

Papillon-Lefèvre syndrome: a highly-suspected case

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Abstract: Papillon-Lefèvre syndrome (PLS) is characterized by severe periodontal disease extending to destruction of the alveolar bone surrounding deciduous teeth and palmoplantar hyperkeratosis of the skin. Increased susceptibility to infection has been reported among individuals with the cathepsin C (CTSC) gene mutation. This article reports a 7-year-old Japanese girl who presented with deciduous tooth mobility and was diagnosed as having PLS. Radiographic examination revealed loosening of deciduous incisors and the right second molar of the maxilla, and destruction of the alveolar bone around the residual deciduous dentition. However, there was no destruction of the alveolar bone around the permanent molars. The patient did not show the typical signs of CTSC polymorphism, which almost always negatively impacts certain activating enzymes. With respect to immune function, analysis of the patient's leukocytes indicated that H₂O₂, chemotactic and phagocytotic functions were within the normal range. However, the special precautions normally applied to prevent infections in PLS patients undergoing dental treatment were taken. (*J. Oral Sci.* 48, 257-260, 2006)

Keywords: Papillon-Lefèvre syndrome; periodontal disease; palmoplantar hyperkeratosis; cathepsin C; infection.

Introduction

Papillon-Lefèvre syndrome (PLS) was first described in 1924 by Papillon and Lefèvre (1), who reported a

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brother and sister affected by palmoplantar hyperkeratosis associated with severe, early-onset periodontitis and premature loss of primary and permanent teeth.

The prevalence of PLS is one to four per million individuals (2), and the disease generally becomes apparent by 2-3 years of age (3). PLS is characterized by erythematous palmoplantar hyperkeratosis and severe periodontal disease (1-3), the latter often leading to partial or complete loss of deciduous and permanent teeth (4). The soles of the feet are severely affected, and erythema always precedes hyperkeratosis. The hands are also affected, but to a lesser degree (2,5).

PLS is a rare condition, characterized by autosomal recessive transmission. The identified genetic defect in PLS involves mutation of cathepsin C (CTSC). PLS patients demonstrate more than a 90% reduction of CTSC activity (6,7). An increased susceptibility to infection has also been reported in approximately 25% of PLS patients (3).

Here we describe a case of PLS in a 7-year-old girl who presented at the Nihon University Hospital at Matsudo, with an existing diagnosis of highly-suspected PLS.

Case Presentation

A 7-year-old Japanese girl was referred to the Nihon University Hospital at Matsudo complaining of deciduous tooth mobility. Intraoral examination revealed progressive loosening of the deciduous incisors and right second molars of the maxilla over a period of several years, and deep pockets (4 mm or more) around the deciduous canines and molars (Fig. 1 and Table 1).

Extraoral examination revealed slight palmoplantar keratosis on one hand, and the soles of both feet, and pigmentation of one knee (Figs. 2, 3 and 4). She had been an outpatient at the Dermatology Department of Juntendo Hospital since 2004. The patient had a younger brother, whose dental history was unknown.

Radiographic examination [panoramic radiograph (Fig. 5) and intra-oral radiographs (Fig.6)] showed loosening

Table 1 Probing depth of patient's periodontal pockets

buccal		666		666	646			656	666	455	566	
palatal		867		666	666			666	666	667	666	
Location	16	A	B	C	D	E	F	G	H	I	J	26
Location	46	T	S	R	Q	P	O	N	M	L	K	36
lingual	-46	666	656	666	866				666	666	666	534
buccal	-33	666	866	666	666				666	656	666	333

Unit: mm

A three digit figure: left, center and right sides depth.



Fig. 1 Intraoral view.



Fig. 2 Palmoplantar keratosis (hand).



Fig. 3 Pigmentation (knee).

of the incisors and the right second molar of the deciduous dentition and destruction of the alveolar bone around the residual deciduous dentition (periodontitis). However, there was no destruction of the alveolar bone around the permanent molars.

The patient's medical history recorded previously by a dermatologist had indicated that the patient suffered from an atypical case of CTSC polymorphism, which quite likely affected her activating enzymes. A functional analysis

of leukocytes indicated that H_2O_2 , chemotactic and phagocytotic functions were within the normal range. However, the granulocyte count was below the normal level, and the shapes of the cells were abnormal. No abnormalities of leukocytes were observed. PLS was highly suspected because of CTSC polymorphism. The residual deciduous teeth were extracted on 23rd April 2005, and the patient is currently receiving treatment and follow-up care.

Discussion

PLS is a rare condition characterized by severe periodontitis and palmoplantar hyperkeratosis of the skin (1-3), in which periodontitis leads to early loss of the deciduous teeth, as observed in the present case. However, the palmoplantar hyperkeratosis in this case was slight.

An autosomal recessive disorder (1), PLS generally

becomes apparent by 2-3 years of age (3). The present patient was 7 years old when she first visited the Nihon University Hospital at Matsudo. The patient had a younger brother, whose dental history, and therefore PLS status, was unknown. She exhibited clinical symptoms indicating periodontitis of the deciduous dentition and slight palmoplantar keratosis of the skin, both of which are common findings in PLS patients.

Due to gene mutations, PLS cases typically demonstrate greatly accelerated onset and progression of periodontitis (6,7). Prepubertal periodontitis is associated with loss of CTSC enzyme activity (6,8,9,10). These immunologic deficiencies are transitory and appear to be related to subgingival infection by periodontal pathogens, particularly *Actinomyces actinomycetemcomitans* (11).

Polymorphisms arise from genetic mutations. An alteration that changes only a single base pair is known as a point mutation. Not all point mutations are repaired, and they can be transmitted by inheritance. The most common class of point mutation is a transition involving substitution of a G-C (guanine-cytosine) pair with an A-T (adenine-thymine) pair or *vice versa*. Variations at the site harboring such changes have recently been termed "single nucleotide polymorphisms" (12). The present case was considered to involve an abnormal CTSC

polymorphism.

In patients with PLS, loss-of-function mutations in CTSC do not affect lymphokine activated killer cell function. NK cells from affected patients contain inactive granzyme B, indicating that CTSC is required for granzyme B activation in unstimulated human natural killer (NK) cells (13). CTSC mutations increase susceptibility to infection, and dental treatment of PLS patients typically involves examination for and treatment of infections. However, the present patient demonstrated no leukocyte abnormalities.

With respect to palmoplantar keratosis, the CTSC gene is expressed in epithelial regions commonly affected by PLS, such as the palms, soles, knees, and keratinized oral gingiva. The CTSC gene is expressed at high levels in various immune cells, including polymorphonuclear leukocytes, macrophages, and their precursors (7,14). While periodontitis and palmoplantar hyperkeratosis are attributable to the same CTSC mutations, skin pigmentation has not been described previously as part of this complex of symptoms. Accordingly, it is unclear whether the pigmentation observed in this case is characteristic of PLS.

Another rare finding in PLS cases is pyogenic liver abscess (15), a rare condition among children. Severe periodontal destruction is a typical radiographic findings in PLS patients (5,6) leading to loosening of the deciduous and permanent dentition. In the present case, the deciduous dentition was clearly affected by severe periodontal destruction, with loosening of deciduous incisors and the right second molar of the maxilla. Atypical of PLS cases, skull radiography showed findings within the normal range and no ectopic calcification of the falx cerebri or tentorium (16).

PLS needs to be differentiated from other conditions showing similar oral and cutaneous clinical features, such as acrodynia, hypophosphatasia, histiocytosis X, leukemia, cyclic neutropenia, and Takahara syndrome, which are also associated with periodontitis and premature loss of

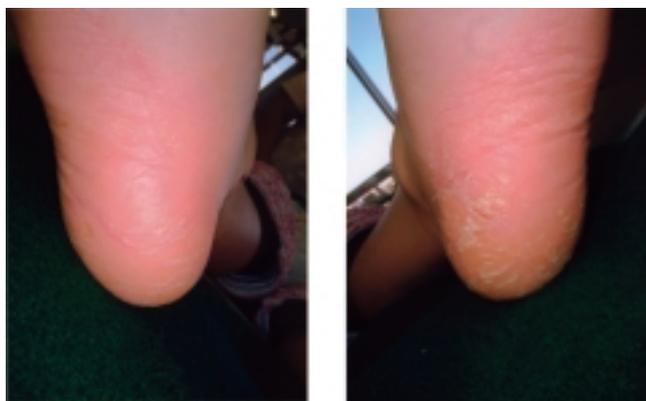


Fig. 4 Palmoplantar keratosis (soles).



Fig. 5 Panoramic radiograph.

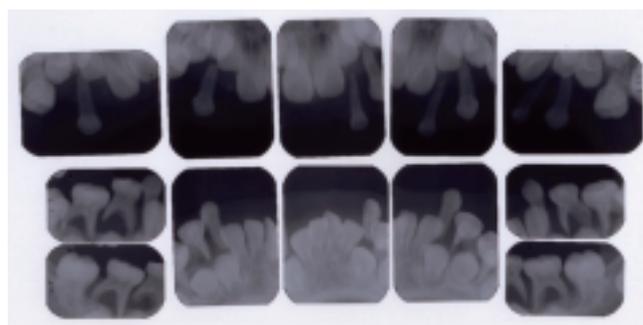


Fig. 6 Dental radiographs.

teeth. PLS differs in that palmoplantar hyperkeratosis is present (16). The present patient underwent extraction of the residual deciduous teeth, and this appeared to halt the progression of periodontitis.

In conclusion, we have described a 7-year-old Japanese girl diagnosed as having highly-suspected PLS who exhibited severe periodontal disease of the deciduous teeth and slight palmoplantar keratosis of one hand and the soles, together with knee pigmentation.

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