

Histopathological Aspects of the Surface Epithelium Associated with Trauma in Reactive Hyperplastic Lesions of the Buccal Mucosa

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Received: 12 Aug 2024

Accepted: 19 Sep 2024

Published: 26 Sep 2024

J Short Name: ACMCR

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Citation:

Silvia Carino, Histopathological Aspects of the Surface Epithelium Associated with Trauma in Reactive Hyperplastic Lesions of the Buccal Mucosa. Ann Clin Med Case Rep. 2024; V14(4): 1-6

Keywords:

Bite fibroma; fibrous hyperplasia; frictional keratosis; irritation fibroma; oral reactive lesion; reactive hyperplasia.

1. Abstract

Objective: To study clinical-pathological aspects of Reactive Hyperplastic Lesions (RHL) of the oral cavity, age frequency, sex, location, and analysis of alterations of the surface epithelium in selected cases with traumatic factors.

Materials and Method: A retrospective study was conducted on 1296 biopsies from the Pathological Laboratory, Faculty of Dentistry. National University of Tucumán, and inter consultations from General Pathology Services. Sixty-eight cases of Fibrous Hyperplasia (FH) with a history of associated traumatic factors, such as suction, local irritation and maladaptive prostheses, were selected.

Results: Out of 1296 biopsies, 346 (26.7%) corresponded to LHR. 59.2% were diagnosed as Fibrous Hyperplasia/ Irritation Fibroma (FH/IF); 23.9% Pyogenic Granuloma (GP); 7.2% Peripheral Giant Cell Granuloma (PGCG); 6.9% Peripheral Ossifying Fibroma (POF) and 2.6% Giant Cell Fibroma (GCF). The mean age was 38.4 ± 19.8 years, range: 2-90 years. 67.8% were women, and the female: male ratio was 2.1:1. The most common location was the gum (37.4%) and the least common was the palate (5.3%). Alterations of the surface epithelium were analyzed in 68 cases of FH; 69.1% were women, mean age 50.8 years SD: 14.1 (range: 12-76 years); located more frequently in the buccal mucosa, labial mucosa, and bottom of the sulcus. 67.6% of the cases were related to suction and bite patterns and 32.3% to maladaptive prostheses. The main epithelial alterations were: Hyperparakeratosis (86.7 %);

epithelial hyperplasia (83.8 %), intracellular edema of keratinocytes (83.8%); elongated epithelial ridges (47.05%); focal atrophy (35.2%) and keratin detachment (35.29%).

Conclusion: The epithelial alterations correspond to histopathological pictures of Secondary Frictional Keratosis (SKS) of the superficial epithelium. Intracellular edema was a remarkable change associated with trauma. The alterations studied in most cases were combined, in the cases analyzed, no isolated cytological atypia or epithelial dysplasia were observed.

2. Introduction

Reactive Hyperplastic Lesions (RHL) are usually triggered mainly by local irritating factors, such as chronic trauma, the presence of foreign bodies, or iatrogenic factors. These lesions represent adaptive responses of tissues to stimuli, manifesting as epithelial and underlying connective tissue hyperplasia. They are of clinical interest due to their variety of presentations. The mucosa reacts to these irritating factors with local hyperplasia with the presence of mature collagen, fibroblasts, mineralized tissue, endothelial cells, and multinucleated giant cells. These lesions are not considered neoplasms, they are hyperplastic or inflammatory reactions. [1,2,3] Clinically, they present as lesions with a sessile or pedunculated base, painless, with a smooth or ulcerated surface, whose size ranges from a few millimeters to several centimeters. The color of the lesion can vary from bright pink to red [1]. The accepted classification of LHR of the oral mucosa includes a spectrum of lesions, which include Fibrous Hyperplasia (FH) or Irritation

Fibroma (IF), Giant Cell Fibroma (GCF), Pyogenic Granuloma (PG), Peripheral Ossifying Fibroma (POF), and Peripheral Giant Cell Granuloma (PGCG). [4,3,5]. FH is a solid, painless, nodular mass with a smooth surface and normal color that can appear in any location of the oral mucosa. Histologically it is composed of connective tissue with dense collagen. [6]. GCF is a relatively rare hyperplastic fibrous lesion of the oral cavity that can only be diagnosed by histopathological examination. Kuo et al, on 24 cases of GCF, observed that they present as a pedunculated or sessile fibrous lesion of the color of normal mucosa, measuring 0.5-1 cm with a granular surface, and that the most distinctive feature is the presence of stellate and multinucleated giant cells in the loose fibrous sub epithelial connective tissue. He also observed that the surface epithelium was atrophic, parakeratinized or orthokeratinized stratified squamous epithelium. [7] PG appears clinically as an erythematous, painless, smooth, lobulated mass that grows rapidly and bleeds easily. It is associated with trauma, poor oral hygiene and increased hormonal levels during pregnancy. It generally appears in the gums but also in less common places such as the lips, tongue and oral mucosa. Histologically, it is composed of hyperplastic granulation tissue with a marked proliferation of endothelial cells that cover the capillary channels and an infiltrate of mixed inflammatory cells. There are two histological types of PG, the first type is characterized by the proliferation of blood vessels that are organized in a lobular shape, this type was called Lobular Capillary Hemangioma (LCH), while the second type consists of a proliferation that resembles to granulation tissue. [8] The natural history of PG can be classified into three different phases, cellular phase, capillary/vascular phase and involution phase. Sternberg et al, 1999 suggested three different phases to describe the course of PG, an “early phase” with compact cellular stroma with little formation of lumens, a capillary phase, with the formation of highly vascularized lobes, and a final phase called “involution” with intra- and perilobular fibrosis. [6]. The surface epithelium usually appears ulcerated. [9]. The differential diagnosis must be made with true Hemangioma. The Lobular Capillary hemangioma is a vascular neoplasm. Circumscribed proliferation of capillaries with plump endothelial cells surrounded by pericytes in a fibromyxoid stroma, arranged in one or more lobules which may show high cellularity. Each lobule has a large central vein surrounded by small capillaries. (IARC, 2022) POF can arise as a result of irritants, trauma, microorganisms, plaque, and stones. Typically located in the interdental papilla, they usually measure less than 1cm in diameter. It has a recurrence rate of 16% to 20%. Histologically, it presents a stratified squamous epithelium that covers a stroma of fibrous connective tissue with bone trabeculae and dystrophic calcifications. [10] PGCG is exclusively a lesion of the gingiva or alveolar mucosa. It presents as a nodular, painless, red to bluish-red, pedunculated or sessile increase in volume. Histologically, it consists of a proliferation of multinucleated giant cells and a pro-

liferation of mesenchymal cells, associated with prominent vascularization, abundant hemorrhage, and hemosiderin deposits at the periphery of the lesion. It may also present chronic inflammation and dystrophic calcifications [11].

3. Materials and Method

A retrospective analysis was carried out on a total of 1,296 biopsies from the FOUNT Pathology Laboratory, as well as from inter-consultations from General Pathology Services during the years 1996-2022. Data were collected from the RHL biopsy protocols age, sex, location, and associated traumatic factors, in all cases, the identity of the patients was protected from the records of the biopsy file. Of the total RHL (346), 68 cases of Fibrous Hyperplasia (FH) of the oral mucosa were selected that had a history of traumatic factors, such as suction, local irritation, and maladaptive prostheses. RHL related to teeth and/or the periodontal ligament were not included. A microscopic protocol was performed on histological sections stained with Hematoxylin and Eosin (H&E) and Periodic Acid Schiff (PAS) in selected cases. The following microscopic patterns in the lining epithelium were analyzed: Type of keratinization, epithelial hyperplasia, elongated ridges, keratin detachment, superficial papillomatosis, intracellular edema, ulcer, exocytosis, contamination, and pool of plasma. The collected data were recorded in detail in a Microsoft Excel® data sheet (Microsoft Corporation, Redmond, USA) and descriptive statistical analysis was performed on all collected data using Microsoft Excel® software.

4. Results

A total of 346 (26.7%) correspond to RH, 58.6% were diagnosed as FH; 23.9% PG; 7.2% PGCG; 6.9% POF, and 2.6% GCF. See (Table-1). The mean age of the RHL was 38.4 ± 19.8 years with a range of 2 to 90 years. Shows the incidence according to sex. 234 female patients, an average age of 78 years, and 112 men, an average age of 37.3 years. 67.8% were women, and the Female: Male ratio was 2.1:1. Most injuries were more frequent in women, see (Tables-2 & 3). FH and PG were more frequent in the age groups of 40-49 years and 20-29 years respectively. POF was more frequent among 30-39 years old. PGCG was more frequent in the age groups of 30-39 and 40-49 years. The most common location of RHL was the gum (37.4%), and the least common was the palate (5.3%). See (Table-4). Reactive alterations of the surface epithelium were analyzed in 68 cases of FH. 69.1% were women, mean age of 50.8 years SD: 14.1 (range: 12-76 years); located in the buccal mucosa, labial mucosa, tongue and bottom of the sulcus (see Table-5). 67.6% of the cases were related to a sucking habit and bite pattern and 32.3% to poorly adapted prostheses. Distribution of epithelial alterations associated with trauma in FH. Results. Hyperparakeratosis was present in 86.7% of cases; combined hyperorthokeratosis and hyperparakeratosis in 11.76% and hyperorthokeratosis alone in 1.47%. Epithelial hyperplasia

was observed in 83.8% and pseudoepitheliomatous hyperplasia in 16.2% of cases. It should be noted that the epithelial alterations occurred in a combined form: intracellular edema of keratinocytes (83.8%); elongated epithelial ridges (47.05%); keratin detachment (35.29%); focal atrophy of the epithelium (35.2%); superficial papillomatosis (29.4%); plasma pool or the so-called Toto Bodies, was a finding in 8.8% of the cases; presence of ulcer (7.3%) and microbial colonies (8.8%). The microscopic findings of lining epithelium concerning trauma are shown in (Table-6).

Histopathological criteria:

1. Increase in the parakeratinized and/or orthokeratinized keratin layer. (Figure-1, 2)

Table 1: Distribution of RHL according to subtype.

RHL Subtype	n° (%)
FH	203 (58,6%)
PG	83 (23.9 %)
PGCG	27 (7,8%)
POF	24 (6.9%)
GCF	9 (2.6%)

Note: Fibrous Hyperplasia (FH), Pyogenic Granuloma (PG), Peripheral Giant Cell Granuloma (PGCG), Peripheral Ossifying Fibroma (POF), Giant Cell Fibroma (GCF)

Table-3. Distribution of RHL according sex

Subtype	n° of Cases	Male n° (%)	Female n° (%)
FH	203	67 (33%)	136 (67%)
PG	83	28 (33,7%)	55 (66,3%)
PGCG	27	9 (33,3%)	18 (66,5%)
POF	24	5 (20,8%)	19 (79,1%)
GCF	9	3 (33,3%)	6 (99,6%)
Total	346	112 (32,4%)	234 (67,6%)

Note: Fibrous Hyperplasia (FH), Pyogenic Granuloma (PG), Peripheral Giant Cell Granuloma (PGCG), Peripheral Ossifying Fibroma (POF), Giant Cell Fibroma (GCF)

2. Epithelial hyperplasia (Figure-1)
3. Elongated and anastomosing crests. (Figure-3)
4. Defleked, macerated epithelial surface. (Figure-4)
5. Swollen epithelial cells. (Figure-5)
6. Cytoplasm of empty keratinocytes (necrotic epithelium) (Figure-4).
7. Superficial papillomatosis. (Figure-6)
8. Bacterial colonies attached to the surface. (Figure-8)
9. Plasma pool. (Figure-7)

Table-2. Distribution of RHL according to subtype, age and age range

Subtype	n° de Cases	%	Range	Average age
FH	203	58,67	Sep-90	45,13
PG	83	23.98	Feb-72	32,8
PGCG	27	7,8	Dec-61	37,5
POF	24	6.93	Dec-63	34,3
GCF	9	2.6	18 - 63	41,5
Total	346	100		

Note: Fibrous Hyperplasia (FH), Pyogenic Granuloma (PG), Peripheral Giant Cell Granuloma (PGCG), Peripheral Ossifying Fibroma (POF), Giant Cell Fibroma (GCF)

Table-4. Distribution of RHL according to location

Location	n°	(%)
Gum	127	37,46
Buccal mucosa	53	15,63
Alveolar mucosa	37	10,91
Tongue	32	9,43
Lip	30	8,84
Vestibular sulcus	25	7,37
Palate	18	5,3
Unspecified	17	5,01

Table-5. Distribution of FH according to location

Location	n°	(%)
Buccal mucosa	23	33,8 %
Lip	14	20,6 %
Tongue	12	17,6 %
Vestibular sulcus	14	20,6 %
Floor of mouth	2	2,9 %
Alveolar mucosa	2	2,9 %
Palate	1	1,5 %
Total	68	100%

Table-6. Types of epithelial alterations

Epithelial alterations.	n°	%
Hyperparakeratosis	59	86,7
Hyperparakeratosis and Hyperorthokeratosis	8	11,76
Hiperortoqueratosis	1	1,47
	68	100%
Epithelial hyperplasia	57	83,8
Pseudoepitheliomatous hyperplasia	11	16,2
	68	100%
Combined epithelial alterations		
Intracellular edema	57/68	83,82
Epithelial atrophy	24/68	35,29
Elongated ridges	32/68	47,05
Keratin shedding	24/68	35,29
Superficial papillomatosis	20/68	29,41
Plasma Pool	6/68	8,82
Ulcer	5/68	7,35

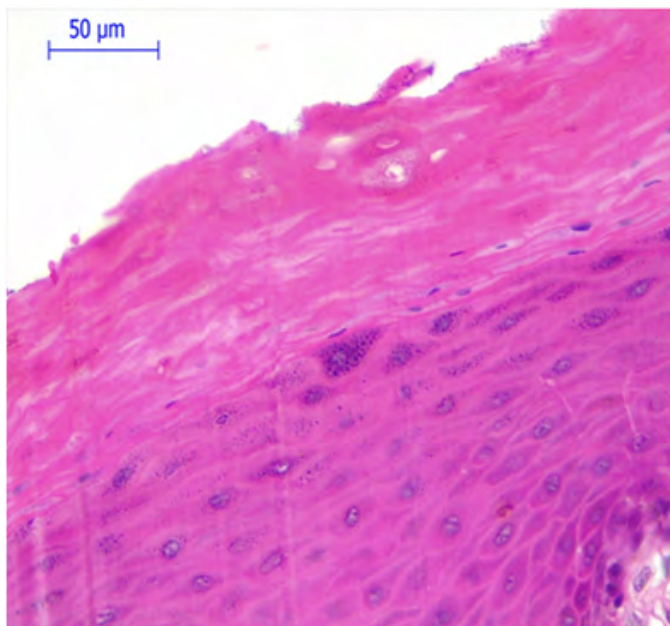


Figure-1. Hyperorthokeratosis, hyperparakeratosis and epithelial hyperplasia. H&E. 200x

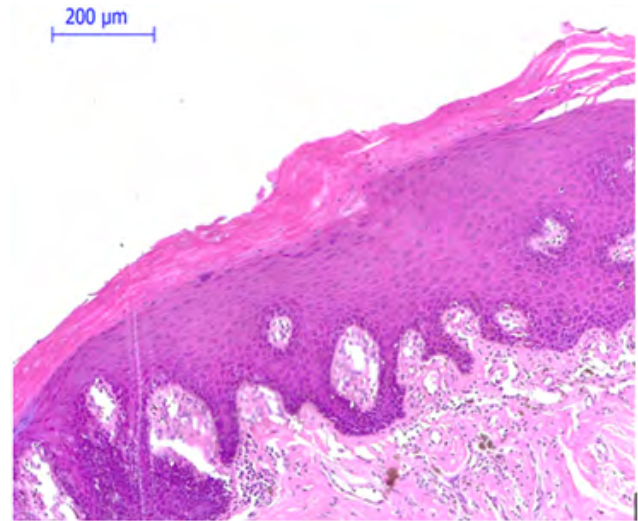


Figure-2. Hyperorthokeratosis, keratohyaline granules are observed. H&E 400x

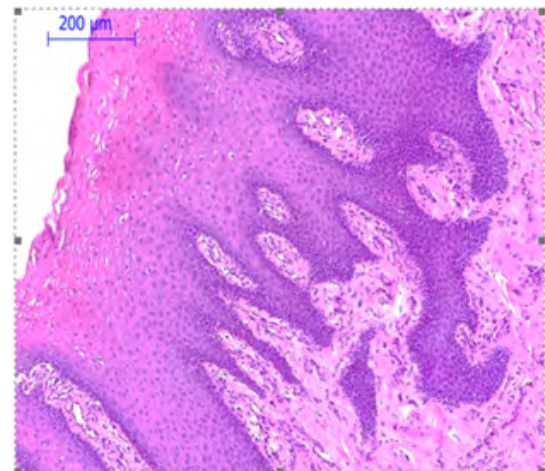


Figure-3: Epithelial hyperplasia and elongated ridges. H&E. 200x.

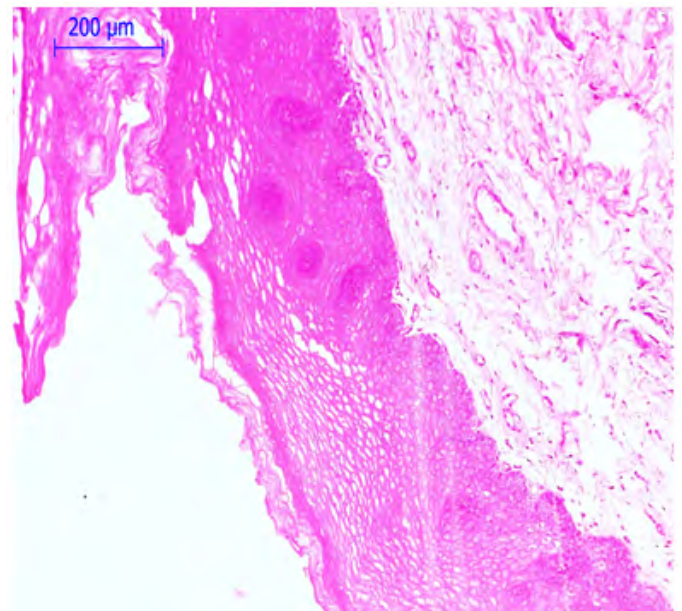


Figure-4: Epithelial acanthosis, areas of epithelial detachment. Necrotic superficial keratinocytes. Optically empty cytoplasm. H&E 200x

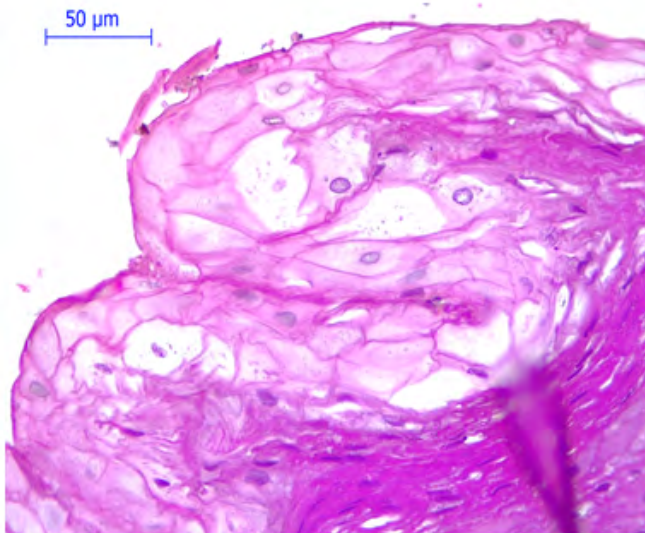


Figure-5: Cellular ballooning, swollen epithelial cells H & E.400x

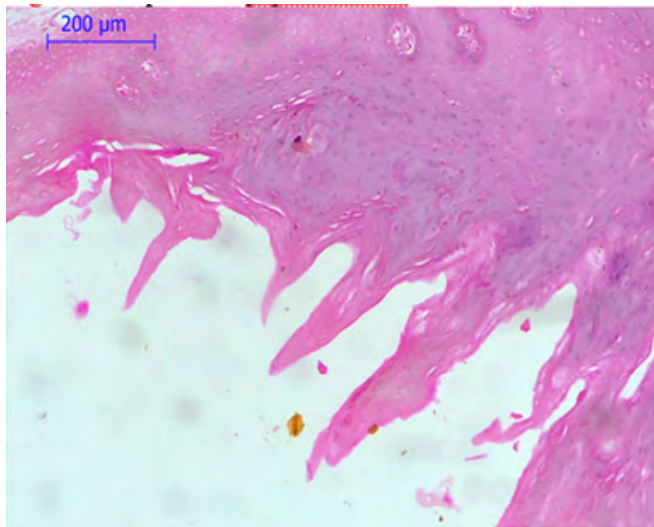


Figure-6: Superficial papillomatosis. H&E. 200x

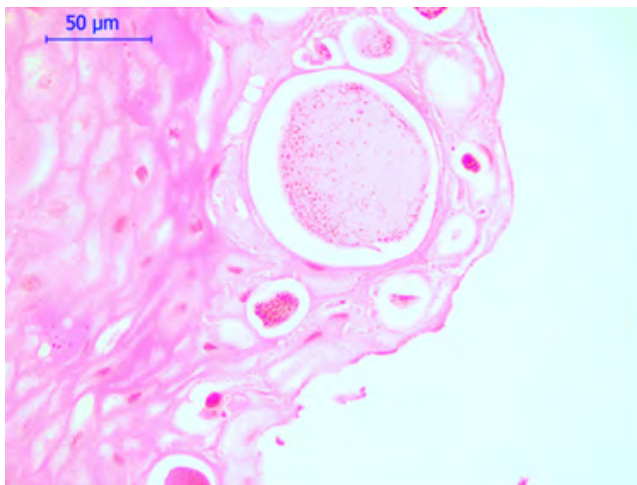


Figure-7: Presence of plasma pool (TOTO bodies) on the epithelial surface. H&E 400x

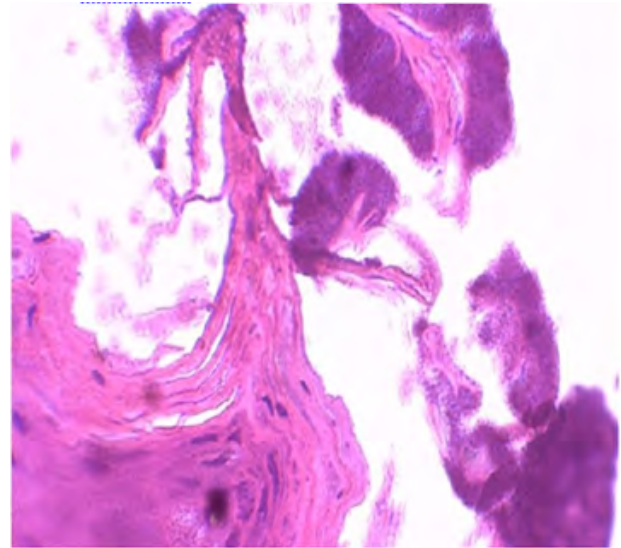


Figure-8: Presence of bacteria on the surface of the epithelium. H&E. 400x.

5. Discussion

RHL is a mucosal response to chronic low-grade irritation caused by biofilm, dental calculus, or other types of local irritating factors. Our report includes various subtypes of RHL of the connective tissue of the buccal mucosa, the clinic-pathological aspects, and in particular the alterations of the surface epithelium in the Fibrous Hyperplasia subtype, in sites other than the gingiva. This subtype was selected to reduce factors close to the gingival tissue. Our general results about frequency, age, sex, and location were similar to the findings obtained in other studies. [12,13, 14,2] The order of prevalence FH (58.6%), PG (23.9%); PGCG (7.2%), POF (6.9%) and GCF (2.6%). Coincidentally with Dutra et al, Awanga et al and Maturana Ramírez et al, HF was the most frequent followed by GP. Most authors record a peak in the 2nd and 3rd decade of life [14,15,16,17,20]. Concerning the analysis of associated epithelial alterations. Epithelial alterations were described in HF such as: Atrophy, signs of continuous trauma, excess keratin, and intracellular edema of the superficial layers or traumatic ulceration [18]. As well as Santana et al, 2014 mentions alterations such as atrophy, hyperkeratosis, and intracellular edema of the superficial layers or traumatic ulceration, in GCGP Muller et al (2019) [19] described Frictional Keratosis of the oral mucosa, produced by a parafunctional habit, the constant friction, chewing or sucking the oral mucosa against the teeth can cause keratosis of the oral mucosa. The alterations of the epithelium that we found are identical to those described in Frictional Keratosis. The epithelium exhibits epithelial hyperplasia and intracellular edema is commonly presenting as ballooned cells in the spinous layer. As well as bacteria on the keratin surface and detachment of the epithelium.

6. Conclusion

From the histopathological analysis it appears that the components of the connective tissue according to their predominance are useful

for diagnosing the subtypes of RHL, Diagnostic criteria: A) Pre-dominance of fibrous tissue and few vessels in FH/IF. B) Vascular neoformation, hemorrhages, hemosiderin and ulcerated with fibrinoleukocyte exudate on the surface, which may have a capillary hemangioma-like pattern in GP; C) Giant cells on a vascularized stroma without bone involvement the PGCG; D) The presence of giant, multinucleated stellate fibroblasts in the GCF and E) The presence of bone tissue in a fibroblastic matrix in the POF. Epithelial alterations are not always included in the diagnosis, we recommend adding for a more detailed diagnosis and we adhere to the term secondary frictional keratosis. mentioned by Dr. Sook Bin Woo (2012). The main histopathological criteria taken in our series were: hyperkeratosis, epithelial hyperplasia, intracellular edema, detachment of superficial keratin layers and bacteria present on the surface. The intracellular edema was remarkable and plasma pools were not always present. The main findings were more conspicuous in the implantation area. No cellular atypia or dysplastic changes were observed in any of the cases analyzed.

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