developing therapies for rare diseases including pachyonychia congenita. *J Investig Dermatol Symp Proc.* 2005;10(1):62-66.
6. Al Aboud A, Al Aboud K. Josef Jadassohn (1863-1936), Felix Lewandowsky (1879-1921), and their syndrome. *Clin Cosmet Investig Dermatol.* 2011;4:179-182.
7. Jackson AD, Lawler SD. Pachyonychia congenita; a report of six cases in one family, with a note on linkage data. *Ann Eugen.* 1951;16(2):142-146.
8. Smith FJD, Hansen CD, Hull PR, et al. Pachyonychia Congenita. In: Pagon RA, Adam MP, Ardinger HH, et al., eds. *GeneReviews(R)*. Seattle (WA); 1993.
9. Agarwal P, Chhaperwal MK, Singh A, et al. Pachyonychia congenita: A rare genodermatosis. *Indian Dermatol Online J.* 2013;4(3):225-227.
10. McLean WH, Rugg EL, Lunny DP, et al. Keratin 16 and keratin 17 mutations cause pachyonychia congenita. *Nat Genet.* 1995;9(3):273-278.
11. Bowden PE, Haley JL, Kansky A, Rothnagel JA, Jones DO, Turner RJ. Mutation of a type II keratin gene (K6a) in pachyonychia congenita. *Nat Genet.* 1995;10(3):363-365.
12. Smith FJ, Jonkman MF, van Goor H, et al. A mutation in human keratin K6b produces a phenocopy of the K17 disorder pachyonychia congenita type 2. *Hum Mol Genet.* 1998;7(7):1143-1148.
13. Smith FJ, Liao H, Cassidy AJ, et al. The genetic basis of pachyonychia congenita. *J Investig Dermatol Symp Proc.* 2005;10(1):21-30.
14. Eliason MJ, Leachman SA, Feng BJ, Schwartz ME, Hansen CD. A review of the clinical phenotype of 254 patients with genetically confirmed pachyonychia congenita. *J Am Acad Dermatol.* 2012;67(4):680-686.
15. da Silva Santos PS, Mannarino F, Lellis RF, Osorio LH. Oral manifestations of pachyonychia congenita. *Dermatol Online J.* 2010;16(10):3.
16. Shah S, Boen M, Kenner-Bell B, Schwartz M, Rademaker A, Paller AS. Pachyonychia congenita in pediatric patients: natural history, features, and impact. *JAMA Dermatol.* 2014;150(2):146-153.
17. Hannaford RS, Stapleton K. Pachyonychia congenita tarda. *Australas J Dermatol.* 2000;41(3):175-177.
18. Mawhinney H, Creswell S, Beare JM. Pachyonychia congenita with candidiasis. *Clin Exp Dermatol.* 1981;6(2):145-149.
19. Kolde G, Hennies HC, Bethke G, Reichart PA. Focal palmoplantar and gingival keratosis: a distinct palmoplantar ectodermal dysplasia with epidermolytic alterations but lack of mutations in known keratins. *J Am Acad Dermatol.* 2005;52(3 Pt 1):403-409.
20. Luo S, Luo Q, Zhang H, Wan C. A novel H1 mutation in keratin 6a in an infant with pachyonychia congenita. *Indian J Dermatol Venereol Leprol.* 2015;81(4):385-387.
21. Marakhonov A, Skoblov M, Galkina V, Zinchenko R. Clouston syndrome: first case in Russia. *Balkan J Med Genet.* 2012;15(1):51-54.
22. Dokal I. Dyskeratosis congenita. *Hematology Am Soc Hematol Educ Program.* 2011;2011:480-486.
23. Jirakova A, Rajska L, Rob F, et al. First case of pachyonychia congenita in the Czech Republic. *Dermatol Ther.* 2015;28(1):10-12.
24. Milstone LM, Fleckman P, Leachman SA, et al. Treatment of pachyonychia congenita. *J Investig Dermatol Symp Proc.* 2005;10(1):18-20.