PAPILLON-LEFÈVRE: A CASE REPORT

CRISTIANA PEREIRA*; GIL CAROTO**; ARLINDO ALMEIDA***; JOÃO SILVA****; PAULO FILIPE*****, SOUSA COUTINHO******; MARIA JOÃO RODRIGO*******, JOÃO FREITAS********

RESUMO

Observámos uma doente do sexo feminino, caucasiana de 13 anos de idade oriunda da ilha da Madeira, com o Sindroma de Papillon-Lefèvre (PLS). Apresentava os seguintes sinais clínicos característicos do Sindroma: hiperqueratose palmoplantar e uma periodontite generalizada. Esta última resultou na perda precoce de ambas as dentições, decidual e permanente.

Efectuámos a extracção dos seis dentes e realizámos biópsias dos tecidos gengivais das respectivas peças dentárias. Os tecidos gengivais e cemento foram observados por microscopia óptica e microscopia electrónica, respectivamente. Os tecidos gengivais apresentaram-se com uma destruição extensa dos ligamentos periodontais e com característica celulares de inflamação crónica, infiltrado de células plasmáticas. O cemento não apresentou alterações morfológicas.

Foram avaliados a capacidade fagocítica e a produção de superóxido pelos fagocitos activados, encontrando-se dentro dos parâmetros normais. As moléculas de adesão dos neutrófilos- CD18/CD11A; CD18/CD11B; CD18/CD11C- também foram avaliadas, apresentando valores normais.

Palavras-chave: Sindroma Papillon-Lefèvre, hiperqueratose, periodontite generalizada.

ABSTRACT

We report a case of Papillon-Lefèvre syndrome (PLS) in a 13-year-old caucasian girl from Madeira island. She exhibited the features of PLS: palmar and plantar hyperkeratosis and an advanced destructive periodontitis resulting in early loss of both primary and permanent dentitions.

Six permanent teeth and associated soft tissue were examined. Periodontal tissues and cementum were examined by light microscopy and electron microscopy respectively. Gum showed extensive destruction of the periodontal ligament, still attached to the root, and severe inflammation of the soft tissues with a predominant plasma cells infiltrate. The cementum didn't show any morphological alterations.

The phagocytic capacity and the superoxide production by activated phagocytes were within the control values, neutrophil adhesion molecules - CD18/CD11A; CD18/CD11B; CD18/CD11C – were also normally expressed.

Key-words: Papillon-Lefèvre syndrome, periodontitis, hyperqueratosis

* Departamento de Biomateriais da Faculdade de Medicina Dentária, Universidade de Lisboa, Portugal

** Departamento de Oclusão da Faculdade de Medicina Dentária, Universidade de Lisboa, Portugal

***Departamento de Medicina Oral da Faculdade de Medicina Dentária, Universidade de Lisboa, Portugal

****Clínica Universitária Dermatologia, Hospital Santa Maria, Lisboa, Portugal

*****Clínica Universitária Dermatologia, Hospital Santa Maria, Lisboa, Portugal

******Clínica Universitária Dermatologia, Hospital Santa Maria, Lisboa, Portugal

*******Clínica Universitária Pediatria, Hospital Santa Maria, Lisboa, Portugal

********Clínica Universitária Dermatologia, Hospital Santa Maria, Lisboa, Portugal

INTRODUCTION

In 1924, Papillon & Lefèvre described two siblings, the products of first- cousin mating, with a condition characterized by diffuse transgradient palmoplantar keratosis and the premature loss of both the deciduous and permanent dentitions. This condition came to be known as Papillon-Lefèvre syndrome (PLS). PLS is an autosomal recessive form of palmoplantar ectodermal dysplasia, characterized by palmoplantar hyperkeratosis and severe early-onset

periodontitis. The presence of severe periodontitis distinguishes PLS from other palmoplantar keratodermas.[1]

CASE REPORT

A 13-year-old caucasian girl from Madeira Island was referred to the Dental School of Lisbon in April, 2000, suffering from early loss of the permanent teeth, and with a history of premature shedding of deciduous teeth. The diagnosis of Papillon-Lefèvre syndrome (PLS) was hypothesising.

The girl was the second of four siblings, one older sister, a brother and a younger sister. The same syndrome affected any of them. The parents, siblings, grandparents and their close relatives were free from similar manifestations. The consanguinity was not proving in the two previous generations.

She had normal development and without complains during the first 2 years of age, when the skin lesions appeared, involving palms and soles, constituted by erythematous and scaly plaques causing discomfort.

Primary teeth erupted within normal chronological time. At the age of three, the gums around the teeth were red, swollen, and sore. A few months later, the first teeth became loose and exfoliated followed by the loss of all deciduous teeth.

The first intraoral examination showed the presence of the following teeth: 18,16,15,23,-25,28,38,37,35,34,45,46. All teeth had mobility scores of II/III. They were drifted and extruded, and gingival recession was evident. The periondontal gingival was bright red, severely inflamed, swollen, tender and displayed dark red granulomatous proliferations (Figure 1a). Purulent exudate was discharge from some periodontal pockets and gingival abscesses upon slightest pressure. The patient had difficulty in chewing and characteristic halitosis. The oral mucosal, including that covering the edentulous area, was normal in colour and consistency.

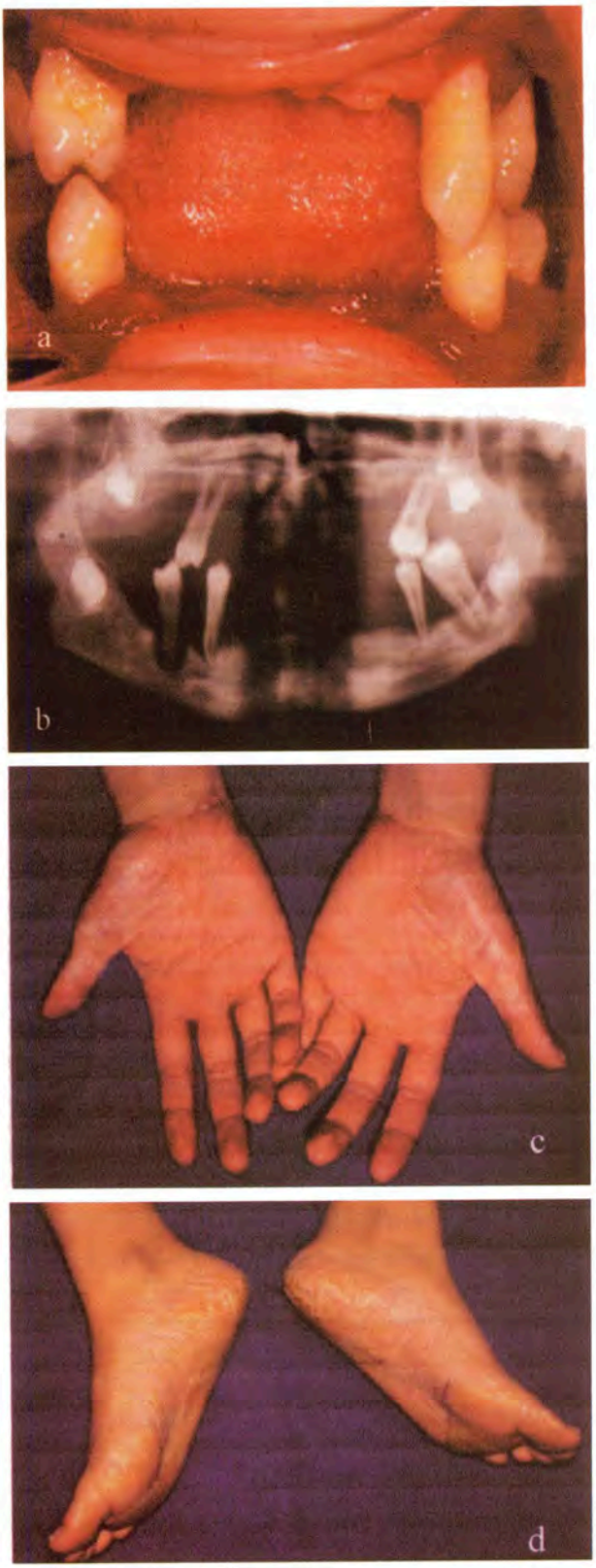

Figure 1 - Clinical Findings: a) - Intraoral examination - All teeth were extinded with gengival recesion and displayed dark red granulomatous proliferations. b) Radiographic imaging revealed a generalised loss of the supporting alveolar bone. c) and d) - Dermatogical examination revealed a symmetrical hyperqueratosis of the palms and soles.

The clinical examination revealed extensive gingival inflammation, profound bleeding and extensive loss of periodontal tissue support, with deep periodontal pockets (at several sites the probing depth was 8 mm). Supragingival plaque deposits were abundant. In contrast, subgingival plaque deposits were scarce.

Radiographic imaging revealed a generalised loss of the supporting alveolar bone. In some teeth the destructive process extended to the apical regions (Figure 1b).

She was absent one year without appropriated follow up and treatment. On returning, the patient exhibited the same clinical manifestations but in addition she lost 3 more teeth. At this occasion were present the following teeth: 18,16,25,-28,38,35,34,45,46,48. The four third molars were unerupted.

All six standing erupted teeth and associated soft tissues were extracted. During the extraction, biopsies were taken from the inner gingival margin. Half of the specimen was used for conventional microscopy. (Figure 2a) The remaining part, used for transmission electron microscopy, was immediately immersed in 3% glutaraldehyde in 0.1 M sodium cacodylate buffer pH 7. The lower left second premolar was also processed for scanning electron microscopy.

Dermatological examination revealed a symmetrical hyperkeratosis of the palms and soles (Figure 1 c, d). The hyperkeratotic, erythematous, and fissured palmar lesions extended to the lateral and dorsal aspects of the hands, while the plantar lesions with the same morpholocic character spread onto the external malleoli and Achilles region. The soles were more severely affected than the palms. Few scattered healed and active pustules were seen throughout the face.

Light microscope examination of the soft tissue specimens revealed deep pockets lined by squamous epithelium, which was hyperplastic in some areas but markedly thinned in others. At the tips of some of the retepegs, there were foci of cellular infiltrates consisting of mainly lymphocytes and plasma cells. In the stroma, underneath the oral gingival epithelium, clusters of mononuclear cell infiltration predominantly composed of plasma cells, were observed. The prominent features of

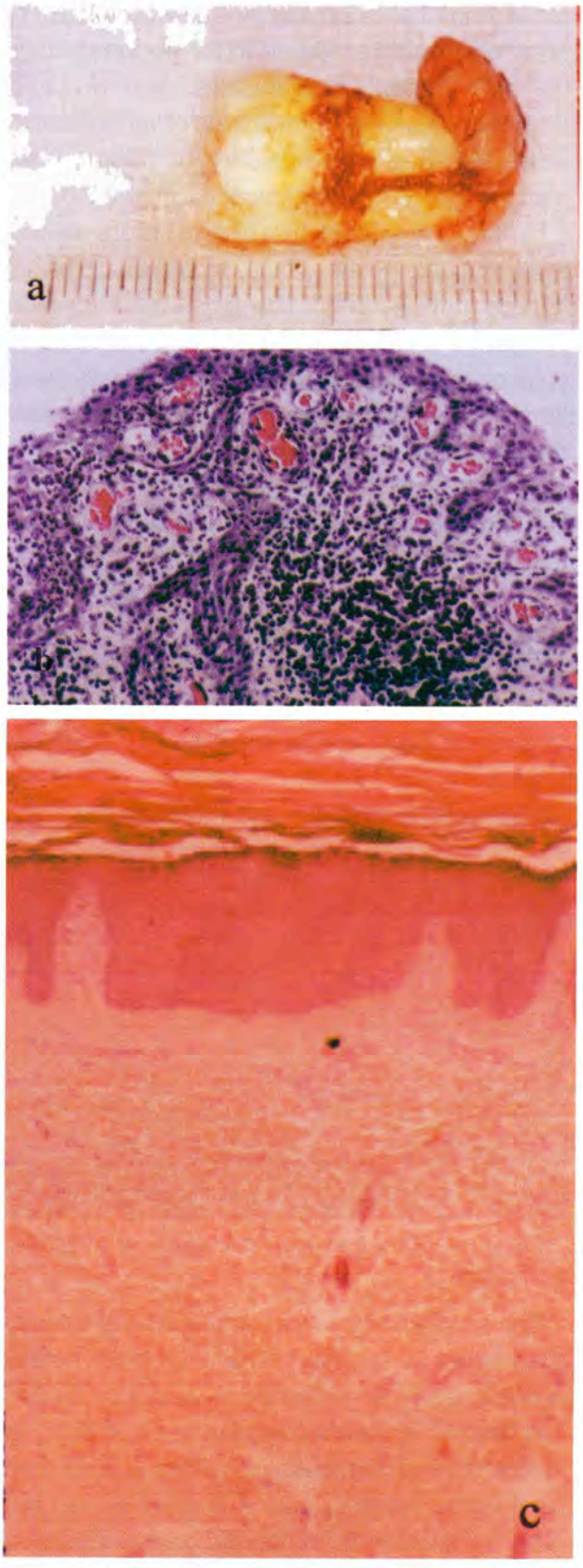

Figure 2 Specimens a) - Extraction of the teeth. b) Light microscope examination of pocket epithelium. c) Histological examination of skin lesions

the pocket epithelium were varying degrees of ulcerations and hyperplasia. In some areas, sepa-

ration from the underlying stroma was noted. The connective tissue subjacent to the pocket epithelium was markedly oedematous, also revealing large perivascular accumulations of inflammatory cells consisting predominantly of plasma cells, many of which were degenerate. (Figure 2 b)

Histological examination of skin lesions showed mild hyperkeratosis, focal hyperparakeratosis, hypergranulosis, mild acanthosis and irregular elongation and widening of the rete ridges in the epidermis. In the upper dermis, a slight perivascular chronic inflammatory cell infiltrate composed mostly of mononuclear cells may be evident, similar to that seen with chronic dermatitis. The mitotic index of cutaneous epidermal cells appears unremarkable. (Figure 2 c)

Ultrastructural examination of the pocket epithelium confirmed disruption of intercellular space, with alterations of hemidesmosomes. Regions of the epithelium were found, where the underlying basal lamina was intact or disrupted. (Figure 3)

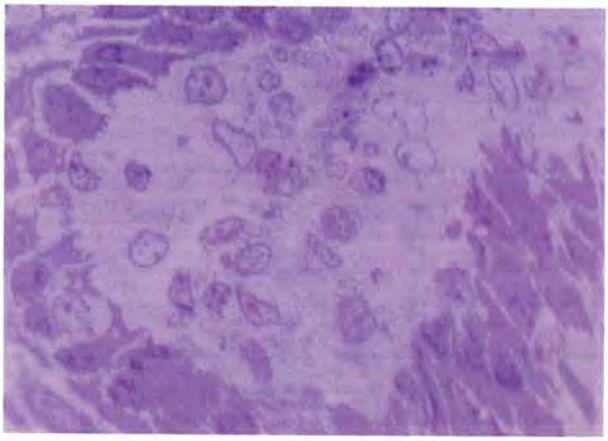

Figure 3 - Ultrastructural examination of the pocket epithelium

The immediately subjacent and deeper connective tissues were lysed. The only other notable qualitative leukocyte feature in the connective tissue was the abundance of plasma cells, many of which showed morphological changes in the form of dilated cisternae, and a number of electron dense profiles similar to Russell bodies. There was a high level of tissue destruction even in the deepest regions of connective tissue.

The scanning electron microscopy of the second premolar showed only distinguishable morphotype at the apical border plaque was a short rod. These occurred either singly, or in small groups, often linked by fibrils.

Haematological investigation including complete blood count was unaltered. The white blood cell count was 8100 / mm^3 with a differential of 63% neutrophils, 29% lymphocytes, 5% monocytes, and 3% eosinophils. In serum creatinine, uric acid, glucose, cholesterol, triglycerides, phosphorus, calcium, sodium, potassium, total protein, albumin, acid phosphatase and electrolytes were within normal values. The serum alkaline phosphatase level of 212U/ml was compatible with her age and growth period. Urine analysis was normal.

The previous studies about the PMN function are contradictory in patients with PLS[2]. PMN phagocytosis was normal. Superoxide radical production upon in vitro activation of neutrophils was also normal.

Radiographic imaging of her skull did not reveal ectopic calcification of the falx cerebri of the dura mater, as well as of the brain. Moreover, radiographic imaging of the hands did not reveal alterations of the fingers, which differentiate PLS from Haim Munk syndrome.[3] (Figure 4)

The patient was rehabilitated with total dentures immediately after the extractions .[4]

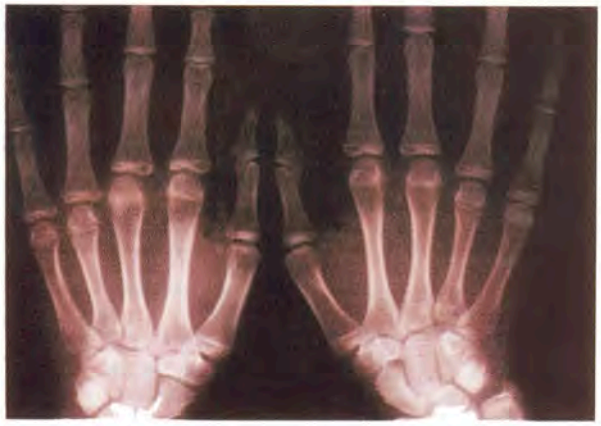

Figure 4 - Radiographic imaging of hands.

CONCLUSIONS

The delay in the diagnosis, made only 10 years after the first manifestations, can be explain by the conjunction of the rarity of PLS and the isolation of the patient in a island far from the major

Portuguese University Centres. This delay made possible oral only one type of treatment: - extraction of the teeth. The four included teeth will be a hope, as soon as their roots become full developed, to remains in oral cavity, with early periodontal management. Rehabilitation using implants will be tried after complete mandible growth.

The fact that the patient lives in an island can predisposes the propagation of the mutated gene (11q14) [5]. In this regard complementary genetic studies of the family would be of interest as well as a correct familial planning program.

REFERENCES

1- Thomas C. Hart & Lior Shapira. Papillon-Lefèvre Syndrome. Periodontology 2000 1994; 6: 88-100.

2- Liu R, Cao C, Meng H, Tang Z. Leukocyte Functions in 2 cases of Papillon-Lefèvre Syndrome. J Clin Periodontol 2000; 27(1): 69-73.

3- T C Hart, P S Hart, M D Michalec. Haim-Munk syndrome and Papillon-Lefèvre syndrome are allelic mutations in cathepsin C. J Med Genet 2000; 37: 88-94.

4- De Vree H, Steenackers K, De Boever JA. Periodontal Treatment of rapid progressive periodontitis in 2 siblings with Papillon-Lefèvre syndrome: 15-year follow-up. J Clin Periodontol 2000; 27(5): 354-60.

5- Thomas C. Hart, Donald W. Bowden, Khaled A. Ghaffar, Wei Wang, Christopher W. Cutler, Irfan Cebeci, Ahmet Efeoglu, Erhan Firatli. Sublocalization of the Papillon-Lefèvre syndrome locus on 11q14-q21. American Journal of Medical Genetics 1998; 79 (2): 134-139.