J Oral Res
research in oral sciences

CASE REPORT

PAPILLON-LEFÈVRE SYNDROME: 17-YEAR DENTAL FOLLOW-UP. CASE REPORT

Síndrome De Papillon-Lefèvre: Seguimiento Dental De 17 Años. Reporte De Caso

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ABSTRACT

Introduction: The present report describes the case of a 12-year-old patient with 17-year follow-up who was previously diagnosed with Papillon-Lefèvre Syndrome (PLS), which is a rare autosomal recessive irregularity in the cathepsin C gene (CTSC) characterized by palmoplantar hyperkeratosis and premature loss of primary and permanent teeth.

Case Report: A specific mutation in the c.203 T > G gene inducing loss of function leading to PLS was detected, as was a mutation in the HLA-DRB1*11 allele, which is associated with this syndrome. There is no consanguinity of the parents, and the siblings are entirely healthy. Early identification of the main characteristics of this syndrome is imperative. Accurate diagnosis by genetic analysis allows differential diagnoses and timely comprehensive dental treatment.

Conclusions: Additionally, it allows consultation with a dermatologist to maintain or improve the quality of life of patients with this condition due to progressive worsening and severity of the main physical manifestations.

Keywords: *Papillon-Lefevre Disease; Keratoderma, Palmoplantar; Cathepsin C; Periodontitis; Skin Diseases, Genetic; Case reports*

RESUMEN

Introducción: El presente reporte describe el caso de un paciente de 12 años de edad con 17 años de seguimiento a quien previamente se le diagnosticó Síndrome de Papillon-Lefèvre (PLS), el cual es una rara irregularidad autosómica recesiva en el gen de la catepsina C (CTSC) caracterizada por hiperqueratosis palmoplantar y pérdida prematura de dientes primarios y permanentes.

Reporte de Caso: Se detectó una mutación específica en el gen c.203 T > G que induce pérdida de función que conduce a PLS, así como una mutación en el alelo HLA-DRB1*11, que se asocia a este síndrome. No presenta consanguinidad de los padres, padres y hermanos totalmente sanos. La identificación temprana de las principales características de este síndrome es imperativa. El diagnóstico certero por análisis genético permite diagnósticos diferenciales y tratamientos odontológicos integrales oportunos.

Conclusiones: Adicionalmente, permite la consulta con un dermatólogo para mantener o mejorar la calidad de vida de los pacientes con esta condición debido al progresivo empeoramiento y severidad de las principales manifestaciones físicas.

Palabras Clave: *Enfermedad de Papillon-Lefevre; Queratodermia Palmoplantar; Catepsina C; Periodontitis; Enfermedades Cutáneas Genéticas; Informes de Casos.*

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CITE AS: **Melchor-Soto M, Arriola-Guillén LE, Ruíz-Mora GA, Rodríguez-Cárdenas YA, Melchor-Soto J, Romero-Quintana J & Aliaga-Del Castillo A.** Papillon-Lefèvre Syndrome: 17-Year Dental Follow-Up. Case Report. **J Oral Res. 2023; 12(1): 119-126. doi:10.17126/joralres.2023.011**

Received: February 13, 2023
Accepted: June 01, 2023
Published online: August 23, 2023

ISSN Print 0719-2460
ISSN Online 0719-2479.

INTRODUCTION

The Papillon-Lefèvre syndrome (PLS) is a rare autosomal recessive irregularity that has recently been nosologically proposed as palmoplantar ectodermal dysplasia.[1-10] The prevalence of PLS ranges from 1 to 4 cases per million in the general population,[2,7] with no sex predominance. It can occur by consanguinity of the parents, hereditary or associated with a syndrome, and in most cases, it has been described that it is the result of a mutation in the alleles of the cathepsin gene C gene (CTSC), particularly on chromosome 11q14.2. CTSCs are found in neutrophils, lymphocytes and epithelial cells.[1-6,8,9] This irregularity in the CTSC gene causes the loss of enzymatic function, leading to an imbalance in organism response to bacterial infections.[1,2,5,9]

More than 113 mutations in CTSCs have been reported, and phenotypic variability among the various mutations has been described.[1,2] The initial signs usually appear during the first 4 years of life as palmoplantar hyperkeratosis and extensive, severe and aggressive pre-pubertal periodontitis, which is responsible for the premature loss of temporary and permanent dentition with the same eruption sequence over time.[3-6]

As such, it is important that dentists know about the dental management of these patients and their approach to provide them with better dental treatment and probably more valued by patients with this complex condition. In this way, this report describes the case of a patient diagnosed with PLS who was studied from 12 years of age with a follow-up of 17 years.

CASE REPORT

The patient was a 12-year-old male with a detailed medical history. The patient's first dental visit was at 9 years old. He reported discomfort when eating as the reason for dental consultation. The patient's mother mentioned having had a dermatological consultation with a specialist who diagnosed atopic dermatitis.

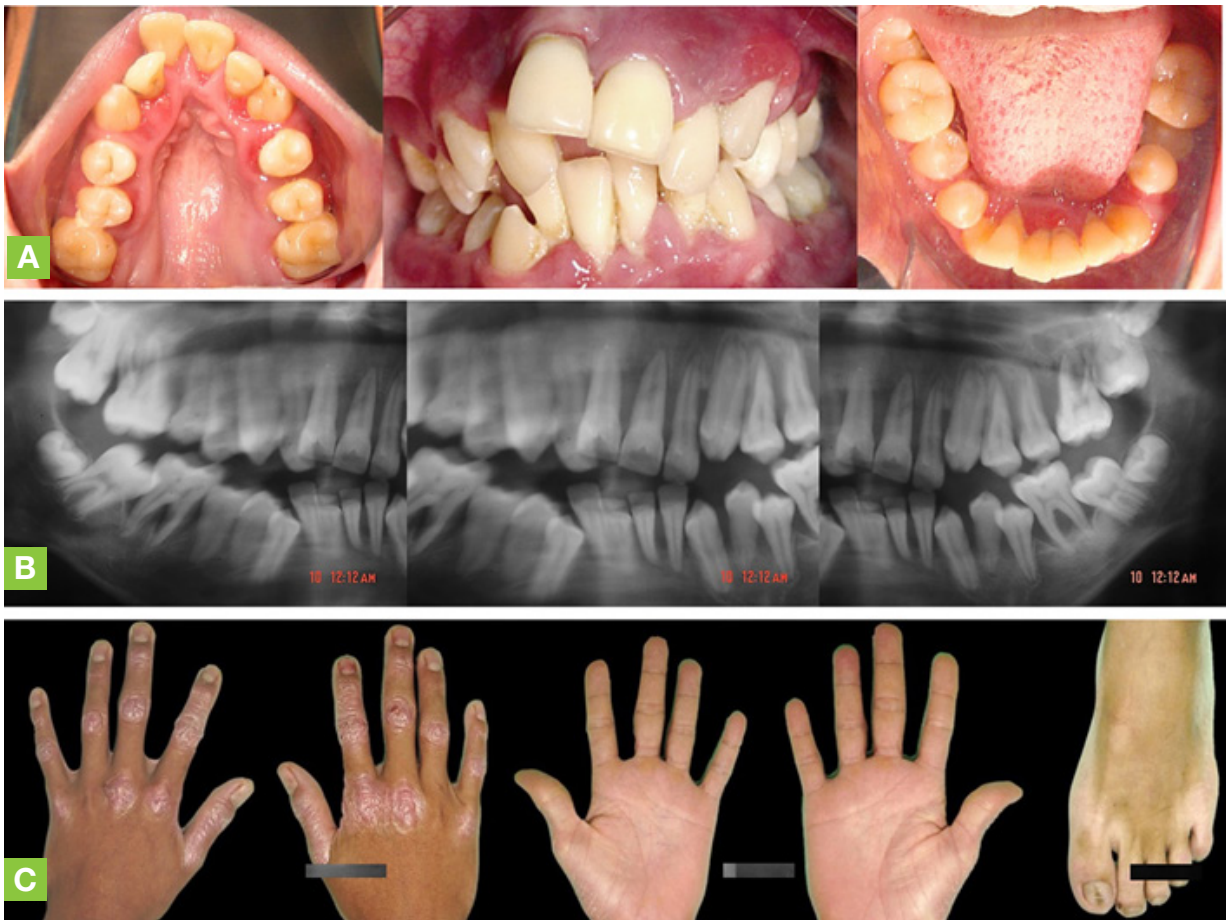
During the physical examination, palmar-plantar hyperkeratosis and involvement of the knees and elbows were observed. The mother commented that she had two other children who had psychomotor retardation and that no relatives (grandparents, parents, or siblings) presented the same dermatological characteristics as the patient. On intraoral examination at the first visit, mixed dentition was observed with generalized tooth mobility, edematous gums with pain on palpation, bleeding on probing, dental plaque, tartar, multiple caries, crowding, maxillary arch collapse, and a triangular and deep palate. Panoramic and periapical x-rays were requested and showed severe alveolar bone loss. Unfortunately, records from that time were lost.

Subsequently, the patient was medically diagnosed with PLS. The treatment included serial extractions of the teeth that presented mobility, and a consultation with a pediatric dermatologist was established for the treatment of hyperkeratosis. Routine blood and biochemical laboratory tests were within normal limits.

The patient returned for consultation at the age of 12 years, and intraoral photographs and x-ray (analog) images of the hands and feet were obtained (Figure 1).

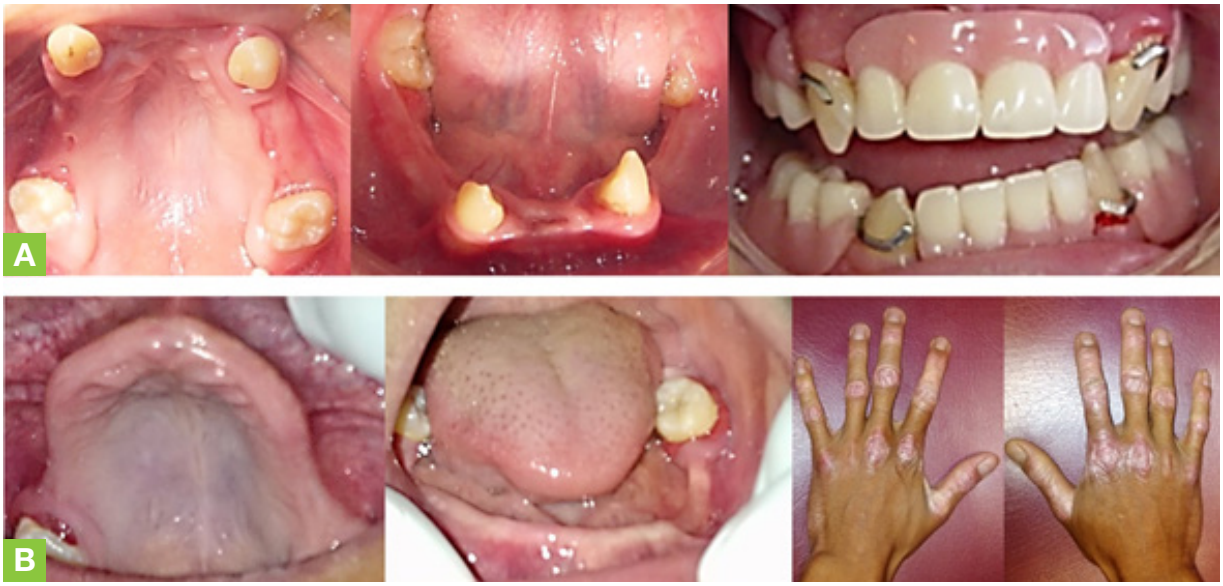
ISSN Print 0719-2460 - ISSN Online 0719-2479.

Figure 1: Patient at 12 years of age.



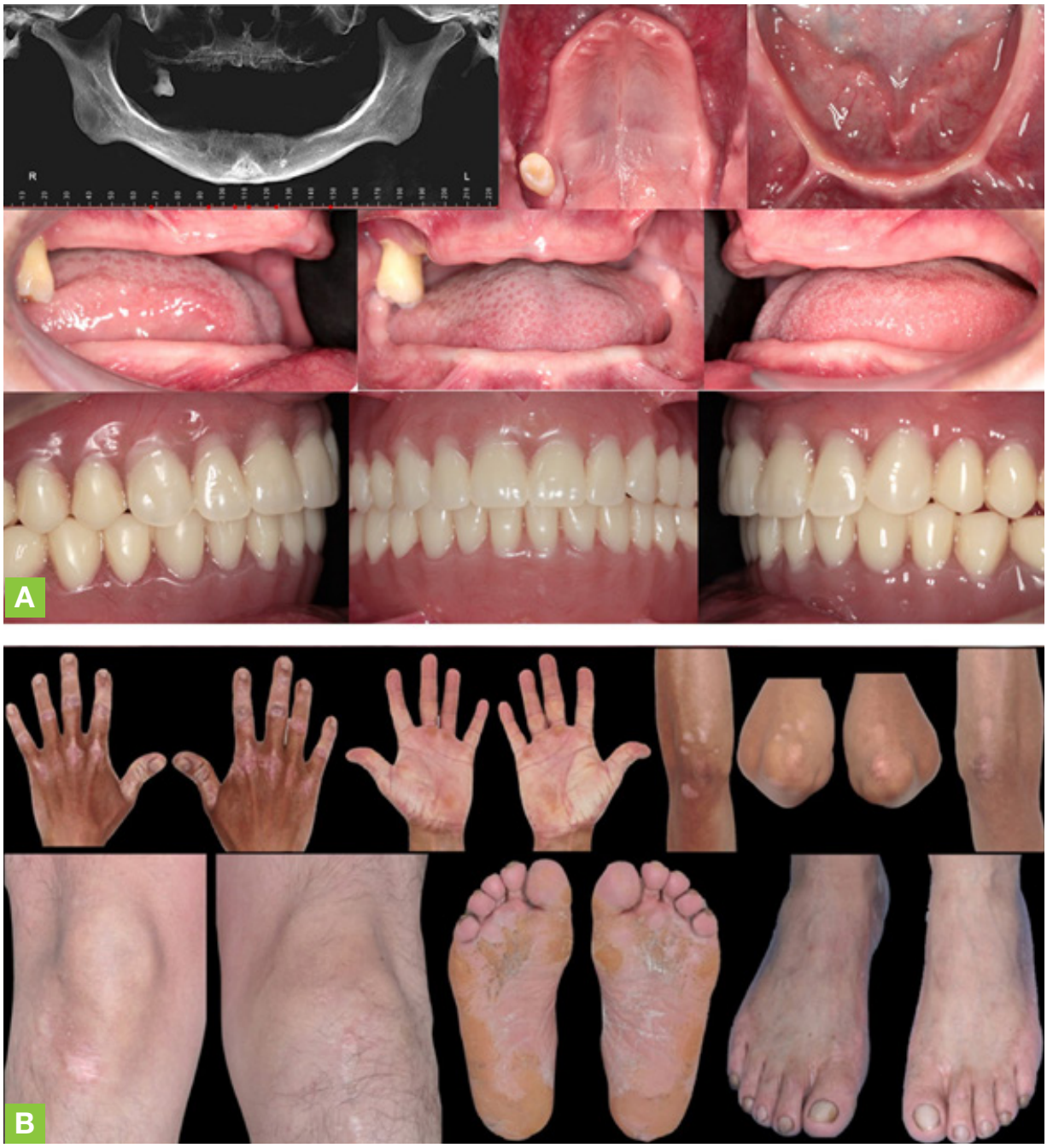
A: Intraoral photographs. B: Panoramic x-ray (right side, anterior area, left side). C: Hands and foot.

Figure 2: Patient at 15 and 17 years old.



A: Patient at 15 years of age with and without the removable partial prosthesis. B: Patient at 17 years of age, intraoral photographs and hands.

Figure 3: Patient at 29 years of age.



A: CBCT-derived panoramic image and intraoral photographs with the maxillary third molar. Complete removable prosthesis was employed after the extraction of the third molar. B: Hands, elbows, knees, and feet.

During the physical examination, palmar-plantar hyperkeratosis with involvement of the knees and elbows were still present. Intraoral examination revealed permanent dentition, anterior crowding in both arches, deep palate, edematous and inflamed gums associated with periodontal disease, bleeding on probing with pain on palpation, Grade III tooth mobility, tartar and halitosis.

X-ray examination showed severe generalized horizontal and vertical bone loss. When the patient was 14 years old, a genetic

ISSN Print 0719-2460 - ISSN Online 0719-2479.

study of the patient and his family was performed as part of an attempt to identify the clinical characteristics, gene expression, enzymatic activity and mutational analysis of CTSCs in patients with PLS from seven different families.[7]

This allowed the corroboration of the previously established diagnosis based on the literature and the signs, symptoms and evolution of dermatological lesions in PLS. The patient was found to have compound heterozygosity mutations at c.203T>G and c.458C>T in the CTSC gene, while the parents were carriers of c.203T>G or c.458C>T, and the two siblings were carriers of c.458C>T but were not affected.

Intraoral photographs were taken when the patient was 15 years old. Clinically, the upper and lower canines and second molars presented Grade III mobility (Figure 2A).

The gums surrounding the teeth were edematous and inflamed, with bleeding upon periodontal probing. Additionally, further evolution of palmoplantar hyperkeratosis was observed on physical examination. Treatment at this time consisted of extraction of the canines and maxillary second permanent molars due to increased mobility caused by the loss of support bone, and placement of a removable complete prosthesis after the extractions.

Once the teeth were removed, the gingival tissues returned to their healthy state; however, as the patient aged, hyperkeratosis evolved unfavorably. At 17 years of age, the patient maintained the maxillary right third molar and mandibular second molars and continued to present characteristics of the syndrome, including hyperkeratosis on the back of the hands (Figure 2B). At this time, extraction of mandibular second molars and removable complete prosthesis in the mandibular arch were indicated.

At an age of 29 years, the patient returned for a control study. The panoramic view showed irregular alveolar edges with loss of height in both arches and the presence of the upper right third molar with severe bone loss (Figure 3A). In the intraoral images, loss of vertical dimension was observed, as was thinning of both alveolar processes, Grade III mobility in the upper right third molar, edematous and inflamed tissue surrounding the teeth and bleeding on periodontal probing. This tooth was extracted and a new complete upper and lower prosthetic treatment was performed (Figure 3A).

On physical examination, the elbows and knees showed small areas of hyperkeratosis; additionally, hyperkeratosis was more predominant on the back of the hands than on the palms and on the soles more so than on the top of the feet (Figure 3B).

The prosthetic treatment began at the age of 12 years, replacing the dental organs with a partial removable denture subsequently until reaching the total removable prosthesis of both arches (18 years), with the growth of the patient the prostheses were misadjusted, prosthetic rebases were made until it was dysfunctional, after the extractions the tissue returned to normal allowing a comfortable adaptation and function of the prostheses, After the patient's growth, the use of implant-supported prostheses was proposed, but the lack of patient resources prevented expensive treatments.

DISCUSSION

The present report describes the case of a 12-year-old patient with a 17-year follow-up who has the diagnosis with PLS. Economic limitations and the patient's place of residence conditioned the comprehensive care received. A genetic study found that the patient was compound heterozygous for a mutation of the c.203T>G and c.458C>T CTSC gene, while both of his parents were carriers of c.203T>G or c.458C>T, and his two brothers were carriers of c.458C>T.
There was no consanguinity between relatives, and his parents and siblings were completely asymptomatic. Currently, the overall prevalence of PLS in Latin-America is unknown and the number of reported cases in journals of dentistry is very low.[7]

The prognosis of PLS is reserved, since it depends not only on medical knowledge of the characteristics of this syndrome but also on complete understanding of the condition by the patient and requires ongoing psychological support. Early and timely care can maintain or avoid severe deterioration of periodontal disease and the risk of bacterial infections of the skin lesions.[3,4,8]

In the present case, medical intervention was provided within the limitations to promote the periodontal and dermatological health of the patient during the 17 years of follow-up.
Oral rehabilitation initially consisted of removable partial prostheses, followed later by complete prostheses, which are associated with a lack of stability and retention that causes discomfort for patients with PLS. Follow-up is recommended to adjust the dentures to ensure patient comfort, and with the goal of preserving as much natural dentition as possible.[4,5,8]

The placement of bone-integrated implants after 18 years of age is another prosthetic option recommended in the literature, with an overall reported survival rate of 16%.[5,8,11] However, medical, physiological and economic factors, as well as the expectations of the patient and professional, determine the final restorative treatment selected.
This case report has sought to present the management of a patient with PLS, properly diagnosed, the timely intervention allowed to establish an initial treatment with serial extractions combined with a prosthetic treatment, it is important to follow up on this type of patients because they require the constant intervention of the dentist, to provide stability to the treatment and a better quality of life.

CONCLUSION

The literature reports PLS has a higher prevalence in children born of consanguineous marriages. However, there was no consanguinity between relatives, and his parents and siblings were completely asymptomatic.[7] For patients with suspected PLS, accurate diagnosis at an early age by genetic analysis allows preventive medical action to be taken and comprehensive and timely dental treatments to be performed.
The participation of a multidisciplinary team in the rehabilitation of patients with PLS is essential for maintaining and improving the quality of life of affected individuals.

ISSN Print 0719-2460 - ISSN Online 0719-2479.

CONFLICT OF INTERESTS

The authors declare no conflict of interest.

ETHICS APPROVAL

The authors certify that they have obtained all appropriate patient consent.

FUNDING

None.

AUTHORS' CONTRIBUTIONS

Arriola-Guillén L: conceptualization, resources, original draft preparation and editing, supervision.
Ruíz-Mora G: conceptualization, original draft preparation and editing.
Rodríguez-Cárdenas Y: conceptualization, resources, original draft preparation and editing.
Melchor-Soto J: conceptualization, resources, data curation, original draft preparation and editing.
Romero-Quintana J: conceptualization, resources, data curation, original draft preparation and editing.
Aliaga-Del Castillo A: conceptualization, resources, original draft preparation and editing

ACKNOWLEDGEMENTS

None.

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PUBLISHER'S NOTE

All statements expressed in this article are those of the authors alone and do not necessarily represent those of the publisher, editors, and reviewers.

PEER REVIEW

This manuscript was evaluated by the editors of the journal and reviewed by at least two peers in a double-blind process.

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ISSN Print 0719-2460 - ISSN Online 0719-2479.
https://www.joralres.com/index.php/JOralRes/issue/archive

REFERENCES.

1. Yu H, He X, Liu X, Zhang H, Shen Z, Shi Y, Liu X. A novel missense variant in cathepsin C gene leads to PLS in a Chinese patient: A case report and literature review. Mol Genet Genomic Med. 202;9(7):e1686. doi: 10.1002/mgg3.1686. Epub 2021 May 5. PMID: 33949806; PMCID: PMC8372118.
2. Ghanei M, Abbaszadegan MR, Forghanifard MM, Aarabi A, Arab H. A novel mutation in the cathepsin C (CTSC) gene in Iranian family with Papillon-Lefevre syndrome. Clin Exp Dent Res. 2021;7(4):568-573. doi: 10.1002/cre2.387. Epub 2021 Feb 14. PMID: 33586345; PMCID: PMC8404484.
3. Patil SM, Metkari SB, Shetty S, Thakkannavar S, Sarode SC, Sarode GS, Sengupta N, Patil S. Dental prosthetic rehabilitation of Papillon-Lefèvre syndrome: a case report. Clin Pract. 2020;10(3):1285. doi: 10.4081/cp.2020.1285. PMID: 33042508; PMCID: PMC7520704.
4. Giannetti L, Apponi R, Dello Diago AM, Jafferany M, Goldust M, Sadoughifar R. Papillon-Lefèvre syndrome: Oral aspects and treatment. Dermatol Ther. 2020;33(3):e13336. doi: 10.1111/dth.13336. Epub 2020 Apr 9. PMID: 32222110.
5. Atarbashi-Moghadam F, Atarbashi-Moghadam S, Kazemifard S, Sijanivandi S, Namdari M. Oral rehabilitation of Papillon-Lefèvre syndrome patients by dental implants: a systematic review. J Korean Assoc Oral Maxillofac Surg. 2020;46(4):220-227. doi: 10.5125/jkaoms.2020.46.4.220. PMID: 32855368; PMCID: PMC7469965.
6. Abou Chedid JC, Salameh M, El-Outa A, Noujeim ZEF. Papillon-Lefèvre Syndrome: Diagnosis, Dental Management, and a Case Report. Case Rep Dent. 2019;2019:4210347. doi: 10.1155/2019/4210347. PMID: 31179131; PMCID: PMC6501246.
7. Romero-Quintana JG, Frías-Castro LO, Arámbula-Meraz E, Aguilar-Medina M, Dueñas-Arias JE, Melchor-Soto JD, Romero-Navarro JG, Ramos-Payán R. Identification of novel mutation in cathepsin C gene causing Papillon-Lefèvre Syndrome in Mexican patients. BMC Med Genet. 2013;14:7. doi: 10.1186/1471-2350-14-7. PMID: 23311634; PMCID: PMC3563609.
8. Sreeramulu B, Shyam ND, Ajay P, Suman P. Papillon-Lefèvre syndrome: clinical presentation and management options. Clin Cosmet Investig Dent. 2015;7:75-81. doi: 10.2147/CCIDE.S76080. PMID: 26203280; PMCID: PMC4507741.
9. Toomes C, James J, Wood AJ, Wu CL, McCormick D, Lench N, Hewitt C, Moynihan L, Roberts E, Woods CG, Markham A, Wong M, Widmer R, Ghaffar KA, Pemberton M, Hussein IR, Temtamy SA, Davies R, Read AP, Sloan P, Dixon MJ, Thakker NS. Loss-of-function mutations in the cathepsin C gene result in periodontal disease and palmoplantar keratosis. Nat Genet. 1999;23(4):421-4. doi: 10.1038/70525. PMID: 10581027.
10. Papillon M. Deux cas de keratodernune palmaire symmetrique famiale (Maladie de Meleda) chez Le frere et la soeur. Coexistece dans les deux cas d'alterations dentaires graves. BUll Soc Fr Dermatol Syp lt. 1924;31:82-4.
11. Nassani MZ, Al-Maweri SA, Veeraganta SK, Al-Shamiri HM, Alaizari NA, Najeeb S. Survival Rates of Dental Implants in Patients with Papillon-Leféve Syndrome: A Systematic Review. J Contemp Dent Pract. 2021;22(1):93-100. PMID: 34002717.

ISSN Print 0719-2460 - ISSN Online 0719-2479.