Idiopathic gingival papillokeratosis with crypt formation: an exclusive entity in the young population?

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Abstract

Idiopathic gingival papillokeratosis with crypt formation (IGPC) is a new and a very rare benign entity, clinically characterized by white-yellowish plaques with papillary architecture located in the upper labial gingiva of adolescent patients. The condition generally exhibits a bilateral symmetrical distribution and is asymptomatic. We report two new cases, one with a classic presentation and the other in an older individual. Through these case reports, we describe and highlight the key clinical and histopathological features associated with IGPC for greater understanding and knowledge by general dentists, oral pathologists, and dermatologists.

Keywords: crypt formation, fibromatosis, gingival, idiopathic, interdental, papilla, papillokeratosis

Introduction

Idiopathic gingival papillokeratosis with crypt formation (IGPC) is a benign entity introduced in 2017 by Noonan et al. [1] to characterize whitish-yellowish plaques with blunt papillary architecture that are located in the labial gingiva of upper anterior teeth, terminating at the mucogingival junction, with symmetrical and bilateral distribution. Less than 20 cases have been reported in the world (from USA, Mexico, and Brazil) and all in patients in the second decade of life without sex predilection [1,2]. Its etiology is still unknown, but some hypotheses have been proposed. These include a manifestation of human papillomavirus owing to the papillary nature of this condition, an acquired condition related to local factors, or the intraoral analogue of a localized congenital epidermal nevus [1]. The histopathologic examination reveals gingival mucosa characterized by a thin layer of parakeratin, accompanied by papillary acanthosis. Additionally, there are multifocal epithelial crypt-like invaginations, each featuring parakeratin plugging. The objective of this case report is to describe the clinical and histopathologic features of this rare condition on the attached gingiva of two patients from Chile, one of which was older than the previously reported cases. Although this injury has been previously documented in patients up to 20 years old [1], notably, one of our cases involves a 52-year-old patient, challenging the notion that this injury is exclusively in younger individuals.

Case Synopsis

Case 1

A 14-year-old girl with a history of atopic dermatitis was referred for a two-week history of painless swelling of the upper lip and was treated pharmacologically with antihistamines, nonsteroidal anti-inflammatory drugs, and analgesics. Angioedema of the upper and lower lips was confirmed by physical examination and a food allergy was suspected. Upon intraoral examination, an extensive white plaque was observed on the labial maxillary attached gingiva in the region of teeth 1.3 to 2.3, along the mucogingival junction, with a rough and slightly papillary surface that was well demarcated and asymptomatic (**Figure 1A**). Wiping with gauze decreased the intensity of the

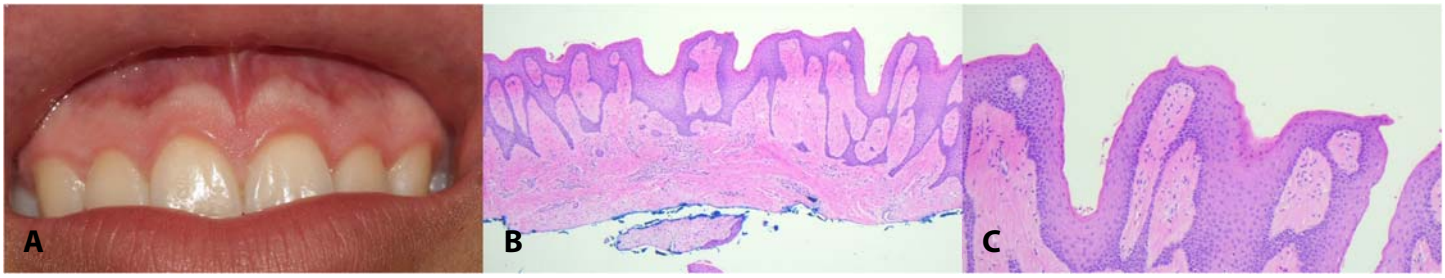

Figure 1. *Clinical and histopathological features of idiopathic gingival papillokeratosis with crypt formation in Case 1.* ***A)*** *White plaque on the labial maxillary attached gingiva in the region of upper anterior teeth, along the mucogingival junction, well demarcated and with a papillary surface.* ***B)*** *Oral mucosa exhibiting a thin layer of parakeratin with papillary acanthosis, elongated, tapered rete ridges, and epithelial crypt-like invaginations. H&E, 4×.* ***C)*** *Crypt-like invaginations with scarce parakeratin plugging, in a epithelium without atypia. H&E, 10×.*

white color, leaving irregular pink papillary plaques. An incisional biopsy was performed on the right side of the plaque. The microscopic features showed oral mucosa with acanthotic, parakeratinized stratified squamous epithelium, without cellular atypia. The papillary surface exhibited crypt-like invaginations with scarce keratin inside. Underlying this, a collagenized fibrous connective tissue with areas of chronic inflammatory infiltrate was found. The histopathological findings were consistent with the clinical hypothesis of IGPC (**Figure 1B**, **C**). The case has been followed up and the patient has not exhibited an exacerbation or modification of the presentation of IGPC.

Case 2

A 52-year-old woman smoker, with a history of arterial hypertension, hypothyroidism, insulin resistance, multiple food allergies, and allergies to non-steroidal anti-inflammatory drugs, was referred for a three-year history of a verrucous lesion on the labial mandibular gingiva of tooth 4.5 suspecting verruca vulgaris. She did not report any symptoms or history of contact dermatitis. We suspected verruca vulgaris. However, upon intraoral examination, a whitish-pink plaque was observed on the labial maxillary attached gingiva in the region of teeth 1.3 to 2.3, along the mucogingival junction. She noted that this was a new finding. The plaque had a rough and papillary surface, was poorly demarcated, and was asymptomatic (**Figure 2A**). An incisional biopsy of the plaque was performed. The histopathological features found in this case were quite similar to the previous case, but the keratin plugging of the crypt-like epithelial invaginations were more pronounced and IGPC was confirmed (**Figure 2B**, **C**). The initial lesion that had been the patient's concern turned out to be a giant cell fibroma after excisional biopsy. The case has been followed up and the patient has not exhibited an exacerbation or modification of the presentation of IGPC.

Case Discussion

In the current cases, the patient in Case 1 maintains all the clinical and histopathological features previously reported by other authors [1,2]. However, the 52-year-old patient in Case 2 presented in the sixth decade. In the case series of Noonan et al., the mean age of IGPC presentation was 16±2.9 years, and for Romo et al., it was 16.6±5.1 years. At the time of the introduction of IGPC as a new entity, it was considered to be distinct from epithelial adnexal formation in the gingiva (EAFG) identified by Bennet et al. and published in 1967 [3]. A series of three cases of EAFG was described in the same family. The index case was a 52-year-old man; adolescent son and daughter showed milder findings. These patients presented with histopathological changes in the oral mucosa of the labial gingiva of maxillary teeth, such as parakeratosis, epithelial invaginations, and papillary acanthosis. Lesions were asymptomatic and symmetric [4]. Clinically, the appearance of EAFG was very similar to that later proposed for IGPC. For these cases, it was proposed that there could be a genetic predisposition, without ruling out that environmental factors could play an important role in its pathogenesis. It is neither clear whether the histopathological features of EAFG represent

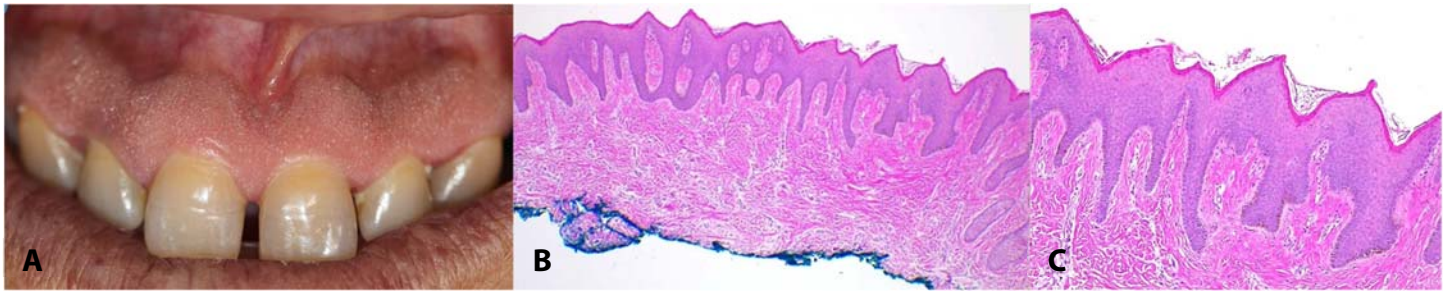

Figure 2. *Clinical and histopathological features of idiopathic gingival papillokeratosis with crypt formation in Case 2.* ***A)*** *Whitish-pink plaque on the labial maxillary attached gingiva in the region of upper anterior teeth, along the mucogingival junction, well demarcated and with a papillary and velvety surface.* ***B)*** *Oral mucosa exhibiting a thin layer of parakeratin with papillary acanthosis, elongated, tapered rete ridges, and epithelial crypt-like invaginations with parakeratin plugging. H&E, 4×.* ***C)*** *Parakeratin buffering the crypt-like invaginations, in an epithelium without atypia. H&E, 10×.*

adnexal differentiation, nor have findings of ductal or sebaceous differentiation been evident in the IGPC series [1,2]. When describing IGPC, Noonan emphasized that the cases in his series were reviewed exhaustively, without finding a familial trend. He did consider that prior IGPC cases in the literature could correspond to a continuum of the same IGPC [5].

Given the clinical and microscopic papillary architecture of this entity, one of the hypotheses proposed regarding its etiology is that it could be human papillomavirus (HPV)-associated. However, in the previous case series, classical HPV histopathological changes have not been observed, such as the presence of cytopathic effects. Only in one of the series was an in situ hybridization test performed for high- and low-risk human papillomavirus, with a negative result [1]. In the current cases it was not possible to find associated cytopathic effects like the presence of koilocytes or dyskeratosis in the thickness of the epithelium [6]. This is especially relevant for the patient owing to the association between human papillomavirus infection and sexual transmission [7].

Furthermore, developmental anomalies have been proposed in the differential diagnosis of IGPC, such as an unusual presentation of an oral epithelial nevus given the young age of most of reported patients [1,2]. The literature indicates that epidermal nevi may manifest towards puberty, becoming more warty over time. A subtype within this group is the linear epidermal nevus that has histopathological characteristics similar to those found in IGPC (papillomatosis, hyperkeratosis, elongated epithelial ridges, acanthosis, epithelial invaginations with keratin plugging). However, the exclusive oral presentation of epidermal nevus is extremely rare and is usually unilateral [8]. In fact, in both of our cases and in all the previously reported [1,2], no skin involvement was found.

In the first case series by Noonan et al., some patients reported food and drug allergies, in addition to habits such as chewing gum, the use of certain toothpastes, or intraoral orthopedic appliances [1]. Romo et al. reported a second series of cases with a history of hypoparathyroidism and the use of orthodontic appliances that were considered relevant [2].

Regarding treatment, the literature indicates that IGPC, being a benign condition, may only require maintaining patients under follow-up in most cases [2]. Previous reports indicate when gently wiping the plaques with gauze, cotton or a toothbrush, they temporarily lose their whitish appearance, probably because of the removal of parakeratin debris trapped in the crypts [1,2]. In our case, the patient in Case 1 underwent this procedure with a moistened gauze and there was indeed a decrease in the whitish color intensity and the accumulation was noted again at a follow-up visit.

Therefore, in more severe cases in which the presence of these plaques affects the patient aesthetically, this mechanical removal could become the most appropriate management. The use of topical corticosteroids has not been tested or described as a treatment alternative and its use does

Box 1. *Conditions associated with idiopathic gingival papillokeratosis with crypt formation.*

Drug allergies
Appliances (intraoral)
-Orthodontic appliances
-Sports mouth guard
-Smokeless tobacco

not seem justified given that this condition is not associated with a chronic inflammatory process that justifies its use. In the diagnosis of IGPC, it is essential to look for potentially associated conditions [1], (**Box 1**).

Idiopathic Gingival Papillokeratosis with Crypt Formation may exhibit resemblances to other clinical conditions, such as Lichen simplex chronicus [9]. (**Table 1**). This underscores the importance of establishing a thorough differential diagnosis to discern between them.

Conclusion

Idiopathic gingival papillokeratosis with crypt formation is a rarely diagnosed condition, typically observed in adolescents. However, it can also manifest in middle-aged adults as noted in our cases. It suggests that this condition may not be exclusive to younger patients, a consideration that becomes important when evaluating it as a potential diagnosis. Treatment is generally unnecessary and a conservative approach to management is sufficient. Familiarity with this entity can aid identifying new patients with similar lesions, contributing to a better understanding of the condition's etiology and clinical relevance.

Potential conflicts of interest

The authors declare no conflicts of interest.

Table 1. *Comparative analysis of idiopathic gingival papillokeratosis and lichen simplex chronicus.*

Histopathological feature	Lichen simplex chronicus	Idiopathic gingival papillokeratosis with crypt formation
Macroscopic appearance	Hyperkeratotic plaque with areas of parakeratosis, prominent and thickened granular layer, marked acanthosis, elongated and thickened rete ridges, pseudoepitheliomatous hyperplasia, papillary dermal fibrosis, and mild spongiosis	Gingival mucosa with a thin layer of parakeratin, accompanied by papillary acanthosis Additionally, there are multifocal epithelial crypt-like invaginations, each featuring parakeratin plugging
Microscopic appearance	Superficial dermis with vertically oriented, thickened collagen bundles, and perivascular and interstitial inflammation characterized by histiocytes, lymphocytes, and eosinophils	Oral mucosa with parakeratinized stratified squamous epithelium, acanthotic, without cellular atypia, and a papillary surface with the presence of crypt-like invaginations with scarce keratin inside
Underlying connective tissue	Collagenized fibrous connective tissue with areas of chronic inflammatory infiltrate	Collagenized fibrous connective tissue with areas of chronic inflammatory infiltrate

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