Papillon-Lefèvre Syndrome

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Papillon- Lefevre syndrome (PLS) is a rare autosomal recessive disorder of keratinzation characterized by palmoplantar hyperkeratosis, periodontopathy and precocious loss of dentition. The exact pathomechanism of these clinical events mainly remains speculative. This paper describes two cases of PLS with classic clinical features and briefly review the relevant literature.

Key words: *Papillon-Lefevre syndrome.*

Papillon-Lefevre syndrome (PLS) is a rare autosomal recessive disorder of keratinization. Its reported incidence is 1-4 per million and both the sexes are equally affected(1). It is characterized by palmoplantar hyperkeratosis, periodontopathy and premature loss of deciduous as well as permanent dentition. It manifests between 1-5 year of life and the patient becomes edentulous in the early teens. Another component of PLS is asymptomatic ectopic calcification in choroid plexus and tentorium. Although this has been taken as a cardinal feature, but being inconsistent it is not considered important for the diagnosis. About 20% of these patients also show an increased susceptibility to infections due to some dysfunction of lymphocytes and leukocytes(2). The diagnosis is mainly clinical.

We describe here two cases of PLS with classic clinical features.

Case 1

This 15-year-old girl presented with palmoplantar hyperkerotosis since the age of four years and total loss of teeth by the age of 12 years. She was the first child born to apparently healthy non-consanguineous parents after an uneventful pregnancy and birth. Her five younger siblings were reportedly normal. History revealed that her deciduous teeth had erupted normally but exfoliated gradually by the age of 4-5 years. Similarly, her permanent teeth too were lost prematurely after erupting normally. There was history of recurrent swelling of gums and foul breath followed by loosening and exfoliation of teeth. At the age of four years, her parents also noticed a progressive thickening of palmoplantar skin. It was associated with marked aggravation of erythema, scaling and dryness during the eruption of teeth, and had improved after complete exfoliation of dentition.

On examination, there was diffuse palmoplantar keratoderma, transgradiens extending up to dorso-lateral aspects and tendo-achillis area (*Fig. 1*). It was diffuse and severe on soles while punctate and striate on palms. No other cutaneous lesion or abnormality of hair, nails or sweating was seen. Intraoral examination revealed completely edentulous ridges with normal overlying mucosa. The two mobile mandibular second molars showed surrounding inflammation and gingival recession. Her systemic examination and routine laboratory investigation including chest and

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skull *X*-ray films were normal. Alveolar healing occurred normally after the extraction of mobile mandibular molars. She was provided artificial dentures subsequently.

Case2

This 10-year-old girl was referred from the dental clinic for the evaluation of cutaneous lesions. She was the second child born normally to non-consanguineous parents. There was no family history of similar complaints. History revealed early loss of her deciduous teeth after normal eruption and development of palmoplantar hyperkeratosis at the age of two years.

Cutaneous examination revealed palmoplantar keratoderma, more on pressure areas with transgradiens extending up to dorsolateral aspects and tendoachillis area. Sweating, hair and nails were normal. Intraoral examination revealed painful, swollen, bleeding gums and fetid odor. The involved gingiva was bright red and margins were hyperplastic. There was loss of gingival stippling and bleeding occurred on probing the involved gums. She was wearing an acrylic splint for multiple loose teeth. The following loose permanent teeth (FDI notation) were present: 15, 14, 12, 11, 21, 22, 24, 25, 26, 36, 35, 34, 33, 32, 31, 41, 42, 43, 44, 45. On removal of acrylic splint for oral prophylaxis, the mandibular central incisors exfoliated spontaneously.

The orthopantograph showed unerupted all second molars and maxillary canines. There was rapid loss of alveolar 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 (*Fig. 2*). Other systemic examination, routine laboratory investigations, *X*-ray films for skull and chest were normal. The acute inflammation improved to some extent with peridontal cleaning and antibiotic therapy. However, the patient did not turn up for further follow up.

Discussion

It is generally accepted that PLS is a

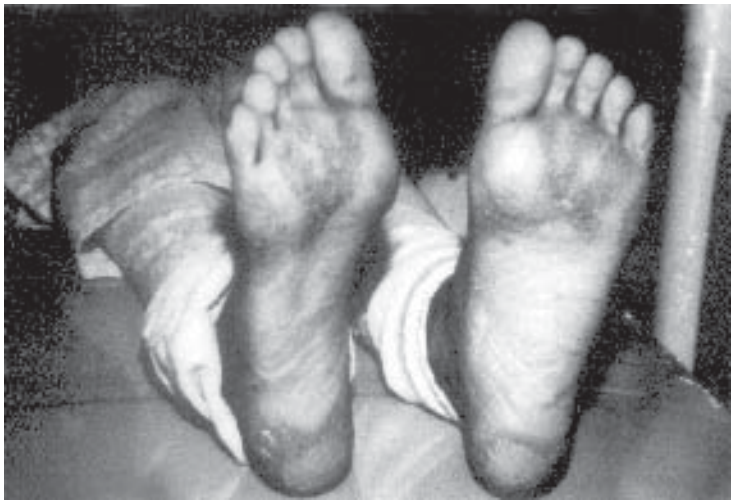

Fig. 1. Plantar keratoderma with transgradiens

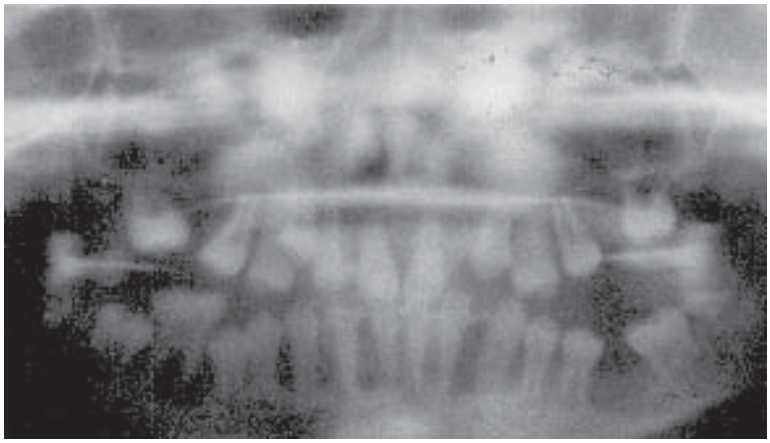

Fig. 2. Floating-in-air appearance of teeth on orthopantograph.

manifestation of homozygosity of autosomal recessive genes with consanguinity as a contributive factor. A major gene locus for PLS has been mapped to a 2.8 cm interval on chromosome 11 q 14 and inheritance of mutations of the cathepsin C gene is found in homozygotes of PLS(3). Variable clinical features and parental non-consanguinity suggest some heterogeneity and variable expressibility of the condition. Both our patients were non-consanguineous and appear to have inherited the condition dominantly.

Swelling of gums and severe periodontitis becomes evident in first year of life itself and loss of primary teeth occurs by the age of 3-4 years. The periodontal inflammation subsides after exfoliation of the deciduous teeth. All the erupted permanent teeth are then lost after periodontal inflammation by the age of 13-16 years. Later the third molars also undergo the same fate. Severe resorption of alveolar bone gives the teeth a " floating-in-air" appearance on dental *X*-ray film. Our both patients showed these classic events of gingivitis, periodontotitis and precocious loss of deciduous as well as permanent dentition at the age of 15 and 10 years. The gingival inflammation subsided and alveolar healing occurred after the extraction of second molars in Case l.

Palmoplantar keratoderma, severe on soles, usually manifests as erythemato-keratotic and sharply demarcated lesion with a tendency for worsening in winter. It may be punctate, striate or diffuse with trans gradient. Hyperkeratotic lesions may also be seen on knees, elbows and achillis tendon areas. Maximum severity of hyperkeratosis coincides with severity of periodontal disease. It tends to improve by puberty and after exfoliation of all the permanent teeth(4). Both are probably interrelated, as the patients are edentulous by that time. Our patients had typical palmoplantar keratoderma but only the first patient showed its severity coinciding with gingival inflammation and tendency towards improvement after exfoliation of all the teeth.

Hair are usually normal and nails may show onychodystrophy and transverse grooving. Claw like phalanges with convex nails (arachnodactyly) and osteolysis(5) described in PLS, are perhaps its variants. No hair and nail abnormalities were observed in

our patients.

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 too 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(6).

Gingival infection, abscess formation, loss of alveolar bone and destruction of the periodontal ligament are probably the causative factors in shedding of teeth. A multitude of etiologic factors appear to be involved in PLS. Page and Baab(7) opined that the defect seems to be with the periodontal component especially the cementum and as the teeth lose their last close relation to bone, the intensity of inflammation subsides. According to Preus(8) the hereditary defect perhaps lie at the epithelial surface barrier leading to reduced defense against virulent periodontopathogens. Furthermore, the severity of palmoplantar hyperkeratosis coinciding with that of periodontal disease and successful retention of teeth by elimination of potential pathogens is also suggestive of their association. There may also exist a direct relation between PLS and psoriasis; both being keratinization disorders and the cutaneous lesions of PLS may sometimes be mistaken for psoriasis unless correlated with orodental findings. Further research at molecular level can only resolve these Issues.

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REFERENCES

1. Griffiths WAD, Judge MR, Leigh IM. Disorders of keratinization. In: Champion RH, Burton JL, Burns DA, Breathnach SM editors. Textbook of Dermatology, 6th edn. Oxford: Blackwell Scientific Publications; 1998. pp. 1569-1571.
2. Bergman R, Friedman-Birnbaum R. Papillon-Lefevre syndrome a study of the long term clinical course of recurrent pyogenic infections and the effects of etretinate treatment. Br J Dermatol 1998; 119: 131-136.
3. Hart TC, Hart PS, Bawden DW, Michalec MD, Callison SA, Walker SJ, et al. Mutations of the cathepsin C gene are responsible for Papillon-Lefevre syndrome. J Med Genet 1999; 36: 881-887.
4. Shaw IN, Rao GS, Mozhi NM, Babu B, Ebenezer G. Papillon-Lefevre syndrome: Improvement of skin lesions after the loss of permanent teeth. Indian J Dermatol Venereol Lepro1 2000; 66: 211-212.
5. Puliyel JM, Iyer KSS. A syndrome of keratosis palmoplantaris congenita, pes planus, onycho-gryphosis, periodontosis, arachnodactyly and a peculiar acro-osteolysis. Br J Dermatol 1986; 115: 243-248.
6. Nazzaro N, Blanchet-Bandon C, Mimoz C. Papillon-Lefevre syndrome. Ultrastructural study and successful treatment with acitretin. Arch Dermatol1988; 124: 533-539.
7. Page RC, Baab DA. A new look at the etiology and pathogenesis of early onset periodontitis. J Periodontol 1985; 56: 748-751.
8. Preus HR. Treatment of rapidly destructive periodontitis in Papillon-Lefevre syndrome. Laboratory and clinical observations. J Clin Periodontol 1988; 15: 639-643.