

## Papillon lefevre syndrome- A literature review and case report

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### Abstract

Papillon-Lefèvre syndrome (PLS) is an extremely rare genetic disorder. This disorder is mostly observed in children from 1-5 years of age. Alteration of CTSC gene which regulates the production of enzyme cathepsin C is responsible for this syndrome. The common characteristics are palmoplantar keratosis and aggressive form of periodontitis. The patient might become completely edentulous in the absence of appropriate and early treatment. Early loss of teeth in young children may have two important concerns- 1. Psychological impact. 2. Prosthetic rehabilitation. Till date, there is no definitive treatment protocol for PLS cases. This article provides a detailed review about the various possible etiologies, clinical features, differential diagnosis and treatment protocols followed for the periodontal management of PLS. This article reports a Case of Papillon Lefèvre syndrome and its management with long term follow up.

**Keywords:** Periodontitis, Papillon Lefevre syndrome.

### Introduction

Papillon-Lefèvre syndrome (PLS) is a rare autosomal recessive heterogeneous disorder. Gorlin RJ et al (1964) stated that "The common characteristics of PLS are palmoplantar hyperkeratosis, early loss of primary and permanent teeth, and associated calcification of the dura mater".<sup>1</sup> It was first described in 1924 by French physicians Papillon and Lefèvre.<sup>2</sup> The PLS syndrome is extremely rare and is observed in one in 4 million cases. It is equally seen in both males and females. Also it is equally distributed among all the human races. There has always been a dilemma regarding the etiology of this syndrome. However, PLS can be hereditary, acquired or even associated with other genetic disorders. Hart et al (1994) stated "If both parents are carriers of the defective gene there is a 25% risk for their children to be affected".<sup>3-7</sup> Hart TC et al (1999) stated that "Mutation of the cathepsin C gene are responsible for Papillon-Lefèvre syndrome". PLS results from genetic mutations on both alleles of the cathepsin C gene (CTSC) on chromosome 11q14.2.<sup>8</sup> This article reports a complete case of this rare syndrome, Papillon-Lefèvre syndrome.

### Case Report

A 12-year-old boy, visited to our department of Periodontology with chief complaint of early loss of deciduous teeth, mobility of teeth and sensitivity of teeth on drinking cold water. He first noticed mobility in his teeth 2 years back, since then it gradually increased. He also complained of bleeding from his gums since 2 years. The bleeding aggravates while brushing teeth in the morning.

A thorough medical and family history was taken for the patient.

He was the first child born to healthy consanguineous parents. History revealed that his deciduous teeth had erupted normally. However they exfoliated gradually by the age of 5 years. Early loss of teeth made it very difficult for him to chew food. This further led to loss of appetite and eventually weight loss.

### Clinical Features

#### Intra-oral findings

Intra-oral examination revealed severely inflamed red colour gingiva. Spontaneous bleeding from the gingiva was seen on probing the gingival sulcus throughout the oral cavity. The consistency of the gingiva was soft and edematous. Teeth 44, 32 and 35 were missing. Severe bone loss resulted in pathological migration of teeth 11, 21, 31 and 41. On assessment, grade III mobility was present in relation with 36 and 46, grade II in relation with 31 and 41. Remaining teeth were present with grade I mobility. There were periodontal pockets of 8-9mm with respect to 36 and 46 and periodontal pockets of 4-5mm with respect to the remaining teeth. [Fig. 1 a,b,c]

#### Extra-oral findings

On extra-oral examination, patient presented with well-demarcated, dry, scaly, keratotic plaques over the skin of palms, elbows and soles extending on to the dorsal surfaces. [Fig. 2 a,b,c]

#### Radiographic findings

Orthopantomogram showed more than 50 % bone loss in the posterior teeth especially in 36 and 46 teeth region. All the third molars were impacted with incomplete root formation. [Fig. 3]

#### Investigations

All biochemical investigations were done for the patient. Complete blood count test, Liver function test, urine analysis and Alkaline phosphatase levels were normal.

Patient was referred for Genetic test (Constitutional Karyotyping) which came to be negative.

#### Management

Papillon Lefèvre patient requires a multi-disciplinary approach for dental and dermatological treatment. The patient was referred to a Dermatologist for his skin lesions. The dental treatment which included aggressive form of periodontitis was managed by the Periodontist.



**Fig. 1:** Pre-operative intra oral findings



**Fig. 2:** Preoperative extra oral findings



**Fig. 3:** Orthopantomogram

#### **Dental treatment protocol for patient with PLS.<sup>6</sup>**

Parental counselling and motivation plays a major role in the treatment plan. Hence, in the beginning the patient's parents

were counselled about the course of the disease and its outcome. The following treatment plan was followed-

1. Patient was explained Modified bass brushing technique. Then, oral prophylaxis in the form of supragingival and subgingival scaling under local anesthesia was performed. This procedure was repeated every month for continues 3 months with regular follow up to evaluate the periodontal status.
2. Patient was instructed to use of 5 ml of 0.2% Chlorhexidine gluconate mouthrinse twice daily for 2 mins for initial 15 days.
3. Desensitizing toothpaste containing Strontium chloride and fluoride was prescribed for the patient.
4. Teeth with advanced periodontal disease, 36 and 46 were extracted.

5. Remaining teeth were maintained with regular oral prophylaxis every three month and regular follow up visits.

Dermatological management- Patient was referred to a dermatologist for the dermatological treatment which included –Acitretin (oral retinoid). The skin lesions gradually increased during winter season. The oral retinoids drastically improved the dermatological lesions with 10 weeks.

Recall after 1 month: There was marked reduction in the gingival inflammation. However the bleeding on probing was still present in the mandibular anterior teeth region. The mobility of teeth was still the same. [Fig. 4 a,b,c]

Recall after 6 month: The gingiva colour changed to pale pink. There was absence in the gingival bleeding. The mobility of teeth was reduced and the patient was able to chew properly. [Fig.5 a,b,c]

Recall after 12 months-The periodontal and dental condition was stable. [Fig. 6 a,b,c]

Recall after 3 years: The periodontal and dental condition was stable. [Fig. 7,8]

Future perspective: Implant supported prosthesis in case of edentulism at later age of life.

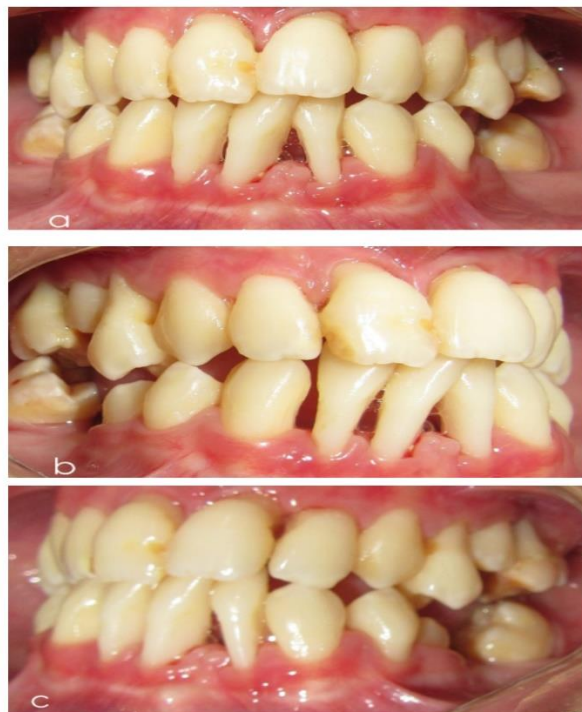


Fig. 5: Recall after 6 months



Fig. 4: Recall after 1 month



Fig. 6: Recall after 12 months



Fig. 7: Recall after 3 years



Fig. 8. Orthopantomogram after 3 years

**Discussion**

Haneke et al (1979) gave important criterias to identify the cases of Papillon Lefèvre syndrome-“(a) Palmoplantar hyperkeratosis; (b) Loss of primary and permanent teeth; and

(c) Autosomal recessive inheritance”.<sup>9</sup> The pathophysiology of Papillon Lefèvre Syndrome is associated with several factors.

**Genetic factors**

The Cathepsin C (CTSC) gene encodes a cysteine-lysosomal protease. This enzyme is also known as dipeptidyl-peptidase I. The function of dipeptidyl-peptidase I is to remove dipeptides from the amino terminus of the protein substrate. Mutations of Cathepsin C (CTSC) gene leads to deficiency of CTSC enzymatic activity.<sup>10-12</sup>

**Immunologic factors**

CTSC encodes variety of serine protease enzymes. Serine protease enzymes play a major role in variety of inflammatory and immune responses. Hence, deficiency of CTSC function makes an individual immunocompromised, leading to increased susceptibility towards various infection. Latest reports by Lundgren et al (2005) stated that the impairment of natural killer cell cytotoxic function is the first consistent immune dysfunction in PLS.<sup>13,14</sup>

**Microbiologic factors**

Various studies were done to prove the microbiological etiological factor involved in the origin of PLS. Robertson et al (2001), found different periodontologic pathogens like *A. actinomycetemcomitans*, *Porphyromonas gingivalis*, and *Prevotella intermedia* in the subgingival plaque of PLS patients.<sup>15</sup> Albandar (2015) conducted a detailed study of the subgingival microbiota of Papillon-Lefèvre syndrome and detected 12 bacterial species. Cultures of the periodontal pocket samples showed high percentage of *A. actinomycetemcomitans* colonies.<sup>16</sup>

**Differential diagnosis**

Hypophosphatasia, Langerhan's cell histiocytosis, Chediak-Higashi syndrome, Acrodynia, Acatalasia, Leukemia and Neutropenia.<sup>17</sup>

**Table 1:** Literature review on its management

S.No	Year	Author	Treatment protocol
1.	1989	Kellum RE et al <sup>18</sup>	1. Scaling and root planning; Oral hygiene instructions and 0.2% chlorhexidine gluconate mouth rinses; 1. Antibiotic treatment therapy in order to control the bacteremia. 2. Antibiotics: Amoxicillin (20–50 mg/kg/d) plus metronidazole (15–35 mg/kg/d). Amoxicillin and Clavulanic acid was also found effective in few cases.
2.	1993	Eronat et al. <sup>19</sup>	Amoxicillin plus Clavulanic acid at a dosage of 1 g per day for 10 days every 6 months.
3.	1995	Baer and Mcdonald et al <sup>20</sup>	1. It was suggested to extract all primary teeth till the age of 3 years. 2. Removable prosthesis after 3 month. 3. Therapeutic dose of tetracycline for 10 days after placement of the dentures;
4.	1995	Kressin S et al <sup>21</sup>	Treatment modalities such as systemic and local antibiotic treatment, and synthetic retinoids have been tried with limited success
5.	2002	Herrera et al <sup>22</sup>	Scaling and root planning along with adjunctive antibiotics in combination with adequate home care is effective in improving the clinical periodontal parameters.
6.	2005	Jain V.Gupta et al <sup>23</sup>	It was suggested to replaced by removable prosthesis during mixed dentition phase. Later on, after the eruption of permanent teeth various other treatment modalities were used to replace the missing teeth like

			conventional complete dentures, modified complete conventional complete dentures, modified complete dentures, implant supported complete dentures, over dentures, or a combination of these.
7.	2005	Lee MR et al <sup>24</sup>	Prolonged use of oral retinoids has been shown to be beneficial in preventing exfoliation of permanent teeth in children
8.	2005	Ullbro C et al <sup>25</sup>	Dermatological lesions were treated by oral administration of Retinoids specifically Acitretin and Etretinate.
9.	2011	Ahmadian et al <sup>26</sup>	Implant-supported overdentures were recommended for the oral rehabilitation of edentulous patients with PLS.
10.	2014	Teughels W et al. <sup>27</sup>	Surgical treatment of such aggressive form of periodontal cases is generally not supported by a lot of studies.

## Conclusion

Under the limitations of this case report, we draw the following conclusions:

1. Edentulism at a young age may have psychological as well physiological impact on children. That's why it is very important to preserve the compromised dentition in such patients.
2. Proper treatment protocol helps to achieve long term preservation of teeth in patients with Papillon Lefèvre syndrome.
3. Parent counselling plays a very important role in the treatment plan.

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## Conflict of interest

None.

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