Case Report

Combined Therapy in a Patient With Papillon-Lefèvre Syndrome: A 13-Year Follow-Up

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**Background:** Papillon-Lefèvre syndrome (PLS) is an autosomal recessive disease characterized by hyperkeratosis of the palms and soles combined with premature loss of the primary and permanent dentition. Several treatment regimens have been recommended in the literature; however, a definitive treatment protocol has not been established. This case report evaluates the success of combined therapy in managing a patient with PLS.

**Methods:** A 6-year-old girl diagnosed with PLS presented with aggressive periodontal destruction of her primary and permanent dentitions. After extraction of periodontally affected teeth, the edentate region was rehabilitated with different temporary dentures until her skeletal growth was complete. At the same time, her orthodontic treatment was performed. The early loss of her incisors resulted in inadequate alveolar bone height and width for esthetic-advanced prosthetic rehabilitation. Alveolar bone augmentation was performed, and 6 months later, two intraosseous dental implants were placed into the central incisor zone.

**Results:** After 13 years of treatment and follow-up, the patient had periodontally healthy permanent dentition. She had practiced meticulous oral hygiene, and the orthodontic treatment was successful and without incident. Alveolar ridge augmentation and placement of an intraosseous implant with guided bone regeneration were performed successfully.

**Conclusions:** This case report demonstrates that individually developed treatment protocols can provide long-term dental/periodontal success in patients with PLS. A multidisciplinary approach with advanced periodontal surgery, orthodontic and prosthetic treatment, and implant therapy may be an appropriate treatment modality for dental rehabilitation in patients with PLS. J Periodontol 2007;78:1819-1824.

**KEY WORDS**

Dental implants; orthodontics; Papillon-Lefèvre syndrome; prosthodontics; regeneration; therapy.

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Papillon-Lefèvre syndrome (PLS) was first described in 1924 as a condition characterized by hyperkeratosis of the palms and soles combined with premature loss of the primary and permanent dentitions.1 Hyperkeratotic lesions of the elbows and knees also may occur, and PLS often involves dental calcification as well. The syndrome is caused by a rare, autosomal recessive trait with a prevalence of between one and four persons per million. Males and females are affected equally, and no racial predominance seems to exist.2 The rate of parental consanguinity is far greater than that for the general population.2,3

The clinical features usually become apparent between the ages of 1 and 5 years. Periodontitis affects the primary and secondary dentitions, resulting in premature tooth loss of both dentitions. Typically, eruption of the primary dentition into the oral cavity is accompanied by severe gingival inflammation and generalized aggressive periodontitis. A close relationship between the presence of Actinobacillus actinomycetemcomitans (Aa) and periodontal destruction in PLS patients has been suggested by microbiologic monitoring and clinical examination following various treatment modalities.4 An improvement in clinical symptoms has been demonstrated with simultaneous elimination of Aa from the gingival crevice and mouthrinse.4,5

All of the permanent dentition may be lost between the ages of 14 and 17 years. After a toothless period, the third molars erupt with no sign of inflammation. Premature tooth loss results in alveolar bone loss and decreased facial height and a senile appearance.

Conventional periodontal treatment and systemic administration of various antibiotics with debridement usually fails in patients with PLS, and the rapid
progression of periodontitis often results in a severe loss of alveolar bone.\textsuperscript{4,6-8}

In recent years, a different therapeutic approach has been proposed. This approach involves elimination of periodontal pathogenic flora, by extracting all of the primary teeth several months prior to eruption of the permanent teeth, combined with antibiotic treatment to reduce the chance of possible infection of the permanent dentition.\textsuperscript{5,9,10}

This report describes the outcome of an interdisciplinary treatment approach for a PLS patient, including 13 years’ follow-up.

**CASE REPORT**

In 1993, a 6-year-old white girl was referred to the Department of Periodontology at Baskent University in Ankara, Turkey. The patient’s intraoral examinations revealed gingival inflammation, pain while chewing, mobility of the anterior incisors, halitosis, and increased secretions. She had hyperemic, edematous gingiva with multiple periodontal abscesses; pus drained on slight pressure. All of the teeth had hypermobility. She had little subgingival plaque; however, subgingival scaling showed abundant plaque deposits. Radiographic examination revealed severe bone loss around all of the primary teeth. The permanent mandibular central incisors and the two first mandibular molars were erupting (Figs. 1A and 1B).

Her medical history indicated mobile primary incisors with gingival inflammation at the age of 4 years and accompanying hyperkeratotic lesions on the palms, knuckles, knees, elbows, and soles that were diagnosed by a dermatologist (Fig. 2).

The medical and dental histories of the patient’s relatives also were investigated. Her parents were cousins. Her mother had severe periodontitis, and the patient’s 25-year-old uncle had lost all of his teeth except for his mandibular third molars; he had been using a complete denture for 7 years. He had a collapsed facial profile and decreased facial height with a prognathic mandible. None of the patient’s relatives had any cutaneous abnormalities.

Initially, the patient and her family were informed about the disease and its impact on oral and dental health. Scaling and root planing were performed under local anesthesia. Oral hygiene procedures were explained to the patient; treatment and oral hygiene were supported with chlorhexidine digluconate mouthrinse (0.2%) twice daily. Routine control appointments were made weekly.

Subgingival plaque samples from periodontally affected sites of the patient and her mother were collected with sterile paper points and transferred to preanaerobitized Ringers solution.\textsuperscript{11} The dispersed
and diluted plaque samples were cultured anaerobi-
cally on a selective medium\textsuperscript{12} and on trypticase soy
blood agar supplemented with hemin and menadione
to detect the presence of \emph{Aa}\textsuperscript{13}.

The patient and her mother were \emph{Aa} positive, and
tetracycline was prescribed (100 mg/day for 3 weeks).
The patient’s involved primary teeth were extracted
while she was taking antibiotics. She visited the clinic
every 3 months for scaling and maintenance of her
oral hygiene. All of her primary teeth were extracted
in 1994, and her treatment then focused on the un-
erupted teeth (Fig. 1C).

The day after the extractions, partial dentures were
constructed to restore masticatory function. Six months
later, periodontal tissues around the first molars were
edematous and hyperemic, with probing depths ap-
proaching 14 mm. Her permanent lower incisors and
first molars were extracted, followed by doxycycline
treatment (100 mg/day for 3 weeks) (Fig. 3). In 1996,
the patient’s permanent upper incisors were extracted
because of severe periodontal destruction and alveo-
lar bone resorption. Her lower canines and upper
lateral incisors erupted uneventfully (Fig. 4).

According to Preus and Olsen\textsuperscript{11}, a systemic antibi-
otic (doxycycline, 100 mg/day for 3 weeks) was pre-
scribed to the mother and brother of the patient to
prevent bacterial transmission. We also recommended
against her sharing spoons, forks, plates, glasses, and
personal belongings.

Temporary dentures for the maxilla and the mandi-
able were planned to restore dentition and maintain the
interocclusal relation.

In 1997, the primary upper first premolars erupted
with no signs of inflammation. One month after the
last extraction, no clinical signs of periodontitis were
detected. The patient’s \emph{Aa} cultures were no longer
positive, but her mother was still \emph{Aa} positive.

The patient visited the clinic regularly for 6 years for
professional teeth cleaning and transitional dentures.
In 2004, orthodontic treatment was planned to correct
the occlusion and tooth positioning (Fig. 1D). Lower
and upper edgewise appliances were placed, and
nitinol arch wires were used for initial leveling. Ortho-
dontic treatment was based on very light forces be-
cause of a fragile periodontium. In the upper arch, the
rotations were corrected and diastemas were
closed. The lower left second molar was set upright
and straightened, and adequate space was obtained
for the first molar. Because of the periodontal condi-
tion of the right upper canine, these teeth were ro-
tated, and all of the remaining teeth on this side
were moved mesially. Orthodontic treatment contin-
ued for 1 year and 6 months.

In 2005, despite orthodontic braces and arch wires,
his oral hygiene was meticulous. She had a healthy
periodontium with a mean probing depth of 2.5 mm.
There was no sign of inflammation. Because she was
18 years old, she demanded a more esthetic and func-
tional prosthesis. Implant-supported fixed dentures
were planned to restore the dentition. The crestal
width and height of the alveolar ridge at the anterior
maxilla (which was inadequate for implant place-
ment) was 3 mm bucco-palatinally because of early
alveolar bone loss and extractions. Alveolar bone
augmentation was planned. Augmentation was per-
formed with a demineralized bone matrix\textsuperscript{8} and a tita-
nium membrane\textsuperscript{i} at the anterior alveolar ridge.
Healing was uneventful (Fig. 5). The membrane was
exposed \textasciitilde{}2 mm; however, there was no inflamma-
tion. The membrane was removed 8 weeks later;
the width of the ridge was 6 mm, which is suitable
for implant placement.

Three months later, two titanium implants\textsuperscript{¶} were
placed into central teeth sites at the anterior maxilla
(Fig. 1E). There was no bony dehiscence around
the implants, and primary stability was optimal; how-
ever, augmentation was repeated to thicken the

\textsuperscript{8} Grafton DBM, Osteotech, Eatontown, NJ.

\textsuperscript{i} CytoFlex mesh, Unicare Biomedical, Laguna Hills, CA.

\textsuperscript{¶} Tapered Screw-Vent, 3.7 mm \times 13 mm, Zimmer Dental, Carlsbad, CA.
surrounding bone for esthetic requirements (Fig. 6). The membrane was removed 6 weeks later (Fig. 7). An objective measurement of implant mobility was made 4 months after surgery using an electronic mobility testing device and was $-1$ and $0$. According to the manufacturer’s instructions, a score of $-8$ to $+90$ indicates a mobile implant abutment. A fixed prosthesis was made (Fig. 8).

For the mandibular incisor zone, distraction osteogenesis was planned for the horizontal deficit of the alveolar ridge. The horizontal bone and soft tissue of the mandibular anterior region were inadequate for guided bone regeneration.

DISCUSSION

PLS is a rare autosomal-recessive entity with palmo-plantar keratosis and early-onset periodontitis in the primary and permanent dentitions. Although many treatment procedures have been performed to prevent early tooth loss, there is no definitive treatment protocol.

PLS patients have a greater incidence of mutations of the cathepsin C gene located on the 11q14-q21 region of the chromosome. Cathepsin C plays a role in the development and maintenance of the skin, as well as immune and inflammatory cells. This gene is responsible for abnormalities in skin development and periodontal disease progression.\textsuperscript{14}

PLS patients are more susceptible to generalized infections. Also, an immune disorder might contribute to this population’s predisposition to periodontitis. Celentiigil et al.\textsuperscript{15} suggested that the etiology of periodontal destruction in PLS shows similarities to other periodontal diseases.

PLS patients have decreased neutrophil chemotaxis and phagocytosis, as well as a decreased phytohemagglutinin response by T lymphocytes.\textsuperscript{16} D’Angelo et al.\textsuperscript{17} found an increased susceptibility to infection with reduced chemotaxis in neutrophils and reduced myeloperoxidase activity in a PLS patient.

Subgingival $Aa$ plays a major role in the etiology of PLS periodontitis, and eradication of this pathogen is a key to successful therapy. The apparent involvement of $Aa$ in many PLS patients may have significant therapeutic implications.\textsuperscript{4,5,18}

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Clinicians have evaluated many specific protocols for treating the periodontal component of PLS syndrome. Van Dyke et al. administered tetracycline treatment for 3 weeks with conventional surgical procedures. Successful treatment of PLS periodontitis, using amoxicillin and metronidazole adjunctive to mechanical treatment, was reported by De Vree et al.

Although mechanical treatment with systemic antibiotics was the first treatment strategy for eradicating periodontal pathogens, a continued breakdown of the periodontium in patients exhibiting resistance to antibiotics has been seen. Possible transmission of Aa to family members was suggested first by Preus and Olsen in 1988. Monitoring and treating family members eliminate possible transmission and re-infection. We also prescribed tetracycline to our patient’s mother, but she remained infected. Therefore, we recommend no sharing of silverware or personal belongings between family members to reduce the probability of Aa contamination. Regular bacteriologic tests may help to prevent or control the potential infection risk. There were no signs of periodontal infection in our patient, and her oral hygiene was meticulous throughout follow-up.

One therapeutic approach to PLS is to eliminate the pathogenic periodontal flora by extracting all of the primary teeth several months before eruption of the permanent teeth, combined with antibiotic treatment to reduce possible infection of permanent dentition. This edentulous period can determine the permanent teeth, combined with antibiotic treatment, was reported by De Vree et al.

After an edentulous period, permanent teeth erupt without guidance, which leads to crowding.Lux et al. treated a PLS patient, who had severe bone loss and poor oral hygiene, with moderate orthodontic tooth movement. This case report is the first successful orthodontically rehabilitated PLS patient treated with a periodontal approach. There were no probing depths >3 mm during treatment.

Palmar plantar hyperkeratosis and the other genetic dermatologic disorders decrease with age. Tinanoff et al. reported decreased neutrophil chemotaxis and adherence in a 9-year-old patient, but these abnormalities were no longer present when the patient reached the age of 24 years. Wiebe et al. also indicated that the risk for developing periodontal disease decreases with age because of the immune response to antigenic challenge. Our patient also showed decreased hyperkeratotic lesions on her hands and feet as she grew older.

Only a few studies have evaluated the prosthetic rehabilitation of PLS patients. Prosthetic rehabilitation provided a psychological boost to the patient by improving her appearance as well as her dental functioning. Implant-based treatments are more important for these patients. Implant therapy in patients with severe periodontitis shows that periodontally compromised patients may be treated successfully with implants. There are no data evaluating osseointegration in patients with PLS. van Steenbergh et al. reported a successful implantation on an edentulous jaw in a patient with PLS, suggesting that hyperkeratosis palmo-plantaris is not a contraindication for implant therapy. Dental implants do not work for growing individuals because they act like ankylosed teeth. Age is an essential consideration for implantation. Ullbro et al. placed five osseointegrated implants in the canine region of a 25-year-old woman, which encouraged other clinicians to place implants in younger patients.

The present case report is the first to our knowledge in which successful implantation was performed in a periodontally healthy PLS patient. Presence of the periodontium increases the possibility of periodontal reinfection, which also may be a risk for peri-implantitis. The inflammatory response of new bone tissue to the infection remains challenging.

Our patient had inadequate alveolar bone for implantation, vertically and horizontally. Guided bone regeneration can assist in preimplant ridge augmentation; however, there are no data about wound healing in PLS patients after guided bone regeneration. The healing period of augmentation was uneventful, and we observed new tissue formation while removing the membrane.

The degree of mobility reveals the supporting bone quality after implant. Electronic mobility testing device measurements are the most common method of measuring osseointegration. These scores, together with radiographic and clinical evaluation of the implants, show successful results for two osseointegrated implants in our patient.

The alveolar distraction osteogenesis process involves mobilization, transportation, and fixation of a healthy bone segment to adjacent defective or deformed bone. Soft tissue and vertical bone level were insufficient in the mandibular incisor region, so an alveolar distraction was planned for future prosthetic or implant rehabilitation.

CONCLUSIONS

Many treatment strategies have been evaluated for functional and esthetic dentition in contemporary dental practice. Damage of the primary or permanent dentition in PLS patients is an inevitable outcome of the disease. Combined therapy that includes
orthodontic, prosthetic, periodontal, and regenerative therapy and implant procedures is essential to provide lifelong functional and aesthetically pleasing dentition.

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