pISSN 2349-3283 | eISSN 2349-3291

Case Report

DOI: 10.5455/2349-3291.ijcp20140514

Palmoplantar keratoderma and edentulous status: two isolated expressions of Papillon-Lefèvre syndrome

Seema Sharma¹*, Vipin Sharma², Milap Sharma¹, Sanjeev Chaudhary¹

Received: 25 April 2014 Accepted: 9 May 2014

*Correspondence: Dr. Seema Sharma,

E-mail: seema406@rediffmail.com

© 2014 Sharma S et al. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Papillon-Lefèvre Syndrome (PLS) is a rare, autosomal recessive disease comprising palmoplantar keratoderma and rapidly progressive and devastating periodontitis, affecting the primary as well as the permanent dentition, attributed to a point mutation of the Cathepsin C gene (CTSC). One of our patients had early onset of severe skin lesions with recurrent pyogenic infections while his elder sibling was edentulous without any other pyogenic infections. This paper describes the clinical variants of PLS in two siblings and briefly reviews the relevant available literature.

Keywords: Keratoderma, Onychodystrophy, Papillon-Lefèvre syndrome

INTRODUCTION

Papillon-Lefèvre Syndrome (PLS) is characterized by keratoderma palmoplantar (PPK) and periodontitis. Its reported incidence is 1-4 per million and both the sexes are equally affected. Patients have an underlying functional or quantitative neutrophil abnormalities, and 50% will be immune compromised. It manifests between 1-5 year of life and the patient becomes edentulous in the early teens. About 20% of these patients also show an increased susceptibility to infections due to some dysfunction of lymphocytes and leukocytes. The incidence of this rare entity is increasing in the recent times, which is associated with irreparable periodontal destruction at an early age, with not so prominent skin lesions in some cases.2 Most of the previous case studies on Papillon-Lefèvre syndrome explained the clinical presentation.^{3,4} In this paper we emphasizes on the variant clinical presentations of PLS in two siblings. Familiarity with clinical presentation of this uncommon disease is essential for accurate clinical diagnosis and appropriate management.

CASE REPORT

Two siblings 15 and 17 years of age presented to us with this disease condition. The younger one had palmoplantar hyperkeratosis since four years of age and currently fever of 2 weeks duration. The fever was persistent, high-grade, and associated with chills and night sweats. There was history of an abdominal mass associated with right upper quadrant pain. The pain was a dull ache, intermittent, non-radiating and unassociated with vomiting, diarrhea, or jaundice. There was significant medical history for recurrent pyogenic infections in the form of pyogenic liver abscesses and empyema thoracis (Figure 1). He was the second of two, born to apparently healthy non-consanguineous parents after an uneventful

¹Department of Paediatrics, Dr. Rajendra Prasad Govt. Medical College and Hospital, Kangra (Tanda), Himachal Pradesh, India

²Department of Orthopaedics, Dr. Rajendra Prasad Govt. Medical College and Hospital, Kangra (Tanda), Himachal Pradesh, India

pregnancy and birth. There was no family history of ichthyosis or hereditary or acquired palmoplantar keratodermas.



Figure 1: CT thorax showing left empyema-thoracis.

On physical examination, both were well developed and well nourished. The younger child was febrile with a temperature of 40°C, but other vital signs were normal. He had a diffuse erythematous palmoplantar hyperkeratosis (PPK) with transgrediens to the dorsae of the hands and feet. He also had multiple, sharply defined, scaly hyperkeratotic plaques over the elbows and knees (Figure 2). The liver was tender and palpable 4 cm below the right costal margin. The spleen was not palpable. No other cutaneous lesion, abnormality of hair, nails or sweating and periodontal disease was noted. Other systemic examination, complete blood count, blood chemistry profile, and liver function tests were normal. Blood, urine, and stool cultures were all negative. Histopathological examination of erythematous plaques revealed orthokeratotic type hyperkeratosis, acanthosis, loss of stratum granulosum and minimal dermal perivascular mononuclear infiltration. Abdominal ultrasound and subsequent Computed Tomography (CT) of the abdomen with contrast showed a solitary liver abscess measuring 7 cm × 6 cm (Figure 3) for which initial differential diagnosis of a pyogenic or amebic liver abscess was kept. Ultrasound-guided drainage was performed, and 100 ml of thick, yellowish exudate was obtained which grew staphylococcus aureus, sensitive to cloxacillin and vancomycin on culture. Because of the rarity of liver abscess in immunocompetent children, and the presence skin lesions, a dermatology consultation was requested, which established the diagnosis of PLS.



Figure 2: Sharply defined multiple hyperkeratotic spots over hands, feet, elbows and knees.



Figure 3: CT abdomen showing single solitary liver abscess measuring 7 cm x 6 cm.

The patient was treated with cloxacillin intravenously for 4 weeks, followed by oral therapy for another 2 weeks. The patient recovered dramatically and was discharged in a good condition. Keratolytic preparations containing 20% salicylic acid were prescribed for the skin lesions.

The elder sibling reported having history of recurrently swollen and friable gums since age of 4 years which started with a chief complaint of loosening teeth and discomfort on eating. All teeth showed mobility, with periodontal pockets, bleeding on probing and gingival recession. Past dental history revealed that since childhood the teeth exfoliated one by one by the age of 14 years. Dental treatment done for this patient included oral prophylaxis, extraction of teeth with poor prognosis followed by replacement with removable prosthesis due to edentulous status (Figure 4). The patient was not diagnosed with PLS previously and he had received only dental treatment. Rest of his past medical history was unremarkable. In view of the above findings and history along with remarkable presentation in younger sibling, the case was diagnosed as PLS. Due to financial issues, genetic testing was not performed to identify responsible mutations.



Figure 4: Edentulous status.

DISCUSSION

PLS was first described by Papillon and Lefèvre in 1924.⁵ The disorder is characterized by diffuse palmoplantar keratoderma and premature loss of both deciduous and permanent teeth. The palmoplantar keratoderma typically has its onset between the ages 1 and 4 years. The sharply demarcated erythematous keratotic plaques may occur focally, but usually involve the entire surface of the

palms and soles, sometimes extending onto the dorsal surfaces of the hands and feet. It may be punctate, striate or diffuse with trans gradient. Hyperkeratotic lesions may also be seen on knees, elbows and achillis tendon areas. Often, there is associated hyperhidrosis of the palms and soles resulting in a foul-smelling odor. The findings may worsen in winter and be associated with painful fissures.

The second major feature of PLS is severe periodontitis, which starts at age 3 or 4 years. The development and eruption of the deciduous teeth proceed normally, but their eruption is associated with gingival inflammation and subsequent rapid destruction of the periodontium. periodontitis The resulting characteristically unresponsive to traditional periodontal treatment modalities and the primary dentition is usually exfoliated prematurely by age 4 years. After exfoliation, the inflammation subsides and the gingiva appears healthy. However, with the eruption of the permanent dentition the process of gingivitis and periodontitis is usually repeated and there is subsequent premature exfoliation of the permanent 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 te same fate. Severe resorption of alveolar bone gives the teeth a "floating-in-air" appearance on dental X-ray film.

Hairs are usually normal and nails may show onychodystrophy, transverse grooving, claw like phalanges, convex nails (arachnodactyly) and osteolysis. In addition to the skin and oral findings, patients may have decreased neutrophil, lymphocyte, or monocyte functions and an increased susceptibility to bacteria, associated with recurrent pyogenic infections. An estimated 17% of patients present with marked predisposition to a variety of usually mild infections like skin pyodermas. Occasionally, fatal infections like multiple abdominal abscesses and cerebral abscesses have been reported.⁶ Pyogenic liver abscess is increasingly recognized as a complication of PLS associated with impairment of the immune system. Other minor features of PLS include calcification of the dura, falx cerebri, tentorium cerebelli, and choroids plexus. Histopathological findings of affected skin have not been well described in the literature.

The cause of PLS is not well understood, but recent studies have suggested loss-of-function mutations affecting both the alleles of the cathepsin-C gene, located on the 11q14-q21 region of the chromosome encoding a lysosomal protease in the interval between D11S4082 and D11S931. The including polymorphonuclear leukocytes, macrophages and their precursors. The cathepsin C gene encodes a cysteine-lysosomal protease also known as dipeptidyl-peptidase I, which functions to remove dipeptides from the amino terminus of the protein substrate. It also has endopeptidase activity. The cathepsin-C gene is expressed in epithelial regions commonly affected by PLS such as palms, soles, knees,

and keratinized oral gingiva. It is also expressed at high levels in various immune cells including polymorphonuclear leukocytes, macrophages, and their precursors. An interesting feature of the cathepsin C gene is that mutations in this gene also result in two other closely related conditions: the Haim-Munk syndrome, and prepubertal periodontitis. A common clinical manifestation in all three syndromes is severe early-onset periodontitis. ⁹

All PLS patients are homozygous for the same cathepsin-C mutations inherited from a common ancestor. Parents and siblings, heterozygous for cathepsin C mutations do not show either the palmoplantar hyperkeratosis or severe early onset periodontitis characteristic of PLS. The exact mechanism of the increased susceptibility to infections is also unknown, but some investigators have demonstrated a dysfunction in neutrophil motility and bactericidal function. Neutrophil and T-cell dysfunctions have been suggested as immunological features of PLS. 10 Chemotactic and phagocytic function of neutrophils is decreased in PLS, and it is associated with a diminished phytohemagglutinin response by T-cell lymphocytes. In consistence with previous reports, consanguineous marriage was found in fifty percent of our patients implying the genetic basis for the disease. 11,12

PLS is an uncommon autosomal recessive type-IV palmoplantar ectodermal dysplasia. Of the palmoplantar ectodermal dysplasias, only PLS and Haim-Munk syndrome (HMS) are associated with premature periodontal destruction.

Haim-Munk syndrome is an autosomal-recessive genodermatosis characterized by congenital palmoplantar keratoderma and progressive early-onset perodontitis. In addition to palmoplantar keratosis and periodontitis, other clinical findings include 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, claw-like volar curve, and pes planus suggestive of HMS being a distinct disorder.

Prepubertal periodontitis is differentiated from PLS by the absence of associated palmoplantar keratoderma. Maximum severity of hyperkeratosis coincides with severity of periodontal disease. It tends to improve by puberty and after exfoliation of all the permanent teeth.

The skin manifestations of PPK are usually treated with emollients. Salicylic acid and urea may be added to enhance their effects. Treatment for the periodontitis includes extraction of the primary teeth combined with oral antibiotics and professional teeth cleaning. Moreover this allows solid base for subsequent use of artificial dentures. Oral retinoids including acitretin, etretinate and isotretinoin are the mainstay of the treatment of both the keratoderma and periodontitis associated with PLS. However, normal dentition is

observed with retinoids only when given before the onset of permanent teeth at 5 years of age. 14

CONCLUSION

This rare yet very fascinating condition requires a careful history and examination for diagnosis. Delayed diagnosis and insufficient treatment of PLS patients can affect patient's life by early edentulism and will impose a great risk of social, psychological, and economical burdens on patients. A multidisciplinary approach is important for management. Stronger evidence is needed to support the use of prophylactic antibiotics in these patients to prevent infections. Further studies are required to discover a genetic basis and to establish appropriate treatment modalities.

Funding: No funding sources Conflict of interest: None declared Ethical approval: Not required

REFERENCES

- Griffiths WAD. Disorders of keratinization. In: Griffiths WAD, Judge MR, Leigh IM, Champion R H, Burton JL, Burns DA, Breathnach SM eds. Textbook of Dermatology. 6th ed. Oxford: Blackwell Scientific Publications; 1998: 1569-1571.
- 2. Radhika Muppa, B Prameela, Mahesh Duddu, and Arthi Dandempally. Papillon-Lefevre syndrome: a combined approach from the dermatologist and dentist a clinical presentation. Indian J Dermatol. 2011;56(6):740-3.
- 3. Canger EM, Celenk P, Devrim I, Yenisey M, Gunhan O. Intraoral findings of Papillon-LeFevre syndrome. J Dent Children. 2008;75(1):99-103.
- Keskin-Yildirim Z, Simşek-Derelioğlu S, Kantarci M, Yilmaz Y, Büyükavci M. Papillon-Lefèvre syndrome: report of three cases in the same family. Turk J Pediatr. 2012;54(2):171-6.

- Papillon M, Lefèvre P. Dens, Cas de Keratodermie, Palmaire et Plantaire, Symetrique Familale (Maladie de Meleda), Chez le Frère, et al. Soeur: co exdistence dans les deux cas d'alterations dentaires groups. Bull Soc Fr Dermatol Syph.1924;31:82-7.
- Kanthimathinathan HK, Browne F, Ramirez R, McKaig S, Debelle G, Martin J, Chapple IL, Kay A, Moss C. Multiple cerebral abscesses in Papillon-Lefèvre syndrome. Childs Nerv Syst. 2013 Aug;29(8):1227-9.
- Patel S, Davidson LE. Papillon-Lefevre syndrome: a report of two cases. Int J Pediatr Dent. 2004;14:288-94.
- 8. Thakker N. Genetic analysis of Papillon-Lefevre syndrome. Oral Dis. 2000;6:263.
- Hart TC, Hart PS, Michalec MD. Haim-Munk syndrome and Papillon-Lefèvre syndrome are allelic mutations in cathepsin C. J Med Genet. 2000;37:88-94.
- Rathod VJ, Joshi NV. Papillon-Lefèvre syndrome: a report of two cases. J Indian Soc Periodontol. 2010;14(4):275-8.
- 11. Patel S, Davidson LE. Papillon-Lefèvre syndrome: a report of two cases. Int J Pediatr Dent. 2004;14(4):288-94.
- 12. Nagaveni NB, Suma R, Shashikiran ND, Subba Reddy VV. Papillon-Lefevre syndrome: report of two cases in the same family. J Indian Soc Pedodont Prev Dent. 2008;26(2):78-81.
- 13. Almuneef M, Al Khenaizan S, Al Ajaji S, Al-Anazi A. Pyogenic liver abscess and Papillon-Lefèvre syndrome: not a rare association. Pediatr. 2003;111(1):e85-8.
- 14. Al-Khenaizan S. Papillon-Lefèvre syndrome: the response to acitretin. Int J Dermatol. 2002;(12):938-41.

DOI: 10.5455/2349-3291.ijcp20140514

Cite this article as: Sharma S, Sharma V, Sharma M, Chaudhary S. Palmoplantar keratoderma and edentulous status: two isolated expressions of Papillon-Lefèvre syndrome. Int J Contemp Pediatr 2014;1:48-51.