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Journal of Kerman University of Medical Sciences
2021; 28(3): 301-305

10.22062/JKMU.2021.91671

Case Report

Papillon-Lefèvre Syndrome: A Case Report

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ABSTRACT

Takayasu's arteritis (TA) is a major chronic vasculitis disorder that its etiology is unknown. Patients are mostly Asian women who often show nonspecific symptoms such as fever, myalgia, arthralgia, weight loss, and anemia. The report relates to a 17-year-old girl suffering from complaints, permanent and uncontinental pain starting from a month earlier, with loss of appetite and weight loss (4 kg), and night sweats. She had no diarrhea or gastrointestinal symptoms but had a pain in the shoulder and chest area since the last 5 months. She got better after seeing a physician and receiving supplements. She had a history of pain in the ear from the last five months leading to otitis, and was treated as a case of brucellosis with a score of 1.20 in the Coombs Wright test. According to the physical examination findings, the patient's left, radial, ulnar, and proximal pulses, and blood pressure were unexplained, and in the supraclavicular region of the left and the umbilical region, bruit was heard and the shape of the left nail was changed. Laboratory tests and imaging were performed for the patient, and after angiography, the left subclavian artery stenosis was detected. Given the age and sex of the patient and the results obtained, she was diagnosed with Takayasu's arteritis.

Keywords: Takayasu's arteritis (TA), Large-vessel vasculitis, Sedimentation rate (ESR)

Citation: Abdal Kh, Roozegar MA. Papillon-Lefèvre Syndrome: A Case Report. *Journal of Kerman University of Medical Sciences* 2021; 28(3): 301-305. doi: 10.22062/JKMU.2021.91671

Received: 05.03. 2020
Accepted: 22.10. 2020
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Published by Kerman University of Medical Sciences

Introduction

Papillon-Lefèvre syndrome (PLS) was first described in 1924 by two French physicians (1). This syndrome is a very extreme autosomal recessive disorder that predominantly demonstrates oral and dermatologic manifestations (2). Because of the autosomal recessive inheritance pattern, the parents and siblings, are typically not affected cause of heterozygous for cathepsin C mutations; consanguinity is noted in approximately one third of the cases. Genetic studies of patients with PLS have mapped the major gene locus to chromosome 11 (q14-q21) and revealed mutation and loss of function of the cathepsin C gene (1,3). This gene is important in the structural growth and development of the epithelial regions such as skin, palms, soles, knees, and keratinized oral gingiva and is critical for appropriate immune response of myeloid and lymphoid cells such as polymorphonuclear leukocytes, macrophages, and their precursors (4). The loss of appropriate function of the cathepsin C gene results in an altered immune response to infection and altered integrity of the junctional epithelium surrounding the tooth. Papillon-Lefèvre syndrome, which is characterized by palmoplantar hyperkeratosis, diffuse follicular hyperkeratosis, nail dystrophy, hyperhidrosis, keratosis on the elbows and knees, and progressive periodontal disease, is seen in both deciduous and permanent dentitions and develops soon after the teeth eruption (3,5). Papillon-Lefèvre syndrome exhibits the prevalence of one to four per million people in the population and both males and females are equally affected with no racial predominance (6). In most cases, the dermatologic manifestations become clinically evident in the first 3 years of life. The lesions are typically present as white light-yellow, brown, or red plaques and patches that develop crusts, cracks, or deep fissures. Some patients describe worsening in the winter and others describe keratotic desquamation, which may be confused with psoriasis (7).

The oral manifestations consist of dramatically advanced periodontitis that is seen in both the deciduous and the permanent dentitions and develops soon after the eruption of the teeth. Extensive hyperplastic, erythematous, edematous, hemorrhage on probing from gingival and halitosis is seen (6,7).

The development of the primary teeth is normal but their eruption is associated with severe gingivitis and periodontitis in the absence of any local etiologic factor (8).

The deciduous incisors are generally affected first and shows mobility at age of four or five years, all the deciduous teeth may be exfoliated (5). With the eruption of permanent dentition, the gingivitis and periodontitis is repeated and most of permanent teeth are lost by the age of 13-16 years and patients are mostly edentulous at an early age (3). A rapid loss of attachment occurs, with the severe resorption of alveolar bone and reveals floating-in-air manifestation on dental radiographs (8). Treatment with oral hygiene instructions, scaling, root planning, systemic antibiotics, and periodontal surgery is unsuccessful (9).

Radiographically, PLS characterized by generalized loss of alveolar bone, calcification of the falx cerebri, and the choroid plexus (10).

Histopathologically, findings of the affected skin shows hyperkeratosis, parakeratosis, acanthosis, increased vascularity, and a mixed inflammatory cellular infiltrate such as polymorphonuclear leukocytes, lymphocytes, histiocytes, and plasma cells (1,2,4).

In this paper, a case of Papillon-Lefèvre syndrome with all of the characteristic clinical features of the syndrome was described.

Case report

An 18-year-old female patient presented to the Department of Periodontology, School of Dentistry, Ilam, Iran, with the chief complaint of severe dental mobility and halitosis since 3-4 years ago. The past dental history showed that she had normal deciduous teeth which erupted at 8-9 months of age but unfortunately she lost deciduous teeth early at age of 5 years. The patient reported gingival bleeding during brushing and eating. In an interview with her family, they reported the presence of rough skin on the plantar surface of his feet and the palmar surface of the hands at age of 5 years. The lesions became worse during winter. There was no family history of resemble complaints. The patient's laboratory tests were normal. Intraoral examination showed severe periodontitis with gingival erythema edematous, and bleeding on probing (Figure 1). Her permanent teeth started mobiling at age of 12 years.

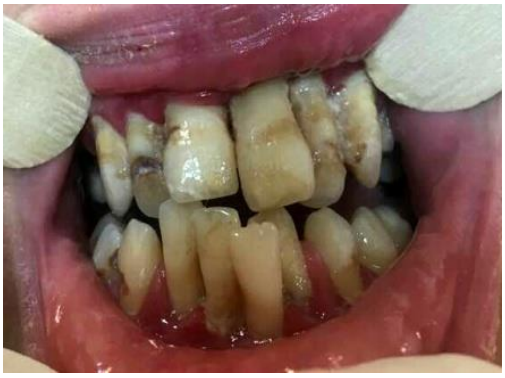

Figure 1. Severe periodontitis with gingival edematous and bleeding on probing.

Panoramic view of the radiograph revealed generalized loss of alveolar bone, complete resorption of bone support around all premolars and second molars (Figure 2). Lateral skull view of patient showing no evidence of intracranial calcification (Figure 3).

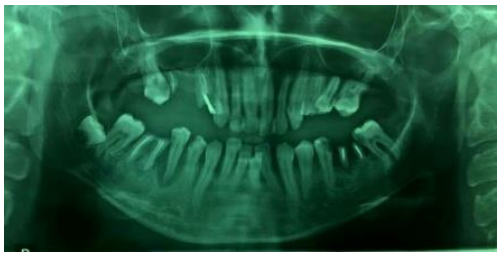

Figure 2. Panoramic view of the radiograph revealed generalized loss of alveolar bone, complete loss of bone support around all premolars and second molars.

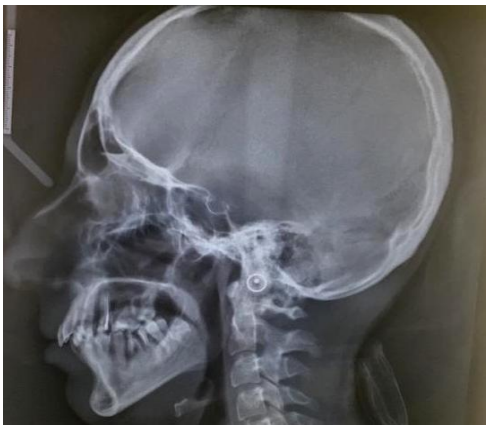

Figure 3. Lateral skull view of patient showing no evidence of intracranial calcification.

Dermatological examination showed well-demarcated, rough, erythematous, hyperkeratotic, scaly lesions on her palms and soles (Figure 4). Successively, skin lesions were reddening and became rough and scaly. Her general growth, hair growth, and mental development were all normal. Routine hematological investigations were normal.

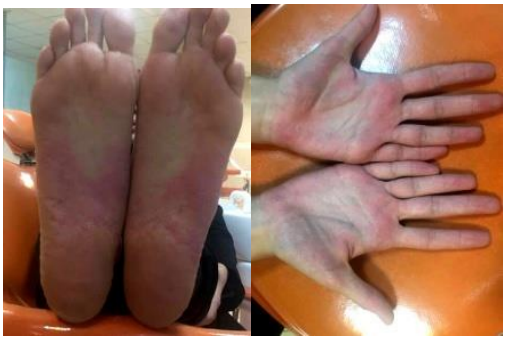

Figure 4. Erythematous areas on soles and palms.

According to the clinical and radiographic features, the final diagnosis of PLS was confirmed. Oral tetracycline was given for two weeks, after clinical improvement, patient refer to the dentist for treatment with removable prosthodontic appliance . The patient was referred to a dermatologist for improvement of skin lesions.

Discussion

In our case, the skin and periodontal findings were strongly similar to the classical descriptions of the Papillon-Lefèvre syndrome. The dental history of the patient showed exfoliation of all deciduous teeth at age of 5 years.

Clinically, the patients had the characteristic skin lesions such as keratotic plaques on the surface of the palms and soles (5). The plaques were diffuse, dry, scaly surface, and rough on palpation. The diffuse, erythematous, and scaly plaques were observed in our case, and her hair and nails was normal.

On based intraoral findings (severe gingivitis and periodontitis) with any etiologic factor as has been described for PLS (6). Our patient demonstrated severe mobility with gingival inflammation, deepening of periodontal pockets, and severe halitosis. Symptoms such as hyperhidrosis, infections, and mental retardation have been reported in PLS (7). No such symptoms were observed in our case.

Radiographically, panoramic radiograph of the patient revealed the extensive alveolar bone resorption of the roots of often all the permanent teeth that were present, giving the teeth a floating-in-air appearance (8,9). Considering the assessment of skin lesions and dental features, all the findings confirmed PLS. The findings such as intracranial calcification may be seen in

these patients but they were not observed in our case (8).

Although pathogenesis of PLS is relatively unclear but immunologic, microbiologic, and genetic bases are suspected (1). Microbiological researches have revealed Actinobacillus actinomycetemcomitans, Porphyromonas gingivalis, Fusobacterium nucleatum, and Treponema denticola organisms, suggesting that they may be involved in the disease development (2). Some studies showed that A. actinomycetemcomitans play an important role in the pathogenesis of aggressive periodontitis in PLS, and also, decreased function (chemotactic and phagocytic function) of neutrophils has been suggested (2,3). Recently, studies have shown deactivation of the cathepsin C gene that is responsible for the skin lesion and periodontal disease (5).

In our case, because of the poor economic condition of the parents, genetic testing could not be performed to determine the gene mutation but the dermatological, periodontal, and radiological features strongly suggested the diagnosis of PLS. In this case, the parents were healthy and there was no family history of the disease, suggesting an autosomal recessive pattern of inheritance.

Histologically, PLS demonstrated hyperkeratosis, parakeratosis, acanthosis, psoriasiform hyperplasia, and superficial perivascular lymphocytic infiltrate (3). This syndrome may be mistaken with other hereditary keratodermas, especially those of Unna-Thost and Mal De Meleda where no odontological features are observable, therefore, for the diagnosis of PLS, it is necessary for the dermatologist and dentist for diagnosis (4). The other differential diagnoses of PLS include Haim-Munk syndrome and Hypophosphatasia. Haim-Munk syndrome is an autosomal-recessive disorder that is characterized by congenital palmoplantar keratoderma and progressive periodontal disease, arachnodactyly, acroosteolysis, atrophy of nails, and deformity of the phalanges in the hands that none of these features were found in the present cases (5). Hypophosphatasia is caused by deficiency of alkaline phosphatase (ALK), but in the our case, ALK was within normal limits, and therefore, this differential diagnosis could be rejected (6).

Treatment: The skin manifestations of PLS are treated with retinoid (e.g., etretinate), which has resulted in a significant improvement with complete removable lesions in the large number of patients (6). Adverse reactions caused by retinoid consumption include angular cheilitis, Chapped lips, hair loss, arthralgia, tendinous, ligamentous calcifications, and teratogenicity. In order to prevent these drug-related adverse reactions, patients with mild dermatologic appearance often are treated with topical lubricants, keratolytic agents (salicylic or lactic acid), corticosteroid agents, or antibiotics medications (2,3).

Attempts at resolution of the periodontal disease often have been unsuccessful (4). Surprisingly, oral retinoids such as acitretin, etretinate, and isotretinoin can improve both the keratoderma and the periodontitis associated with PLS (9).

The periodontitis associated with PLS is usually difficult to control with ordinary periodontal therapy methods. Effective treatment of periodontitis includes extraction of the hopeless teeth, systemic antibiotics with the use of mouthwashes, oral hygiene training and professional scaling and root planning of the teeth (3,8). Tetracycline was successful in preventing the recreation of periodontitis in the permanent teeth after the extractions, as well as in the resolution of the infection in the deciduous dentition (5). However, penicillin, erythromycin, metronidazole, and tetracycline were all unsuccessful in resolving active sites of periodontitis (6). Treatment with high-dose amoxicillin and metronidazole, rigorous oral hygiene with strong supportive periodontal treatment has been effective in the elimination of A. actinomycetemcomitans (7).

Generally, periodontal therapy, oral hygiene instruction, and antibiotic therapy is not sufficient, and however, teeth are extracted and replaced by partial or complete denture prosthetic (10).

A course of antibiotics must be given for patients with PLS to avoid bacteremia, and subsequently, pyogenic liver abscess. Fever of unknown origin in these patients should be evaluated (9). Recently, findings of researches show that stem-cell therapy can be useful in the dental treatment (1).

Conclusion

Early diagnosis and intervention are necessary for PLS. Edentulous patients required removable or fixed prosthetics according to their age. Overall, in the case of observation of keratotic plaques on the palms or plantar surfaces of the feet of their child, parents are

suggested to consult with a dermatologist until receiving early treatment with retinoids that can prevent the creation of more skin lesions and to delay the course of periodontitis. Generally, more studies are recommended for determining a treatment strategy that can lead to the maintenance of teeth.

Ethical issues

This report was prepared with the consent of the patient.

Acknowledgments

The authors would like to thank Ilam University of Medical Sciences for supporting this research.

Conflict of interests

The authors declare that they have no conflict of interests.

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