ABSTRACT

It is a rare, autosomal recessive disorder occurring between the first and fifth years of life and is characterized by palmoplantar keratoderma and periodontitis followed by the premature shedding of both primary and permanent teeth. The teeth are affected in the order of their eruption, exhibiting inflammation of the periodontal tissue, bleeding of the gums, pocket formation, loosening of teeth, and finally spontaneous exfoliation without showing definite signs of root resorption by about age five. After an edentulous interval, the same process begins shortly after the second dentition. PLS (Papillon Lefevre Syndrome) is transmitted as an autosomal recessive trait. In addition, some patients manifest excessive sweating, the growth of fine body hair and the development of dirty colored skin on the affected parts. Genetic analysis of several affected families suggests that the disorder may result from mutations of a gene that regulates production of an enzyme known as cathepsin C. A case of PLS is presented along with management of this condition. The result was satisfactory with limited resources. The patient was satisfied with improved esthetic, speech and chewing abilities.

Conclusion: Any young patient who exhibits palmar hyperkeratosis should be examined carefully for periodontal breakdown

Key words: Papillon Lefevre Syndrome; Haim-Munk syndrome; Cathepsin C mutation, Allelic mutations, Periodontitis.

INTRODUCTION

Papillon Lefevre Syndrome (PLS) was first described by two French physicians, Papillon and Lefevre in 1924. They reported two children with skin lesions on the hands and feet. These children also experienced severe periodontal disease and the premature loss of the primary and secondary dentitions.

It is a rare, autosomal recessive disorder occurring between the first and fifth years of life. It is characterized by palmoplantar keratoderma (thickening of the stratum corneum of the skin on the palms of the hands and soles of the feet) and periodontitis followed by the premature shedding of both primary and permanent teeth. In addition, some patients manifest excessive sweating (hyperhidrosis), the growth of fine body hair and the development of dirty colored skin on the affected parts. Calcifications of the falx cerebri of the dura mater, as well as other areas of the brain have been reported. From a dental standpoint, young patients with PLS have juvenile periodontitis, severe destruction of the alveolar bone as early as two years of age in both primary and permanent dentitions. There is usually gingival enlargement, gingival ulceration and the formation of deep periodontal pockets but in some cases, there is no inflammatory reaction and only the periodontium of the secondary teeth is affected. This disease eludes all known forms of therapy and results in edentulousness after only few years.
In most cases, the periodontal lesions begin shortly after the start of both the primary and the permanent dentitions. The teeth are affected in the order of their eruption, exhibiting inflammation of the periodontal tissue, bleeding of the gums, pocket formation, loosening of teeth and finally spontaneous exfoliation without showing definite signs of root resorption by about age five. After an edentulous interval, the same process begins shortly after the second dentition. Without treatment, most of the permanent teeth may also be lost by approximately age 14 years. Additional symptoms and findings associated with PLS may include frequent pyogenic skin infections, nail dystrophy and mental retardation, have often been seen in these patients and may thus be regarded as facultative signs.

PLS is transmitted as an autosomal recessive trait. Genetic analysis of several affected families suggests that the disorder may result from mutations of a gene that regulates production of an enzyme known as cathepsin C. The gene is located on the long arm (q) of chromosome 11. Cathepsin C participates in both intracellular and extracellular cleavage of proteins and activation of serine proteases in immune and inflammatory cells. 1,2,3

Individuals affected with PLS have genetic changes in both copies of their cathepsin C genes. Parents and other family members who have a single cathepsin C gene alteration do not appear to show early onset periodontitis, nor do they appear to have the palmoplantar skin lesions. To date more than 25 different cathepsin C mutations in individuals with PLS and related conditions have been identified. 4

Cathepsin C is normally expressed in palmar, plantar, and gingival epithelium tissues affected by palmoplantar keratoderma (PPK) and severe early onset periodontitis. 7 In addition to being expressed in skin, cathepsin C is present in large amounts in osteoclasts. 8 Osteoclasts are multinucleated giant cells that play an important role in bone resorption and hence in bone modelling and remodelling. Osteoclasts are considered to develop from haematopoietic stem cells. The formation of osteoclasts is regulated by many cytokines, which are known to be influenced by severe inflammatory states, as occurs in PLS. Inflammation and destruction of the oral gingiva occur only when teeth are present. 9 Histologically, teeth are attached to the surrounding epithelium by a developmentally unique epithelium, the junctional epithelium. 9,10 Junctional epithelium is not keratinised, is relatively thin, and is much more permeable than adjacent keratinised oral gingiva. Episodes of gingival inflammation and destruction occur in PLS only, when the junctional epithelium is present, which no longer exists after exfoliation of teeth.

CASE REPORT

A five year old school going girl came to the dental OPD of Children's Hospital, Pakistan Institute of Medical Sciences, Islamabad with progressively loosening of teeth and discomfort during eating.

Upon intra oral examination of the patient only four primary second molars were found, which were very loose. Intraoral examination also revealed painful, swollen, bleeding gums and fetor oris. The involved gingiva was bright red and margins were swollen. Patient looked very shy, non communicating and anxious.

History revealed early loss of her primary teeth after normal eruption and development of palmoplantar hyperkeratosis at the age of two years. There was loss of gingival stippling and bleeding occurred on probing the gums. Her permanent teeth were not erupted yet but the orthopantograph showed presence of unerupted all teeth (fig 2). There was rapid loss of periodontal attachment and the affected teeth lacked osseous support. The alveolar bone around the mobile teeth was devoid of definable lamina dura and showed indurated periodontal membrane pockets. An extensive alveolar bone loss was noted, giving the teeth a "floating-in-air" appearance. No hair and nail abnormalities were observed.

It was thought that periodontal disease is a result of microbial infection and poor oral hygiene. The susceptibility gene for PLS, Haim-Munk syndrome, and prepubertal periodontitis is cathepsin C. Cathepsin C is an enzyme which processes and activates several granule serine proteases critical to immune and inflammatory responses of myeloid and lymphoid cells. Loss of function mutations in the gene in these three disorders should, therefore, result in an altered immune response to infection. This would explain both the oral and dermatological phenotypic spectrum of the three syndromes. In 1997-98, three independent groups 11-14 mapped the gene for PLS to 11q14-q21.

On general physical examination except for palmer and planter hyperkeratosis, no other medical disorder was detected (Fig 2). There was no family history of similar complaints.
Papillon Lefevre Syndrome should be differentials from Langerhans’ Cell Histiocytosis (Histiocytosis X), Hypophosphatasia, and Haim & Munk Syndrome.

1. Langerhans’ Cell Histiocytosis (Histiocytosis X): The presenting signs include pain, swelling, ulceration and loose teeth, and alveolar bone loss. Radiographically, the teeth often appear to be “floating in air” surrounded by large radiolucent regions. Mandible is most frequently effected. The presence of alveolar bone loss in young children with precocious exfoliation of primary teeth suggest the possibility of histiocytosis X.

LCH represents a spectrum of clinical disorders ranging from a highly aggressive and frequently fatal leukemia like disease affecting infants to a solitary lesion of bone. The term eosinophilic granuloma is used when a solitary lesion is found, but multiple lesions may develop later. The cause of LCH is unknown. It may be triggered by an unusual reaction of the immune system to something commonly found in the environment. It is not a known infection or a cancer and, although there may be a more than one patient in certain families, it is usually not hereditary. Around 10-20% of patients, usually infants, die. In other patients there may be long term sequelae due to damage caused by the disease. Not all children require specific treatment.

2. Hypo phosphatasia is autosomal recessive disorder characterized by low level of serum alkaline phosphatase. Teeth are lost without any evidence of inflammation of gingival or periodontal disease. A radiograph shows extensive alveolar bone loss.

3. Haim and Munk syndrome is a condition with congenital palmoplantar keratosis, progressive early onset of periodontal destruction, recurrent pyogenic skin infections, acro-osteolysis, atrophic changes of the nails, arachnodactyly, and a peculiar radiographic deformity of the fingers consisting of tapered, pointed phalangeal ends.

On the basis of clinical and radiographic finding she was diagnosed with Papillon Lefevre Syndrome. Treatment planned for her was extraction of all her four very loose primary second molars under local anaesthesia and antibiotic therapy followed by full denture construction. Denture was constructed up to distal surface of second primary molar region.

DISCUSSION

It is a rare genetic condition and it is usually not necessary to treat cutaneous lesions unless they interfere with patient’s activities. Frequent periodontal cleaning, oral hygiene instructions and antibiotic therapy only delay the shedding of teeth. Early extraction of teeth has been advocated to prevent bony loss. Moreover, this allows solid base for subsequent use of artificial dentures. Etretinate, isotretinoin and acitretin have all been successful in improving the cutaneous as well as gingival lesions. However, normal dentition is observed with retinoids only, when given before the onset of permanent teeth at 5 years of age.

Although the patient in present case was too young, but she was very conscious about her teeth and appearance. Full dentures were constructed for her, which were extended up to distant surface of second primary molar region. Provision of full denture had markedly improved her self confidence due to better esthetics, improved speech and eating ability and she was very happy with her denture. On follow up visit she was more confident verbally and in communication. To prevent any interference with normal tooth eruption, it was decided that during eruption of permanent teeth, the denture would be hollowed with fissure bur at eruption sites of the teeth.
It was also planned that use of mouth rinses with periodontal treatment under antibiotics cover will be performed soon after the eruption of her permanent teeth. Retinoid therapy is quite expensive, and as the patient was from lower middle class she could not afford the costly treatment (approx Rs 3000/- or 50 US Dollars per month). Retinoid treatment will be started when we will find a pharmaceutical company, which could provide her financial support.

Various approaches to treat the periodontal condition associated with PLS have been reported. These include oral hygiene instructions, use of mouth rinses, frequent debridement, multiple antibiotic regimens, periodontal surgery, extraction of very loose teeth, and extraction of all primary teeth. As PLS is rare, most publications are case reports, and there are very few documented long-term successful treatment details of the periodontal condition.\(^{17}\)

Gelmetti reported that retinoid therapy could positively influence the development of normal dentition in Papillon Lefevre Syndrome, if it is started during the eruption of the permanent teeth, and suggests that this result can be maintained for a long time even after stopping therapy.\(^{18}\)

Treatment consisted of extractions of periodontally involved teeth under antibiotic cover and treatment with etretinate resulted in a marked improvement of the palmar and plantar skin lesions.\(^{19}\)

**CONCLUSIONS**

1. Any young patient who exhibits palmar hyperkeratosis should be examined carefully for periodontal breakdown.
2. Historically, PLS was thought to lead to the inevitable loss of both the primary and permanent dentitions. However, recently proposed treatments involving antibiotic coverage, extraction of the primary dentition and a period of edentulism have been shown to be effective in maintaining the permanent dentition.
3. Health care providers should educate the parents for early counseling which should eventually benefit the patient.
4. Provision of full dentures can significantly improve esthetics and self confidence of the patient.
5. The use of implants could considerably enhance future therapeutic options for the severely dentally compromised patients with Papillon-Lefevre syndrome.

**REFERENCES**