THE TYPICAL APPEARANCE AND CBCT IMAGES OF THE PATIENT WITH PAPILLON–LEFEVRE SYNDROME: A CASE REPORT**

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Abstract

Papillon–Lefevre syndrome is a rare autosomal recessive genetic disorder, which is transmitted with an estimated frequency of one to four per million individuals. It is characterized by palmar-plantar hyperkeratosis, and rapid destruction of the alveolar bone and periodontium of both the primary and permanent dentitions, commencing at the time of tooth eruption.

Early diagnosed and rehabilitation of children with Papillon-Lefevre syndrome will go a long way in helping them interact normally and integrate with their peers. However, the rarity with which this entity appears, along with its complex characteristics, often make it difficult to treat.

The aim of this case report is to present the early diagnosed of a 5-year-old boy with Papillon–Lefevre syndrome associated with severe periodontitis in which the premature exfoliation of primary maxillary and mandibular incisor teeth and maxillary primary first molars are observed, and with hyperkeratosis of the palms, knees and soles.

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Introduction

Papillon-Lefevre syndrome (PLS) was first described by two French physicians, Papillon and Lefevre, in 1924[1]. It is a rare autosomal recessive trait in which the main features are hyperkeratosis of the palms and the soles, and severe early-onset periodontal disease that results in premature exfoliation of primary and permanent dentitions[2,3]. Calcification of the falx cerebri and the choroid plexus, and retardation of somatic development is often an associated feature[3,4].

The prevalence of PLS is 1-4 per million individuals with no sex predilection and no racial predominance[1,2]. A genetic predisposition, with greater frequency of occurrence in consanguineous offspring, has been reported[2]. The gene responsible for PLS has recently been localized to chromosome 11q14-21 [OMIM 245000][5], which involves mutations of cathepsin C[6]. Studies in PLS patients have shown more than 90% reduction in cathepsin C activity[6,7]. Despite these advances in characterizing the genetic basis of the syndrome, the pathogenic mechanisms leading to the periodontal involvement remain elusive. An impaired chemotatic and phagocytic function of polymorphonuclear leukocytes (PMNs) has been described in various reports[8-10]. In contrast to the above studies[11,12], however, reported normal PMN chemotaxis. Few reports have addressed lymphocyte function in PLS.

In Papillon-Lefevre syndrome, the eruption of primary teeth occur at the expected ages and in the normal sequence, with the teeth

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being of normal form and structure. Eruption of the primary dentition into the oral cavity is accompanied by severe gingival inflammation and a generalized aggressive periodontitis, resulting in tooth mobility. Severe resorption of alveolar bone gives the teeth a 'floating-in-air' appearance on dental radiographs. There is dramatic alveolar bone destruction, often leaving atrophied jaws[13,14]. Plaque accumulates in the deep crevices and halitosis can ensue. The primary incisors are usually affected first and can display marked mobility by the age of 3 years. By the age 4 or 5 years, the primary teeth frequently become loose and exfoliate[1,4]. After exfoliation of the primary dentition, the gingival inflammation resolves. As the permanent teeth erupt, the same sequence of events recur and, without intervention[1], most of the permanent teeth are lost by 14-15 years of age[1,4,15].

The aim of this case report is to present the early diagnosed of a 5-year-old boy with PLS associated with severe periodontitis in which the premature exfoliation of primary maxillary and mandibular incisor teeth and maxillary primary first molars are observed, and with hyperkeratosis of the palms, knees and soles.

Case Report

A 5-year-old boy presented with complaints of thickening of the skin, palms and soles, and walking difficult. His history revealed that this condition, together with loss of teeth, was noticed by his family at the age of 3. His family history was unremarkable.

His intraoral examination disclosed the absence of maxillary and mandibular primary incisor teeth and maxillary left and right primary first molars. Oral hygiene was poor with significant plaque accumulation, and a buccal swelling associated with the mandibular right primary second molar. There were gingivitis together with generalized recession, periodontal pocketing and mobility affecting most of the teeth. The mandibular right first and second primary molars were carious (Figures 1,2). No other abnormality was detected in relation to soft tissues.

Extraoral examination revealed hyperkeratosis of the knees, the elbows, the palms of the hands, soles of the feet, also extending onto the dorsal surfaces of the hands and the feet (Figures 3A,B,C).

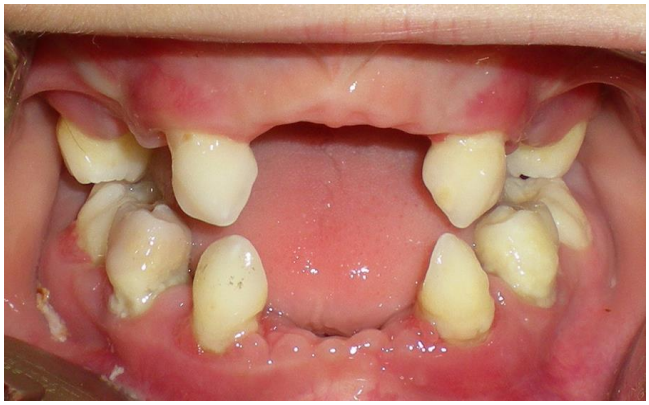

Figure 1. Primary dentition showing significant plaque accumulation and severe periodontal destruction.

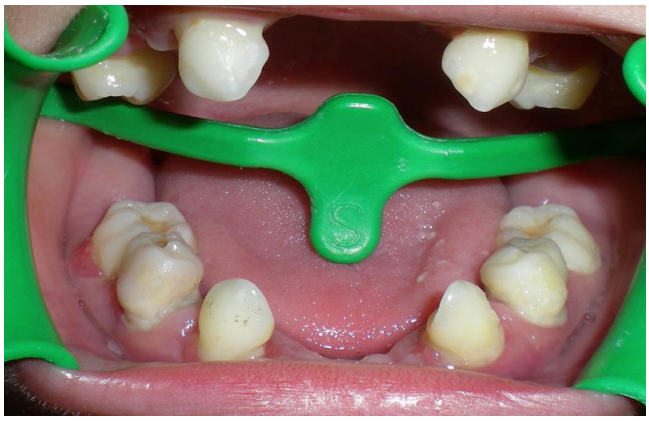

Figure 2. Absence of maxillary and mandibular primary incisor teeth and maxillary left and right primary first molars.

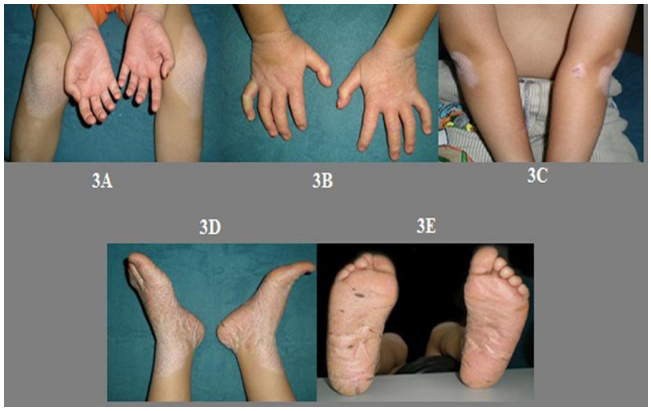

Figure 3A. Hyperkeratosis of the knees and the palms of the hands. **3B.** Hyperkeratotic lesions on the dorsal sides of the hands. **3C.** Hyperkeratosis of the elbows. **3D.** Hyperkeratosis of the soles extends to the achilles tendon, ankles and external malleoli. **3E.** Soles of the feet showing extensive hyperkeratosis. Crustations and fissures are evident.

Moreover, hyperkeratosis of the soles extends to the achilles tendon, ankles and external malleoli (Figure 3D). The soles affected more severely than the other regions, which make walking difficult (Figure 3E).

Laboratory investigation was carried out, which included normal complete blood count (CBC), blood biochemistry, immunoglobulins, C-reactive protein and sedimentation rate. The results were within normal limits.

Radiographic examination confirmed the presence of generalized destruction of the alveolar bone around the primary dentition (Figure 4). In view of the above findings, the case was diagnosed as PLS.

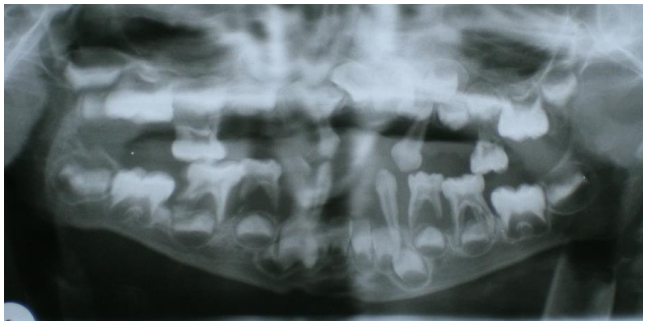

Figure 4. Panoramic radiography showing extensive destruction of the alveolar bone around the primary dentition.

The patient was being treated by Acitretin prescribed by the consultant dermatologist, which markedly improved the hyperkeratosis, but provided no improvement in the periodontal lesions. Because of the severe periodontal destruction, it was necessary to undertake a dental clearance of the primary dentition. Treatment in this case was including periodontal therapy and initiation of an exhaustive prevention program involving instructions for oral hygiene (with implication of the parents). The patient has been periodically recalled at six-months intervals.

A year later intraoral examination of the patient showed that the primary teeth had been completely exfoliated which resulted from severe gingival inflammation and a generalized aggressive periodontitis. However, first molar teeth was realized to erupt. Three-dimensional (3-D) cone beam computed tomography (CBCT) (i-CAT®, Model 17-19, Imaging Sciences International, Hatfield, Pa USA) was used in order to obtain more detailed examinations of non-erupted permanent teeth and their positions[16] (Figures 5A,B,C).

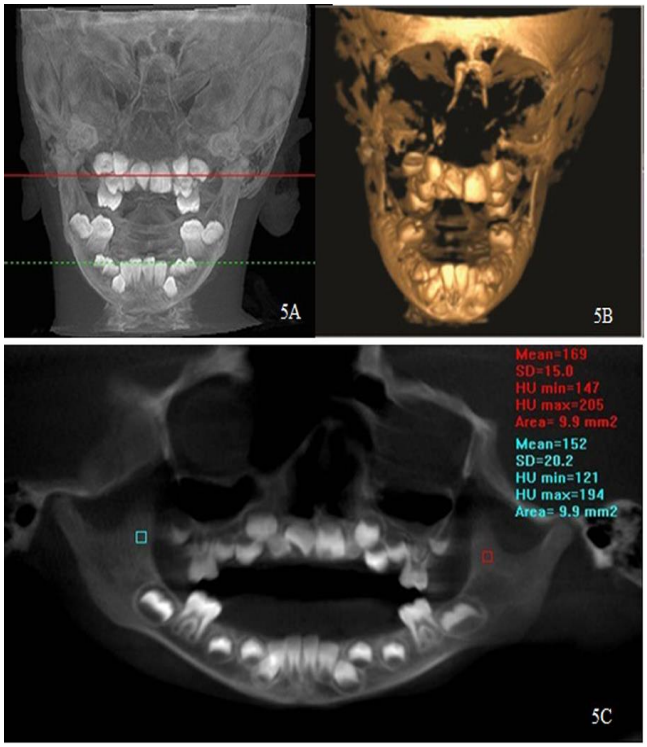

Figure 5 A,B,C. Three-dimensional (3-D) cone beam computed tomography images. All images were obtained with 440 projections and the voxel dimension in the reconstructed image is 0.3 X 0.3 X 0.3 mm. The x-ray emission time was 3,5 seconds. Exposures were made with 5.0 mA, 120 kV and an exposure time of 4 seconds. From the volume obtained after a reconstruction time of ~ 30 seconds.

Orthodontic consultation was established and the management of this was postponed until the other mandibular and maxillary permanent teeth erupted.

Discussion

Papillon-Lefevre syndrome can adversely affect growing children esthetically, psychologically, and socially. Thus, early dental evaluation and parental counseling as a part of preventive dental treatment is essential for providing complete psychosocial rehabilitation for PLS children; a multidisciplinary approach may improve the prognosis and quality of life of these children.

The pathogenesis of PLS is not completely understood. While the skin lesions were thought to derive from a combination of ectodermal and mesodermal malformations, there has never been any explanation for the

cause or the rapidity of the loss of all teeth in the order of their eruption. Two new aspects of PLS have been discovered. Firstly, some PLS patients were found to exhibit either a cellular immune defect with a decreased PHA (phytohemagglutinin) stimulation of lymphocytes or deficient chemotaxis and phagocytic function of neutrophilic granulocytes[12]. Secondly, an association of gram-negative anaerobic rods such as bacteriodes gingivalis, actinobacillus actinomycetemcomitans and capnocytophaga and spirochetes have been observed[17]. Moreover, recent research has shown that inactivation of the cathepsin C gene is responsible for the abnormalities in skin development and periodontal disease progression[18]. These various factors contributing to the etiopathogenesis of this disease ensure that successful treatment of the rapid periodontal destruction seen in this syndrome remains a challenging problem.

The PLS is easily misdiagnosed at initial presentation since the skin lesions can be mistaken for eczema. Skin lesions usually present from 6 months to 3 years of age, approximating the time of tooth eruption. These may start as diffuse red and scaly patches on the palms of the hands and soles of the feet. Lesions are well demarcated and predominantly affect the palms extending to the thenar eminences and to the volar wrists. Involvement of the soles extends to the Achilles tendon and frequently spills over the edges. There can be occasional involvement of the eyelids, cheeks, labial commissures, knees, elbows, thighs, external malleoli, toes and dorsal fingers. The soles are frequently affected more severely than the other regions, which may make walking difficult[1,4]. The presence of skin lesions, along with complete loss of teeth due to severe periodontitis enabled us to diagnose the present condition as PLS.

The differential diagnoses include Hiam-Munk syndrome and hypophosphatasia. Hiam-Munk syndrome also exhibits arachnodactly, acroosteolysis, atrophy of nails, and deformity of the phalanges in the hands[19]. None of these features was found in the present cases. In hypophosphatasia, deficiency of alkaline phosphatase activity is seen, but in our case's values were within normal limits and therefore this differential diagnosis could be excluded.

A multidisciplinary approach is important for the care of patients with PLS. The skin manifestations are usually treated with emollients and oral retinoids. Oral retinoids including acitretin, etretinate, and isotretinoin are the mainstay of treatment of both the keratoderma and periodontitis associated with PLS[20]. Treatment may be more beneficial if it is started during eruption and maintained during the development of permanent teeth. But the periodontitis in PLS is usually difficult to control. A definite treatment regime is not yet reported; however, to control periodontal destruction, several treatment modalities have been suggested, e.g., conventional periodontal therapy, oral hygiene instructions, and systemic antibiotics[21]. However, treatment with oral hygiene instructions, scaling and root planing has been reported unsuccessful[15,22]. Non-surgical treatment combined with use of systemic antibiotics[23,24] and additional periodontal surgery[23] has also been reported to fail. Patients are often edentulous at an early age. For edentulous patients, oral rehabilitation is required; this includes partial or complete denture prosthetic replacement (according to the age of the patient). Osseointegrated implants are an option for the future and can have a great impact psychosocially by restoring esthetics as well as function.

Conclusion

Papillon-Lefevre syndrome threatens children and their parents with the prospect of edentulism if left untreated. Thus, early diagnosis and intervention is essential. The diagnosis and treatment of the periodontal constituent of PLS are both very difficult. Further research is required for defining a treatment strategy that can save the smiles of these children.

The pediatric dentist is the first member of the health team to see and treat children afflicted with unusual syndromes such as PLS and, therefore, awareness of this syndrome is essential if the dentist is to provide appropriate and comprehensive dental care. In addition, greater awareness of this syndrome will be helpful in identifying more cases for further study.

Declaration of Interest

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