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Papillon-Lefevre syndrome with arachnodactyly and associated aggressive periodontitis: A rare case report with review of literature

Mehak Tariq

Postgraduate 3rd year, Oral medicine Diagnosis and Radiology. Vyas dental college and Hospital, Jodhpur
Email: mehaktariqrs@gmail.com

Munaf Maknoja

M.D.S. Periodontist and Implantologist, Mumbai
Email: mak.muna@gmail.com

Sandeep Saurabh

Postgraduate 3rd year. Pedodontics. Vananchal dental college and Hospital, Jharkhand
Email: drsandeepsaurabh.01@gmail.com

Amarnath

MDS Orthodontics, Associate Professor. SB Patil institute for dental sciences and research. Bidar
Email: dr.amarbiradar@gmail.com

Shubhangi Rajbhoj

M.D.S. Periodontics and Oral Implantology, Senior Lecturer, Sinhgad Dental college and Hospital, Pune
Email: shubhangirajbhoj@gmail.com

Sugandha Arya

MDS, Oral medicine Radiologist, Associate Professor, Vyas dental college and Hospital, Jodhpur
Email: suggusuggu53@gmail.com

Abstract---Papillon-Lefevre Syndrome (PLS) is a autosomal recessive genetic disorder. The prevalence of this disorder has been reported to be 1 to 4 per million in the general population. The prime features of PLS include palmar-plantar hyperkeratosis along with premature loss of deciduous and permanent teeth due to aggressive periodontitis. Radiological feature involves severe destruction of alveolar bone giving

teeth a typical “floating in air” appearance along with intra-cranial calcifications. Clinical findings of disease specific dermatologic manifestations and periodontal involvement forms the framework of the diagnosis. Clinical significance: As PLS involves severe irreparable destruction of alveolar bone and tooth loss, both dental clinicians and dermatologists opinion is required for both initial and long term management of this disease followed by psychological counselling.

Keywords---aggressive periodontitis, arachnodactyly, papillon lefevre syndrome, palmar-plantar hyperkeratosis.

Introduction

Papillon-Lefevre Syndrome (PLS) is a rare genetic disorder of autosomal recessive inheritance. The prime features associated with this syndrome are palmoplantar hyperkeratosis associated with aggressive periodontitis, leading to premature loss of both primary and permanent dentitions.¹ It was first described by two French dermatologists Papillon and Lefevre in 1924 as “Mal de Meleda”.² In 1964, Gorlin et al added the third feature of dural calcification in making the diagnosis of PLS.³ The disorder is first seen in children in the age group of 1-4 years⁴ and is found to affect both males and females without any racial predominance.⁵ Parental consanguinity is found to be one of the cause behind its occurrence and is seen affecting 20% and 40% of the cases.⁶ Calcification of the falx cerebri and the choroid plexus along with retardation of somatic development is often a prime feature associated with this syndrome but because of inconsistency it is not considered relevant for the diagnosis.⁷ Its prevalence is estimated to be 1 to 4 per million in the general population with a carrier rate of 2 to 4 per 1000.⁸ The dental surgeon is usually the first to diagnose the syndrome due to severe periodontal breakdown involved at such an early age.⁹ The cutaneous lesions present as sharply demarcated erythematous keratotic plaques on the palms and soles, which tend to spread onto the dorsal surfaces and are usually manifested simultaneously with the intra-oral presentations.⁴ PLS creates a psychological impact on children and their parents if it affects at an early stage along with the prospect of edentulism. Thereby, early diagnosis and a interdisciplinary approach involving both dental professionals and dermatologists is imperative, with equal emphasis on psychological boost up and counselling of the affected individual.⁴ This paper presents a rare case report of Papillon-Lefevre syndrome existing along with arachnodactyly and associated aggressive periodontitis.

Case report

A 24-year-old male reported to the Department of Oral medicine and Radiology complaining of missing teeth in both upper and lower jaw and inability to eat the food properly since 6 years. History dates back to 7-8 years when patient first noticed loosening of his teeth earlier it involved the lower front teeth and gradually in a span of 2 years it involved multiple teeth followed by complete loss of certain teeth. In addition, presence of greyish white patches on his palms and soles was reported since childhood that exacerbates in winters. Parent consanguinity history was not obtained due to physical absence of his family

members except the wife accompanying him had been unaware about it. His wife revealed that 2 months back he had got high-grade fever which was gradual in onset, continuous and was associated with shivering with peaks reported in the morning and evening hours. His fever got relieved with certain unknown medications. Associated symptoms being reported by the patient were anorexia and moderate weight loss. Patient reported chewing 1-2 pouches of gutkha and tobacco from past 6 years and keeps the quid in his right buccal vestibule. No other family member suffered from such condition. Patient was conscious and slightly disoriented to time, place and surroundings. Overall body built was thin, lean and mental status was abnormal. Consent of the patient was obtained for examination and photographic records. On Extraoral examination Bilateral Malar prominence (Figure 1) with positive palor was observed. On the skin grayish white, keratinized well demarcated and consolidated patches affecting palms, soles and even dorsum of hand and feet had been observed. The palmoplantar lesions were mostly symmetric. (Figure 2) Scarring was observed on right side of his head with loss of hair in that region. (Figure 3) Arachnodactyly was observed on left hand with no signs of atrophy seen in the nails. (Figure 2) On Intraoral examination both maxillar and mandibular arches were edentulous except maxillary right and left second molar and mandibular right canine and first premolar with resorbed ridges. (Figure 4a and 4b) Severe gingival recession with grade III mobility was noted.



Figure 1. Showing bilateral malar prominence



Figure 2. Showing presence of hyperkeratotic patch on dorsal of Right hand region as well as arachnodactyly



Figure 3. Showing scarring present on right side of head with loss of hair in that region



Figure 4 a and 4 b. Showing partially edentulous maxillary and mandibular ridges without any evidence of calculus

Based on history and clinical manifestations, a provisional diagnosis of Papillon-Lefevre syndrome with arachnodactyly and associated aggressive periodontitis was given. The extraoral radiography (Panoramic and Cephalometric) confirmed alveolar bone loss in both maxillary and mandibular arch. The characteristic radiographic hallmark “floating in air” or “teeth in space” appearance was well appreciated in right mandibular canine and first premolar (Figure 5) and may be attributed to the extensive loss of bone support around the remaining teeth. Bone loss was typically arc shaped suggestive of vertical defects. No intra-cranial calcifications were observed. Laboratory investigations were carried out to rule out the haematological and biochemical changes. On Haematological investigations, Hb was found out to be 10.4g/dl and Random blood glucose was

found to be in normal range. The neutrophils and lymphocytes were reported to be lowered and may be correlated to the extensive periodontal tissue destruction (defective neutrophil/lymphocytic chemotaxis). Based on the history, clinical findings and both radiographic and haematological investigations a final diagnosis of Papillon-Lefevre syndrome with arachnodactyly and associated aggressive periodontitis was given. Patient was given oral hygiene instructions and was advised with multiple extractions followed by prosthodontic consultation. Patient was then given referral for dermatological consultation along with psychiatric counselling.

Discussion

Palmoplantar keratoderma (PKK) is defined as heterogeneous group of disorder which is characterized by thickening of the palms and soles.¹⁰ These disorders can be classified as hereditary, acquired, or found to be associated with syndromes. The Papillon-Lefevre Syndrome is a type of PKK.^{10,11} The Three criteria which are used to classify a case as PLS was given by Haneke. They are (a) palmoplantar hyperkeratosis; (b) loss of primary and permanent teeth; and (c) autosomal recessive genetic disorder.¹² Our case matched the first two criteria but the third criteria was not confirmed due to physical absence of family members.

Controversy behind the pathogenesis of PLS is ongoing till date. The cause behind occurrence of the skin lesions is explained on the basis of disturbances in ectodermal and mesodermal components but there is no reasonable explanation behind the rapid loss of all the deciduous as well as permanent teeth in the order of their eruption.¹³ Three major bases (immunologic, microbiologic, and genetic) have been suggested in the literature: a) Hereditary: The loss of functional mutations of the lysosomal protease cathepsin C gene which is located on chromosome 11q14.1-q14.3 and is recognized in progression of PLS. The cathepsin C gene is expressed in the integument system such as palms, soles, knees, and keratinized oral mucosa. It is also found to be expressed in immune cells like polymorphonuclear leukocytes (neutrophils), macrophages, and their precursors. In addition, every patient of PLS is reported to be having homozygous alleles for the identical cathepsin C gene mutation which is found to be inherited from a particular ancestor. However, the delayed onset of PLS without causal cathepsin C gene mutation has also been reported in some case reports; b) Immunological: Reduced immunologic response as well as increase susceptibility to infection could be explained because of the decreased phagocytosis, and impaired reactivity to T and B cell mitogens; c) Microbiological: Gram-negative microbes are known to be causative factors in the occurrence of periodontitis. The elevated antibody titers to *Actinobacillus actinomycetemcomitans* and *Campylobacter* in PLS patients confirms the involvement of this bacterium in periodontal pathologies found to be associated with PLS.¹⁴⁻²⁰

Early onset periodontitis is the most significant finding in the field of dentistry, which usually get started at the age of 3-4 years. Other oral manifestations includes inflamed gingival which bleed on slight provocation and leads to rapid destruction of underlying periodontium. In such individuals, the development and eruption of the deciduous teeth is found to occur normally but shedding occurs prematurely mostly by the age of 3-4 years. After the shedding the gingival

appears to be normal but with the eruption of the permanent teeth condition worsens again. All permanent teeth get exfoliated by the age of 13-16 years. Third molars also go through the same fate as that of permanent teeth.⁹ In our case patient lost most of his permanent teeth around the age of 17-18. In this syndrome, the cutaneous lesions usually include keratotic plaques on the palms and soles which vary from mild psoriasiform scaly skin to overt hyperkeratosis.⁴ The level of dermatologic involvement and level of periodontal infection may not be related. PLS patients may include other features like frequent pyogenic skin infections, nail dystrophy and mental retardation, thus are considered as facultative signs.²¹ In our case mental retardation has been observed with scarring present on right side of his head suggestive of some infection. In PLS, skin lesions usually show manifestations approximately at the time of primary tooth eruption from age of 6 months to 3 years. Furthermore, soles of the feet are also affected more severely and more frequently than the other regions. In our case, the skin lesions had appeared in childhood but patient does not remember the exact age of commencement of the lesions.

Investigation and diagnosis: Radiological feature is severe destruction of alveolar bone which gives the teeth a "floating in air" appearance and could be associated with intra-cranial calcifications as has been observed in our case in mandibular right canine and first premolar because of resorption of underlying alveolar bone, teeth appeared as floating in air.⁷ Histopathological findings consists of hyperkeratosis, occasional patches of parakeratosis, acanthosis and a slight perivascular inflammatory infiltrate.²² The most favourable differential diagnosis for PLS includes Haim-munk syndrome (HMS). Both PLS and HMS are found to be allelic variants of cathepsin c gene mutation and are classified as type IV palmo plantar - ectodermal keratodermos but clinically HMS and PLS differ in atrophic changes seen in nails as well as arachnodactyly. In addition to PPK with periodontitis, additional symptoms reported by HMS includes; recurrent pyogenic skin infections and acroosteolysis. Deformity of tapered, pointed phalangeal ends, claw-like volar curve, and pes planus seen on a radiograph confirms the HMS diagnosis.⁹ Furthermore, Haim Munk syndrome, Olmsted syndrome, Huriez syndrome, Epidermolysis bullosa herpetiformis, Cole disease which shows palmar-plantar keratosis like PLS but doesn't show juvenile periodontitis.²³ Acrodynia also known as Feer's syndrome, should be considered when there is premature loss of deciduous and/or permanent teeth. It is a condition seen in children between ages of six months and four years and is usually caused by mercury intoxication. This condition manifests itself as a red desquamative process involving both the extremities is observed but palmoplantar hyperkeratosis is not seen in this condition as seen in PLS. Additional symptoms reported are erythrocyanosis, muscle pain, insomnia, sweating, tachycardia and psychic disturbances. Premature eruption of teeth with dystrophic enamel are noticed and are found to shed prematurely.⁹

Hypophosphatasia can also be considered as differential diagnosis for PLS. It is autosomal recessive disorder in which clinical features like knock-knee, bowing of femur and tibia and enlarged wrists are observed. Hypoplastic teeth, premature shedding reported without any evidence of inflammation of gingival or periodontal disease. Extensive alveolar bone loss can be appreciated on a radiograph and on basis of increased amounts of phosphoethanolamine in the urine and low level of

serum alkaline phosphatase, diagnosis can be framed.⁹ Acatlasemia or Takahara's syndrome, an autosomal recessive trait described by progressive gangrenous lesions involving the gingiva and alveolar bone, leading to exfoliation of the teeth but this condition has rarely been observed outside Japan.⁹

In addition, Langerhans Cell Histiocytosis can also be included in differential where the presenting signs include pain, swelling, ulceration and loose teeth, and alveolar bone loss. Radiographically, the teeth appear to have characteristic "floating in air" appearance surrounded by large radiolucent regions. Mandible is most frequently affected. The presence of alveolar bone loss in young children with precocious exfoliation of primary teeth suggest the possibility of its occurrence.⁹In pathologies like acrodynia, hypophosphatasia, histiocytosis X, leukemia, cyclic neutropenia associated with periodontitis and premature loss of teeth doesn't show palmar-plantar keratosis.²³ Other entities like palmoplantar hyperkeratosis of Unna Thost, Mal de Meleda, Howel-Evans syndrome, keratosis punctata, keratoderma hereditariummutilans (Vohwinkel's syndrome), and Greither's syndrome could also be kept in the category of differential diagnosis.^{9,11,21-31} Although, these pathologies are associated with palmoplantar hyperkeratosis but there is no periodontopathy seen which is associated with PLS.

Recently, Antonella Tammaro *et al* had reported severe palmar hyperkeratosis in a coronavirus (COVID-19) patient indicating that the skin may be affected by the virus during the course of the infection but without any periodontal involvement.³² Furthermore, skin manifestations of PLS, may be mistaken for psoriasis unless they are correlated with oral dental findings.⁷ To diagnose PLS clinically specific dermatologic manifestations and periodontal involvement should be observed .¹ In our case all the characteristic features of PLS had been reported along with arachnodactyly but without any evidence of atrophy of nails, recurrent pyogenic skin infections and acroosteolysis thereby, our diagnosis was restricted to Papillon-Lefevre Syndrome with arachnodactyly and associated aggressive periodontitis instead of HMS as described by Begum S *et al*² justifying our case as a rare novel case report.

Management

PLS can badly affect the psychological, social, and esthetic well-being of the patient at early age, as it is a devastating disease process associated with cutaneous involvement and partial or complete edentulism.³³On very rare occasions, PLS may be associated with squamous cell carcinoma and malignant melanoma.³⁴Hence, for the management of this condition, a multidisciplinary method is imperative.³³The skin manifestations are usually treated topically with emollients, keratolytics including salicylic acid and urea. There are reports that oral retinoids, such as etretinate, acitretin and isotretinoin, have been beneficial in treating keratoderma seen in PLS; although retinoids are not well tolerated in general.^{1,35} But it slows the resorption of the alveolar bone on the remaining teeth.³⁴The dental practitioner is usually the first to diagnose this syndrome due to the involvement of the periodontium.³³Standardized dental treatment protocol for patients with PLS has been mentioned in Table 1.³⁶

Table 1
Showing Standardized dental treatment protocol for patients with Papillon-Lefevre Syndrome

| PRIMARY DENTITION | PERMANENT DENTITION |
|---|--|
| Oral hygiene instructions and prophylaxis every third month | Oral hygiene instructions and prophylaxis every third month |
| Extraction of teeth with advanced periodontal disease | Mouthrinses with chlorhexidine gluconate 0.2% twice daily |
| Extraction of all primary teeth atleast 6 months prior to the eruption of first permanent tooth. | For Teeth with moderate periodontal disease (bone loss < 30% of tooth length, probing pocket depth < 5mm : 1. Dental scaling and prophylaxis once a month 2. Systematic antibiotic treatment for 4 weeks |
| Recommended Antibiotics: Amoxicillin , amoxicillin and clavulanic acid with a dose of 20-50mg/kg/day or 20-40mg/kg/day respectively in divided doses every 8 hours. | Recommended Antibiotics: Amoxicillin ,metronidazole with a dose of 20-50mg/kg/day or 15-35 mg/kg/day respectively in divided doses every 8 hours |
| Antibiotics for 2 weeks post extraction to avoid post operative complications | For Teeth with advanced periodontal disease (bone loss > 30% of tooth length, probing pocket depth ≥ 5mm: 1. Extraction |

A course of antibiotics should be prescribed to control the active periodontitis in an effort to preserve the teeth and to prevent bacteremia and subsequently pyogenic liver abscess. Psychological boost-up and counselling of the affected individual alongside periodontal maintenance visit is advised every 3 months.³³ Further studies in the field of microbiology and genetics with larger samples of larger duration are required to diagnose the exact cause of periodontal destruction in such patients, so that best possible treatment could be administered.¹

Conclusion

Papillon-Lefevre Syndrome (PLS) is a rare autosomal recessive genetic syndrome which is associated with palmoplantar hyperkeratosis and aggressive periodontitis eventually leading to premature loss of both deciduous and permanent dentition. Since PLS involves extensive irreparable periodontal destruction and also affects the psychic of the patient due to sudden loss of teeth at a young age, thereby, multidisciplinary approach involving dental clinicians, dermatologists and psychologists is required for the management of this disease with special emphasis on psychological counselling.

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The patient in this manuscript had given written informed consent to publication of his case details

Conflict of interest

The authors declare no potential conflict of interest

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