PALMOPLANTARIS KERATORIS PERIODONTITIS- A RARE CASE INVOLVING HAND, FOOT AND MOUTH; REVIEW OF PAPILLON–LEFÈVRE SYNDROME

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Abstract
Papillon–Lefèvre syndrome (PLS) a extreme rare case with a incidence of 1- 4 cases per million, is an autosomal recessive genetic disorder caused by a deficiency in cathepsin C. PLS is characterized by periodontitis and palmoplantar keratoderma. The severe destruction of periodontium results in loss of most primary teeth by the age of 4 and most permanent teeth by age 14. Hyperkeratosis of palms and soles of feet appear in first few years of life. Destructions of periodontium follow almost immediately after the eruption of last molar tooth. The teeth are involved in roughly the same order in which they erupt. An 18 year old female patient presented to the Department for removal of her excessive mobile posterior teeth in upper and lower jaw, with thickening, flaking, and scaling of the skin on the palms and soles of the feet. On oral examination, the female patient presented completely resorbed maxillary and mandibular alveolar ridges with retention of only the third molars in upper and right lower jaw and only canine was present in upper left jaw. Based on complete history and clinical examination findings, a final diagnosis of PLS was made. The clinical presentation, differential diagnosis, complications and management of this syndrome are discussed.
Key words: Papillon- lefevre syndrome, Cathepsin, Hyperkeratosis, Periodontitis.

Introduction

This 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 one and four years.[1] The sharply demarcated erythematous keratotic plaques may occur focally, but usually involve the entire surface of palms and soles resulting in foul-smelling odor (Gorlin et al., 1964). Well-demarcated psoriasiform plaques occur on elbows and knees (Siragusa et al., 2000). This may worsen in winter and be associated with painful fissures. The keratosis of the plantar surface extends to the edges of the soles and occasionally onto the skin overlying the Achilles tendon and the external malleoli. Other sites that may be affected include the eyelids, cheeks, labial commissures, legs, thighs and axillae. The hair is usually normal but the nails, in advanced cases, may show transverse grooving and fissuring. The second major feature of PLS is severe periodontitis, which starts at the age of three or four years.[2,3]

The development and eruption of the deciduous teeth proceeds normally, but their eruption is associated with severe gingival inflammation in the absence of any local etiologic factor. The gingiva is bright red, edematous and bleeds easily. The periodontal pockets rapidly deepen, with severe loss of alveolar bone and marked fetor exoris. Although gingival inflammation and alveolar resorption is usually so severe that the alveolar process is completely destroyed, even during the most active phase of periodontal destruction, the rest of the oral mucous membrane is reported to be completely normal.

Primary dentition is usually exfoliated prematurely by the age of 4 years. After exfoliation, the inflammation subsides and gingival appears healthy. With the eruption of permanent dentition, the whole process of gingivitis Primary dentition is usually exfoliated prematurely by the age of 4 years. After exfoliation, the inflammation subsides and gingival appears healthy. With the eruption of permanent dentition, the whole process of gingivitis and periodontitis is repeated and there is subsequent premature exfoliation of the permanent teeth 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 radiographs. The degree of dermatologic involvement may not be related to the level of periodontal infection. Nail changes such as transverse grooving and fissuring are apparent in advanced cases.

In addition to the dermatologic and oral findings, patients may have decreased neutrophil, lymphocyte or monocyte functions and an increased susceptibility to bacterial infection, leading to recurrent pyogenic infections of the skin. Pyogenic liver abscess is a complication of PLS and is associated with impairment of the immune system. Radiographic features are characterized by generalized loss of alveolar bone. Gorlin et al. have added the third feature of dural calcification.[4] Reyes also observed radiographic evidence of intracranial calcification.

Histopathologic findings of affected skin consist of hyperkeratosis, occasional patches of parakeratosis, acanthosis, and slight perivascular inflammatory infiltrate. An increased prevalence of parental consanguinity has been reported in PLS patients.

All PLS patients are homozygous for the same cathepsin-C gene mutation inherited from a common ancestor.

It would be pertinent to mention that there are reports of at least six cases of late onset variation of PLS without underlying cathepsin-C gene mutation. This case report describes a case of PLS with clinical features and brief review of literature.

Case Report

An 18-year old female patient came with a chief complaint of loosening of molar teeth in the upper and lower jaws and wants the removal of her teeth (Figure 1).

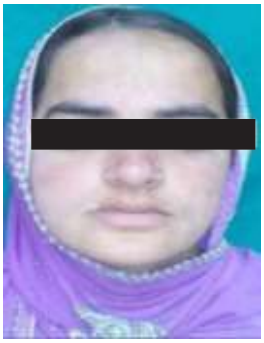

Figure 1: Profile image of patient

The patient noticed loosening of teeth since the age of 8 years, which aggravated in the past five years. The patient apparently also had early exfoliation of her primary teeth. Past history revealed that dry scaly skin started at the age of six, as noticed by her family, over the feet which later extended to bilateral hands and knees. The family history was positive for consanguinity of parents. The patient has two siblings who were clinically unaffected. On intra oral examination only 4 teeth were present out of which three were molars, one in each quadrant and one maxillary left anterior tooth (Figure 2).

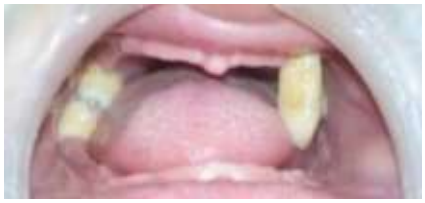

Figure 2: Intra oral image of patient

General physical examination revealed well demarcated lesions of dry scaly skin present bilaterally on knee, dorsum surface of hands and feet (Figure 3, 4).

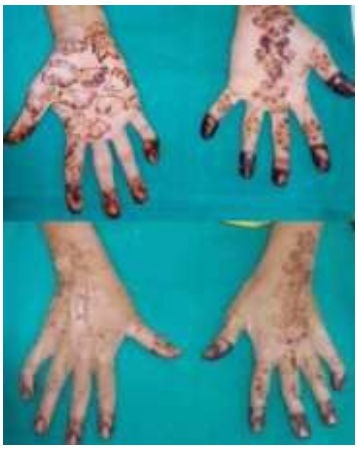

Figure 3: Palmar Keratoris

The lesions involved metacarpal and interphalangeal joints in the hands. These keratotic lesions were dry, scaly, and rough on palpation.

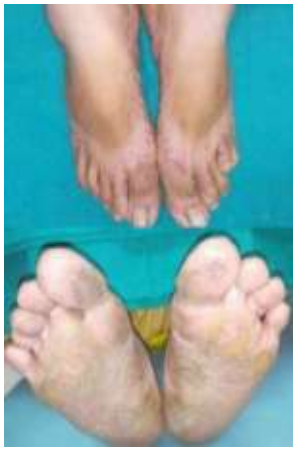

Figure 4: Plantar Keratoris

She was receiving treatment for the same for the past seven years. Patient was well oriented and showed independent ability to understand and communicate. Panoramic view radiograph showed the classical "floating-in-air" appearance with generalized horizontal and vertical bone loss of all the existing teeth (Figure 5). Thus a diagnosis of PLS was made, and extraction of remaining mobile teeth was done under local anaesthesia. Patient was then referred for prosthodontic rehabilitation.

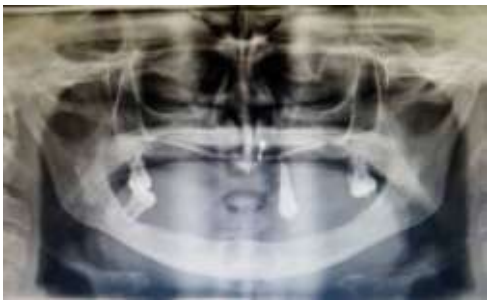

Figure 5: OPG showing extreme resorption of ridges and severe bone loss around teeth

Differential Diagnosis

Symptoms of the following disorders can be similar to those of Papillon-Lefèvre Syndrome. Comparisons may be useful for a differential diagnosis. Cochin Jewish Disorder, also known as Keratosis Palmoplantaris with Periodontopathia and Onychogryposis is a rare inherited disorder. It is characterized by reddening and overgrowth of skin on the palms of the hands and soles of the feet (palmoplantar hyperkeratosis) and overgrowth of the fingernails and toe nails (onychogryphosis).[5]

Affected individuals may also have flat feet (pes planus); abnormally long, slender fingers and toes (arachnodactyly); and/or a heightened sensitivity to cold temperatures and loss of bone tissue in the fingers and

toes (acroosteolysis). Degeneration of the structures that surround and support the teeth (periodontosis) may also be present. Cochin Jewish Disorder is inherited as an autosomal recessive genetic trait. Some researchers believe the disorder may be a variant of Papillon- Lefèvre Syndrome. Schopf-Schulz-Passarge Syndrome is a rare inherited disorder characterized by the development of dry scaly skin on the palms of the hands and the soles of the feet (palmoplantar keratosis), fragile nails, and/or the development of cysts on the eyelids. Other symptoms may include the early loss of primary (deciduous) teeth, absence of some or all of the permanent teeth (hypodontia), and/or lack of body and/or scalp hair (hypotrichosis).

Schopf-Schulz-Passarge Syndrome is believed to be inherited as an autosomal dominant genetic trait. Jadassohn-Lewandowsky Type Pachyonychia Congenita is a rare inherited disorder characterized by reddening, dryness, and a scaly appearance of the skin on the palms of the hands and soles of the feet (palmoplantar hyperkeratosis), and/or overgrowth of the finger nails and toenails (onychogryposis). In addition, affected infants may have teeth that are present at birth (neonatal teeth). Additional features may include loss of hair, excessive sweating (hyperhidrosis) of the hands and feet, hoarseness, and/or, in some cases, respiratory distress. Mental retardation may be present in some cases.

Jadassohn-Lewandowsky type Pachyonychia Congenita is believed to be inherited as an autosomal dominant genetic trait. Mal de Meleda is an extremely rare disorder characterized by the slow progressive development of dry scaly skin on the palms of the hands and soles of the feet (palmoplantar hyperkeratosis). Affected skin may be unusually red and become abnormally thick. Affected children may also exhibit abnormalities of the nails, excessive sweating (hyperhidrosis) associated with an unpleasant odor, and/or development of small, firm raised lesions (lichenoid plaques). In addition, some affected children may have heart defects (cardiac abnormalities), such as an abnormally large heart (cardiomegaly). Mal de Meleda is believed to be inherited as an autosomal recessive genetic trait.[6,7]

Ichthyosis, Sjogren-Larsson Syndrome is a rare inherited disorder characterized by the development of dry scaly skin (ichthyosis), hardened reddened skin on the palms of the hands and soles of the feet (palmoplantar hyperkeratosis), and/or discoloration of certain areas of skin (ecchymosis). In addition, affected infants may exhibit mental retardation, lack of voluntary movements of the arms and legs (spastic tetraplegia), seizures, and/or eye abnormalities. Ichthyosis, Sjogren-Larsson Syndrome is thought to be inherited as an autosomal recessive genetic trait. (For more information on this disorder, choose "Ichthyosis, Sjogren Larsson Syndrome" as your search term in the Rare Disease Database.) Fitzsimmons Syndrome is an extremely rare inherited disorder characterized by slow progressive development of dry scaly skin on the palms of the hands and soles of the feet (palmoplantar hyperkeratosis), mental retardation, and lack of control of voluntary movements of the legs (spastic paraplegia).
In some cases, children may exhibit an abnormally high arch of the foot (pes cavus).[8] Fitzsimmons Syndrome is thought to be inherited as an X-linked genetic trait. There are several additional disorders that are characterized skin abnormalities similar to those seen in Papillon-Lefèvre Syndrome. These may include Psoriasis, Dyskeratosis Congenita, Epidermolytic Hyperkeratosis, and some of the Ectodermal Dysplasias.[9]

Discussion

Papillon-Lefevre syndrome is an autosomal recessive disorder characterized by palmoplantar hyperkeratosis and aggressive periodontitis. Papillon-Lefevre syndrome usually appears in childhood. Males and females are equally affected. Patients are normal at birth. Skin lesions develop concurrently with oral lesions and may extend to dorsal surfaces of hands and feet. Another form of disease associated with palmoplantar keratosis and severe aggressive periodontitis has been named Haim-Munk syndrome. It differs from Papillon-Lefevre syndrome in symptoms such as arachnodactyly, acroosterolysis and onychogryphosis. [1] In Papillon-Lefevre syndrome there is severe periodontopathy and premature loss of primary and permanent dentition. Teeth are lost in eventually the same sequence in which they are erupted. When the last tooth is lost gingiva acquires a normal appearance.
The permanent dentition starts to erupt at proper time, but around 8-9 years of age periodontal destruction is repeated in the same manner as in primary dentition. All permanent teeth are usually lost before 14-16 years of age. In subjects with Papillon-Lefevre syndrome there is defective cathepsin C production. The gene for cathepsin C lies on chromosome 11. Cathepsin C is a lysosomal protease and it is distributed to many tissues.[2] Cathepsin C is involved in the activation of T cells. The exact biochemical defect leading to periodontal disease is still unclear. It is suggested by other authors that Papillon-Lefevre syndrome was due to a combination of ecto and mesodermal malformations. It is also suggested that a functional imbalance of collagenolytic activity in the periodontal ligament was responsible for periodontitis in Papillon-Lefevre syndrome.
In 1984, Van Dyke suggested that neutrophils from an individual with Papillon- Lefevre syndrome exhibit decreased receptor affinity for chemotaxins such as formyl peptides [5]. Page RC *et al*. in suggested defective cementum formation to be the cause for periodontitis in Papillon-Lefevre syndrome.[3] Papillon-Lefevre syndrome is associated with myeloperoxide deficiency, low integrin expression, defective phagocytosis and chemotaxis. Neutrophils from individuals with Papillon-Lefevre syndrome exhibit decreased affinity for chemotaxins.[4,5]

Hattab *et al*., reported four cases of Papillon-Lefevre syndrome affecting two Jordanian families with eight children. In all patients there was a relationship between

increased severity of skin lesions and seasonal variations and intensified periodontal destruction. [8]

Lass *et al*. in three multiplex families, one Ethiopian and two German, demonstrated linkage of Papillon-Lefevre syndrome with chromosome 11q13-q14.[7] Fischer *et al*., conducted a primary genome wide search by homozygosity mapping in a large consanguineous family with four affected siblings. Homozygosity and linkage was demonstrated in region 11q14 of chromosome. Toomes *et al*., showed that in patients with Papillon-Lefevre syndrome gene for cathepsin C which lies in chromosome 11 had undergone mutation resulting in decreased cathepsin C production. [8] Hart *et al*., reported mutations in cathepsin C gene in patients with Papillon-Lefevre syndrome from five different countries. [9]

Conclusion

Papillon-Lefèvre syndrome (PLS) is a rare ectodermal dysplasia characterized by palmoplantar keratoderma associated with early-onset periodontitis. The prevalence is estimated between 1/250,000 and 1/1,000,000 individuals. The male to female ratio is 1:1. PLS is found in all ethnic groups.

Diffuse palmoplantar keratoderma with erythematous plaques develops between the first and fourth years of life, with the soles being usually more severely affected than the palms. Psoriasiform hyperkeratosis can overflow onto the dorsal surfaces of the hands and feet (transgredient spread) and, less frequently, lesions can be seen on the limbs (knees, elbows). Skin lesions are followed by intense gingivitis that rapidly progresses into periodontitis with alveolar bone lysis and early loss of primary dentition. The skin lesions are aggravated by cold and during episodes of severe periodontitis.

Antenatal diagnosis is theoretically possible but has never been reported. Transmission is autosomal recessive. Genetic counseling should be offered to the parents of an affected individual informing them of the 25% chance their offspring has of inheriting the disease causing mutation. Treatment is based on oral retinoids which attenuate the palmoplantar keratoderma and slow the alveolar bone lysis. Antibiotics, along with oral hygiene and use of mouth rinses, are also recommended for slowing the progression of periodontitis. Ultimately, primary or remaining teeth are extracted and are replaced by dental implants. Antibiotic therapy is also used in the treatment of recurrent infections. Etretinate (a synthetic retinoid) shows promising results in the treatment of PLS.

In conclusion, we have reported a case of Papillon-Lefevre syndrome. Further studies in the field of microbiology and genetics are necessary to find the exact cause of periodontal destruction in such patients, so that best possible dental treatment can be given.

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