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Papillon–Lefèvre syndrome: a report of two cases

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Summary. Papillon–Lefèvre syndrome is a rare disease characterized by skin lesions caused by palmar-plantar hyperkeratosis, and severe periodontal destruction involving both the primary and permanent dentitions. It is transmitted as an autosomal recessive condition and consanguinity of parents is evident in about one-third of cases. This paper describes two preschool children who presented at the Paediatric Dentistry Department, Sheffield, UK, with progressively loosening teeth and discomfort during eating. The medical history revealed scaling on the hands and feet, which had been medically diagnosed as eczema. Papillon–Lefèvre syndrome was diagnosed in both cases.

Introduction

Papillon–Lefèvre syndrome (PLS) was first described in the literature by Papillon and Lefèvre in 1924 [1], with more than 200 cases having subsequently been reported. The syndrome is a rare autosomal recessive trait with an incidence of between one and four persons per million. Parental consanguinity is demonstrated in between 20% and 40% of cases [1,2]. There has been no gender preference detected to date [3].

Papillon–Lefèvre syndrome 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. Calcification of the falx cerebri and the choroid plexus, and retardation of somatic development is often an associated feature [2,4,5]. It has been suggested that 20–25% of patients show an increased susceptibility to infection [1,5,6], of which otitis media is a common example [12].

The syndrome 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].

Periodontal effects appear almost immediately after tooth eruption when gingivae become erythematous and oedematous. 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 of 4 or 5 years, all the primary teeth may have exfoliated [1,4]. Following such tooth loss, the gingival appearance resolves and may well return to health only for the process to be repeated as the permanent dentition starts to erupt [1]. The majority of the teeth are lost by the age of 14–15 years [1,4,6]. There is dramatic alveolar bone destruction, often leaving atrophied jaws [6].

The two cases described below of 4- and 3-year-old boys, respectively, serves to illustrate the periodontal effects on the primary dentition.

Case report

Case 1

A 4-year-old Bangladeshi male was referred to the Paediatric Dentistry Department of the Charles

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Fig. 1. Case 1: Hyperkeratosis of the palms of the hands and knees.

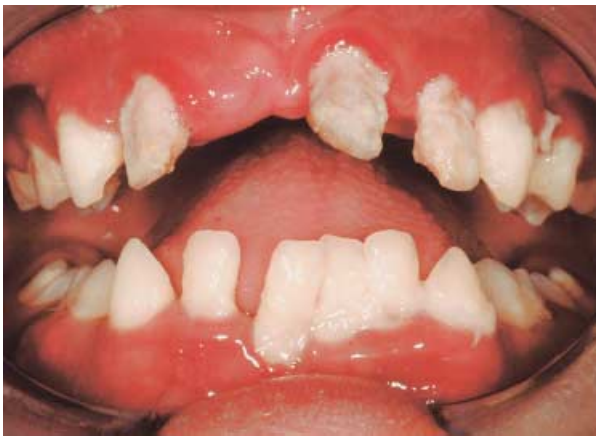

Fig. 2. Case 1: Primary dentition showing significant plaque accumulation and severe periodontal destruction.

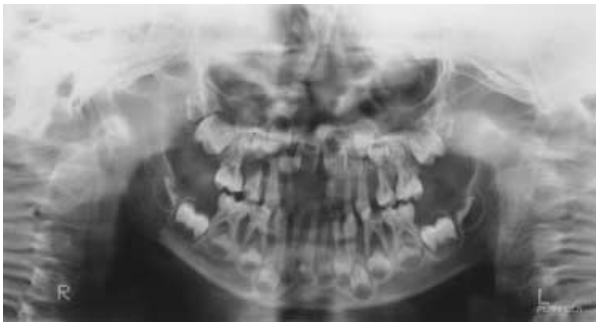

Fig. 3. Case 1: Orthopantomogram showing extensive destruction of the alveolar bone of the primary dentition.

Clifford Dental Hospital from the Oral and Maxillofacial Department of the Leicester Royal Infirmary, Leicester, UK. The patient presented with progressively loosening teeth and discomfort on eating. A medical history revealed eczema on the hands and feet, and the child had been recently diagnosed with PLS (palmoplantar keratosis with periodontitis) by the dermatologist. The clinical geneticist confirmed consanguinity of the parents (first cousins), neither of whom appeared affected, and offered genetic counselling in relation to the autosomal recessive nature of the condition.

Extraoral examination revealed hyperkeratosis of the palms of the hands, soles of the feet and the knees (Fig. 1).

Intraoral examination revealed that all the primary teeth were present with the exception of the upper right primary central incisor. Oral hygiene was poor with significant plaque accumulation and a buccal swelling associated with the lower right first primary molar. There was gingivitis together with generalized recession, periodontal pocketing and mobility affecting most of the teeth. Both the lower left and right first primary molars were carious (Fig. 2).

Radiographic examination (orthopantomogram and periapicals) confirmed the presence of generalized destruction of the alveolar bone around the primary dentition (Figs 3 and 4).

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.

In view of the age of the patient, together with the number of teeth and quadrants involved, this was carried out under general anaesthesia. The recovery was uneventful and the patient was subsequently lost to follow-up.

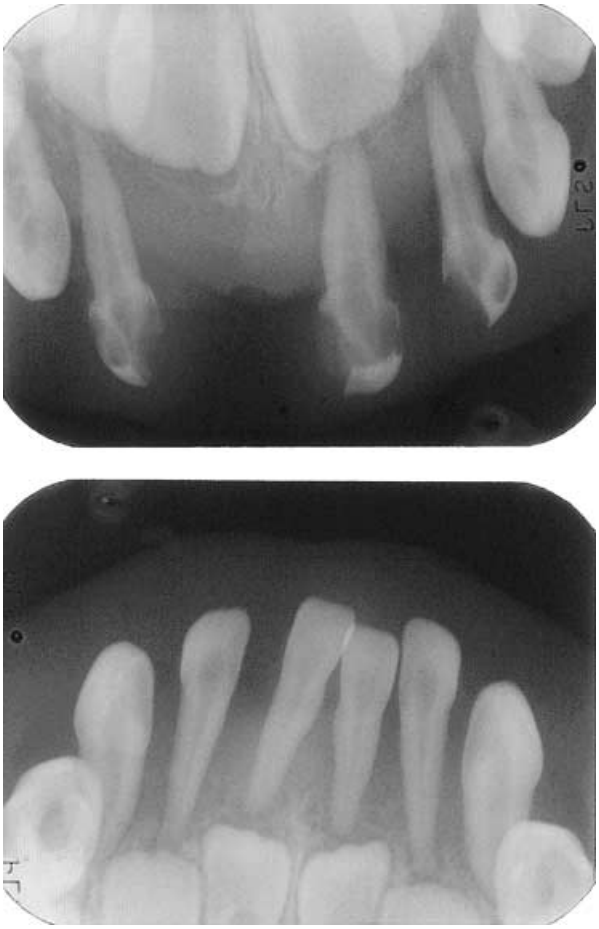

Fig. 4. Case 1: Periapical radiographs showing severe alveolar bone loss around the maxillary and mandibular anterior teeth.

Case 2

A 3-year-old Pakistani male was referred to the Charles Clifford Dental Hospital by his general dental practitioner for advice regarding the mobility of the maxillary and mandibular primary incisors, and 'deep' pockets around the mandibular first primary molars. These teeth were becoming progressively looser and the patient was experiencing discomfort on eating. His mother was concerned regarding halitosis. There was no history of trauma. Medically, the patient had been diagnosed with eczema of both hands and feet at 3 months of age, and was now using a topical steroid cream. The family history was unremarkable, but questioning revealed that the parents were consanguineous (first cousins), neither of whom appeared affected.

Extraoral examination confirmed keratosis of the palms of the hands and the soles of the feet (Figs 5 and 6).

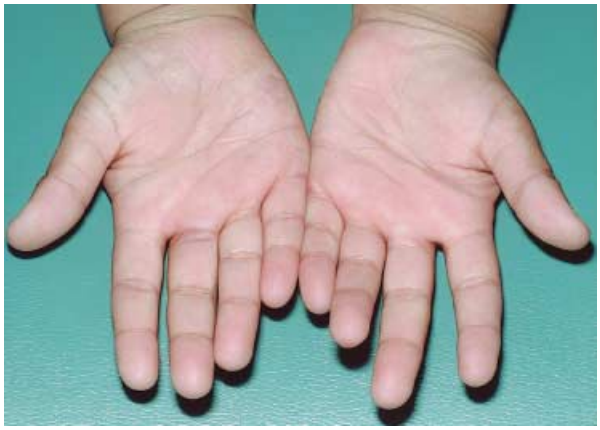

Fig. 5. Case 2: Hyperkeratosis of the palms of the hands.

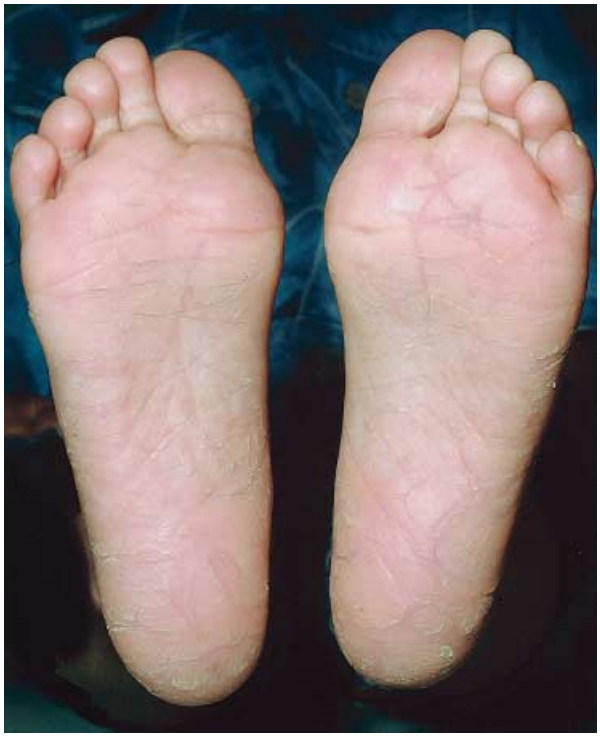

Fig. 6. Case 2: Hyperkeratosis of the soles of the feet.

On intraoral examination, there was a full complement of primary teeth, although the lower right primary lateral incisor and canine were geminated. There was generalized recession, marginal gingivitis and severe mobility affecting the majority of the teeth (Fig. 7).

Radiographic examination (orthopantomogram and upper standard occlusal) revealed severe alveolar bone loss affecting the entire primary dentition and the

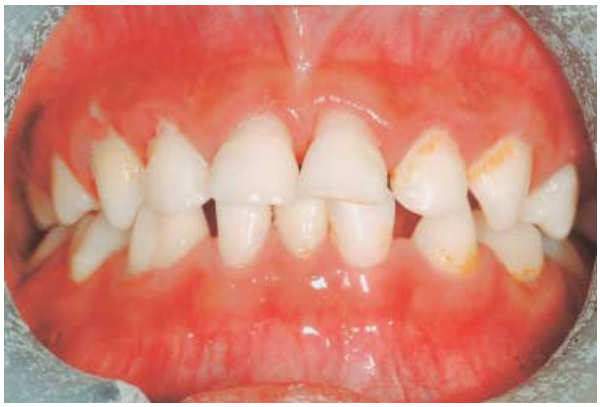

Fig. 7. Case 2: Intraoral photograph showing generalized recession and severe periodontal destruction.

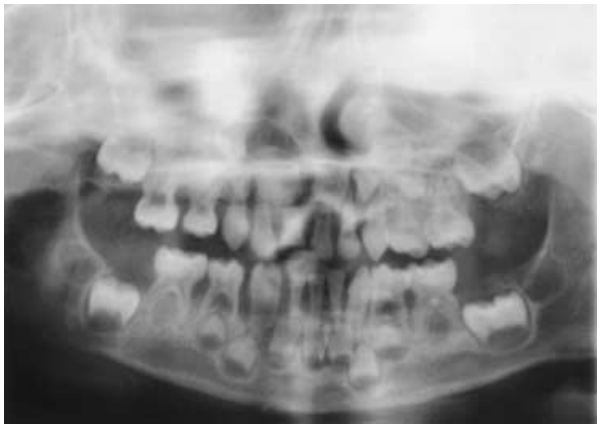

Fig. 8. Case 2: Orthopantomogram showing extensive destruction of the alveolar bone and absence of the lower right permanent lateral incisor.

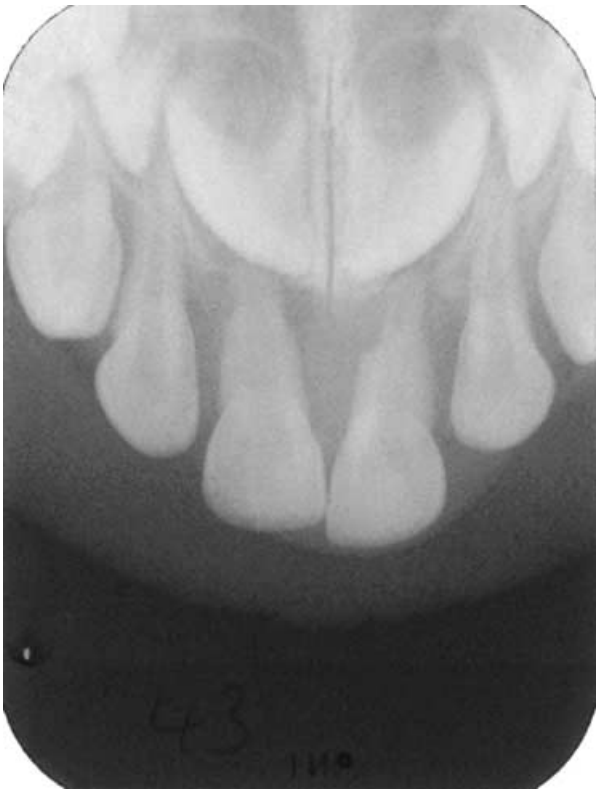

Fig. 9. Case 2: Upper standard occlusal radiograph showing severe bone loss around the maxillary incisors and resorption of the roots.

absence of the lower right permanent lateral incisor (Figs 8 and 9).

Differential diagnoses comprised hypophosphatasia, Chediak–Higashi, PLS, Hiam–Munk syndrome, agranulocytosis, cyclical neutropenias and lazy leucocyte syndrome. Localized Langerhan's histiocytosis and congenital indifference to pain syndrome were considered, but the clinical findings were most similar to hypophosphatasia and PLS.

Haematological investigations included full blood count (FBC) calcium, phosphate, alkaline phosphatase and urinary phosphoethanolamine assessment. The phosphethanolamine levels were raised, but not diagnostic of hypophosphatasia, and all other tests were within normal limits. Thus, the other differential diagnoses were excluded.

A referral was made to the Sheffield Children's Hospital to the Professor of Paediatric Bone Disease where the provisional diagnosis of PLS has been confirmed. Dental treatment options for this patient are currently under consideration, and include extraction of teeth with poor prognosis, possible treatment with bisphosphanates or Doxycyclin, or treatment with extraction of all the primary dentition prior to the permanent dentition erupting. The possible prescription of Doxycyclin has now been discounted because of the patient's age and the possible effects on the permanent dentition. Although a definitive treatment regime is not yet reportable, in view of the progressive mobility of all the primary units (particularly the primary molars) and since extraction of all standing teeth has been thought to be the most effective treatment to date, a primary clearance is the most likely course of action. Should this become inevitable, this will be undertaken under general anaesthesia, together with a bone biopsy. The opportunity to perform a bone biopsy will be taken if the extractions are required, against the use of bisphosphanates being considered as a possibility in the future.

Discussion

Although over 200 cases have been reported in the literature, PLS is a rare condition with an incidence of between one and four persons per million [1]. The aetiology of PLS is not completely understood, and the literature has looked into anatomical defects, microbiological factors, viral agents and host response as causative factors [6]. The two cases reported here are associated with consanguinity of both sets of parents. Both children are of Asian origin, and in both cases, the skin lesions observed at the initial presentation were mistaken for eczema.

Recent studies have suggested a greater incidence of mutations of the capthasin C gene located on the 11q14-q21 region of the chromosome. Capthasin C plays a role in the development and maintenance of the skin, and the immune and inflammatory cells [6]. Previous studies have suggested that the gene is responsible for the abnormalities in skin development and periodontal disease progression [5,6]. A similar mutation on this chromosome occurs in Hiam–Munk syndrome, which is associated with prepubertal periodontitis and palmoplantor hyperkeratosis [1]. Hiam–Munk syndrome is similar to PLS in this respect, but sufferers also exhibit arachnodactly, acroosteolysis, atrophy of the nails and deformity of the phalanges of the hand [6].

Evidence has suggested that PLS patients have decreased chemotatic and phagocytic functions of neutrophil leucocytes, or a cellular immune defect involving decreased phyto-haemaglutinin response by T lymphocytes. Products of the Gram-negative organisms isolated from PLS patients' periodontal pockets may directly or indirectly contribute to leucocyte dysfunction, and there may be genetic component in the white cell dysfunction [12].

It has been suggested that the presence of periodontal pathogens alone is not sufficient for the expression of PLS, and other factors, such as host response, play an important role in the pathogenesis of the disease process [8]. Several authors have suggested an abnormal neutrophil dysfunction with PLS [5,7,10] to explain the pathogenesis, whereas others have reported cases where they appeared within normal limits [5].

Microbiological studies have demonstrated a greater prevalence of *Actinobacillus actinomycetemcomitans* in patients with PLS, and these findings have suggested that it has a significant role in the pathogenesis and progression of rapid periodontal breakdown [5–10]. Other pathogens have also been implicated, including *P. gingivalis*, *F. nucleatum*, *B. forsythus*, *T. denticola* and *P. intermedia* [5], suggesting a multifactorial aetiology of pathogen involvement.

There is conflicting evidence to demonstrate whether anatomical defects in root cementum, such as resorption, are required for the periodontal lesions to develop [4,6]. It was noted in our second case report that the patient had resorption of the maxillary primary central incisors, but this may have been age-related.

Severe periodontal and alveolar bone destruction in children necessitates that a diagnosis should be reached to exclude any life-threatening disorders. These include leukaemia and neutropenias, where loosening of the teeth is an associated feature, along with extensive gingivitis, haemorrhage and ulceration [13]. Other disorders where premature loss of primary and/or permanent teeth occur include hypophosphatasia, Langerhan's cell histiocytosis, Chediak–Higashi syndrome, acrodynia and acatalasia [1,13]. The patients discussed in this paper presented with prepubertal periodontal destruction with concomitant palmar-plantar hyperkeratosis diagnosed as PLS. Hiam–Munk syndrome, which also presents with these features, was excluded since none of the other associated findings, which include arachnodactly, acroosteolysis, atrophy of the nails and deformity of the phalanges of the hand [6], were noted.

If left untreated, patients who develop PLS will be rendered edentulous in their early teens. Several treatment regimes have been recommended in the literature, but a definitive treatment protocol has yet to be established. Various treatment modalities have been suggested, including: early extraction of primary teeth to eliminate all pathogens involved and allow the remaining teeth to erupt without infection [4,5]; a combined approach employing systemic and local antimicrobial therapy as an adjunct to non-surgical periodontal therapy [2,9]; or the use of synthetic retinoids, which have a positive effect on the skin lesions [6]. There are varying data suggesting that the use of retinoid medication has proved beneficial in the treatment of the periodontal lesions [6,11], but a combination of retinoid therapy and periodontal therapy has been reported to improve both conditions [3,5].

Several papers have adopted two different extraction protocols for the treatment of PLS, including the extraction of all primary teeth [4,6], followed by a period of edentulousness and elimination of

pathogens, to allow the permanent teeth to erupt without subsequent infection and allow for healthy periodontium. An alternative approach is dependant on the timing of the extractions, where all the erupted teeth present at that time are extracted to inhibit the pathogens spreading to the gingival crevices of the succeeding dentition [6,7]. Unfortunately, since PLS is rare, the majority of publications are case reports with little documentation of the long-term successful treatment of PLS.

Conclusion

The diagnosis and treatment of the periodontal component of PLS are both very difficult. In this paper, one of the patients was treated by extraction of the entire primary dentition. Unfortunately, this patient was lost to follow-up, and therefore, no long-term observations can be reported. Treatment options for the second patient are still under consideration, so a definitive treatment regime is not yet reportable, although extraction of all standing teeth has been suggested as the most effective treatment to date. Since the symptoms associated with PLS are likely to decrease with increasing age, it is suggested that teeth erupting after this period may be less susceptible to periodontal disease, thus allowing the possibility of retaining some of the dentition into later life [6].

Résumé. Le syndrome de Papillon-Lefèvre est une maladie rare caractérisée par des lésions cutanées d'hyperkératose palmo-plantaire et une destruction parodontale sévère concernant les dents temporaires et permanentes. Sa transmission est autosomique récessive et la consanguinité des parents est mise en évidence dans environ un tiers des cas. Cet article décrit deux enfants pré-scolaires suivis dans le Département de Dentisterie Pédiatrique de Sheffield et présentant une perte progressive des dents, avec inconfort à l'alimentation. L'histoire médicale révèle une atteinte des mains et des pieds qui avait été diagnostiqué médicalement comme de l'eczéma. Un syndrome de Papillon-Lefèvre a été diagnostiqué dans les deux cas.

Zussamenfassung. Papillon-Lefevre Syndrom ist eine seltene Erkrankung charakterisiert durch palmo-plantare Hyperkeratosen und schwere parodontale Destruktionen beider Dentitionen. Es wird autosomal rezessiv vererbt und konsanguinität der Eltern ist in einem Drittel der Fälle erkennbar. Diese Arbeit beschreibt zwei Vorschulkinder, die in der Kinderzahnheilkundeabteilung der Universität Sheffield vorgestellt wurden. In der Anamnese fanden sich Hautveränderungen, die als Ekzem vordiagnostiziert worden waren. In beiden Fällen wurde ein Papillon-Lefevre Syndrom festgestellt.

Resumen. El síndrome de Papillon Lefèvre es una rara enfermedad caracterizada por lesiones dermatológicas de hiperqueratosis palmo-plantar y destrucción periodontal severa implicando tanto a la dentición decidua como a la permanente. Se transmite de forma autosómica recesiva y es evidente la cosanguinidad de los padres en aproximadamente un tercio de los casos. Este artículo describe dos preescolares asistentes al Departamento de Odontopediatría, Sheffield, con movilidad progresiva de los dientes y molestias al comer. La historia médica reveló descamación de manos y pies, que habían sido diagnosticados médicamente como eczema. Se diagnosticó en ambos casos el síndrome de Papillon-Lefèvre.

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