Histopathological review of 667 cases of oral mucoceles with emphasis on uncommon histopathological variations

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ABSTRACT

Mucoceles can occur in the oral cavity, appendix, bladder, paranasal sinuses, and lacrimal sac. In the oral cavity, mucoceles arise from pathological alterations in the minor salivary gland ducts. In this study, we aimed to histologically reevaluate cases of oral mucoceles to identify possible variants. A total of 667 slides containing tissue sections stained with hematoxylin and eosin diagnosed as a phenomenon of mucus extravasation were analyzed under light microscopy by 4 previously trained examiners. In 128 cases (19.1%), 1 or more histopathological changes were identified. Twenty cases (2.9%) exhibited collagenous globular structures compatible with myxoglobulosis. In 30 cases (4.49%), dissociation of collagen fibers after mucin extrava-sation was observed. Fifty-four cases (8.09%) exhibited papillary synovial metaplasia-like change, and 32 (4.79%) showed a significant reduction in the lumen of the cavity due to large papillae. Twenty cases (2.9%) were compatible with superficial mucoceles, and in 11 cases (1.64%), the foamy macrophages showed an unusual solid arrangement, known as clear cell change. It is essential to recognize the possible histopathological changes in oral mucoceles to avoid diagnostic pitfalls.

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1. Introduction

Mucoceles can occur in the oral cavity, appendix, bladder, paranasal sinuses, and lacrimal sac. In the oral cavity, mucoceles arise from pathological alterations in the minor salivary gland ducts. There are 2 types: the phenomenon of mucus retention and mucus extravasation; the latter is caused by a ruptured duct [1]. Oral mucoceles are common lesions that appear as a painless swelling of the smooth surface which measures 0.1 to 2 cm in diameter and has a blue to normal mucosa color [2–4].

The microscopic findings include the extravasation of mucus into a cavity surrounded by a granulation reaction in the absence of epithelial tissue [5,6]. Despite relatively common histopathological findings, some mucoceles can exhibit wide morphological diversity [4]. Within this context, studies have shown some uncommon histopathological features of mucoceles, such as myxoglobulosis, mucoceles presenting papillary synovial metaplasia-like changes, superficial mucoceles, and clear cell changes [1,5,7–11].

Myxoglobulosis appears as a globular structure that lacks epithelial tissue and whose center contains eosinophilic, lamellar, and amorphous or fibrillar material [1]. These spherules can be found either in the lumen or in the connective tissue surrounding the mucin extravasation [1,5]. Shah [1] described the progression of mucus extravasation; first, there is a separation of collagen fibers that occurs immediately after mucus extrava-sation, followed by the formation of a pathological cavity and, finally, resolution of the lesion.

Mucoceles with papillary synovial metaplasia-like change are characterized by the partial replacement of the granulation tissue lining the mucin extrava-sation with a folded membrane exhibiting villi. The more superficial portion of this membrane consists of a thin amorphous and eosinophilic matrix with an underlying condensation of histiocytes, fibrohistiocytes, and/or multinucleated giant cells. Within this spectrum, alterations in the extent of the lumen of the cavity characteristics of oral mucoceles have been described, with the occasional observation of a marked reduction in the cavity due to the presence of broad papillae that project into the cavity. This presentation is known as collapsed lumen [5,9].
Superficial mucocele was first described by Eveson [7]. Clinically, this lesion appears as a small translucent vesicle measuring less than 5 mm. Microscopic features include a mucin-containing subepithelial blister, atrophic surface epithelium, partial epithelial regeneration at the base of the mucin-filled cavity, and the absence of signs of subepithelial separation at the periphery of the lesion [7].

More recently, Piña et al [11] reported an unusual variant of oral mucocele composed almost exclusively of macrophages that exhibited extensive clear cytoplasm and signet ring alterations. This uncommon presentation of oral mucocele was described by the authors as clear cell change [11].

In view of the above considerations, the present study reviewed the histopathological features of oral mucocele cases to better understand the possible histological variants that can be found within the spectrum of microscopic findings of oral mucoceles.

2. Material and methods

The study was approved by the Ethics Committee (permit no. 675.422). All slides containing hematoxylin and eosin–stained sections of oral mucoceles diagnosed as mucus extravasation phenomenon between 1970 and 2013 and stored at the Pathological Anatomy Sector of the Department of Oral Pathology were reviewed. The slides were analyzed under a light microscope (Olympus CH30; Olympus Japan Co, Tokyo, Japan) at magnifications of 40×, 100×, and 400× by 4 previously trained examiners. The clinical findings of superficial mucocele cases were retrieved from the clinical medical records that accompanied the material sent for histopathological analysis to the above service.

The following histopathological variations described in the literature were investigated: myxoglobulosis [1,8], papillary synovial metaplasia-like changes [9], collapsed cavity lumen [9], postextravasation separation of collagen fibers [1], superficial mucocele [7], and clear cell change [11].

3. Results

Among the 11,589 cases diagnosed between 1970 and 2013 and stored at the Pathological Anatomy Sector of the Department of Oral Pathology, 667 (5.75%) were oral mucoceles. Most lesions exhibited the usual histopathological features, including a cavity filled with amorphous eosinophilic material compatible with extravasated mucus, permeated with inflammatory cells, especially foamy macrophages and neutrophils. In most cases, the cavity was surrounded by granulation tissue. Normal appearing, or sometimes chronically inflamed salivary gland parenchyma was observed in adjacent areas.

One or more histopathological variations were observed in 128 (19.1%) cases. Twenty (2.9%) cases exhibited collagenous and hyalinized globular structures, sometimes free floating in the lumen or adhered to the surrounding granulation tissue (Figure A), histopathological findings compatible with myxoglobulosis. The dissociation of collagen fibers after mucin extravasation was observed in 30 cases (4.49%) (Figure B). Fifty-four (8.09%) cases exhibited papillary synovial metaplasia-like changes (Figure C). A significant reduction in the cavity lumen due to the presence of broad papillae was observed in 32 cases (4.79%) (Figure D). Twenty (2.9%) cases showed clinical (size smaller than 5 mm) and histopathological features of superficial mucoceles.

Figure. (A) Collagenous and hyalinized globular structures free floating in the lumen compatible with myxoglobulosis. (B) Dissociation of collagen fibers after mucin extravasation. (C) Papillary synovial metaplasia-like changes. (D) Significant reduction in the cavity lumen. (E) Superficial mucoceles. (F) Clear cell change (hematoxylin and eosin, scale bar).
4. Discussion

Although mucoceles are frequent nonneoplastic lesions of the oral cavity and the most common affecting the minor salivary glands [3], some unusual histopathological features have been described in the literature and prompted new approaches to this topic [1,5,7–11].

In the present study, myxoglobulosis was observed in 2.9% of the sample. This variant was first described by Li et al [8] in 1997, who observed a globular intraluminal organization of mucus content in a mucocele removed from a 10-year-old child. At that time, this peculiar finding had only been described as a histopathological variation in appendiceal mucoceles. Today, several reports of this finding in oral mucoceles are available in the literature, including case reports and large case series [1,5,6,9,12]. However, the etiology and pathogenesis of these globular organizations remain unclear [6]. According to Shah [1], mucus extravasation triggers a host response that initially consists of neutrophils, followed by macrophages. This extravasation of cellular and acellular material into connective tissue induces the separation of collagen fibers, which corresponds to the early stage of a mucocele and occurs immediately after rupture of the salivary duct. The dissociation of collagen fibers was observed in 4.45% of the present sample.

Shah [1] also reported that the dissociated collagen fibers become surrounded by macrophages and acquire a globular appearance, which may be the result of mechanical fragmentation due to the presence of mucus or enzymatic breakdown mediated by macrophages. Before fragmentation, the globular structures also contain inflammatory cells and vessels, corresponding to the early stage of myxoglobulosis. Paremala et al [6] emphasized that, although the diagnosis of mucus extravasation phenomena is not challenging for the pathologist, the intraluminal globular organization surrounded by granulation tissue is an unusual histopathological feature of these lesions.

Histopathological findings compatible with papillary synovial metaplasia were identified in 8.08% of the cases studied. In contrast, in a series of 1824 cases of oral mucoceles, Chi et al [5] observed this finding in only 0.1% of the sample. According to Chi et al [9], it is important that the pathologist recognizes this rare histopathological variant of oral mucocele to avoid a misdiagnosis. Particularly, Warthin tumor should be included in the differential diagnosis because of its cystic papillary growth and eosinophilic surface. However, the authors [9] emphasize that features such as the preferential location of mucocytes in the lower lip, in contrast to salivary tumors that rarely occur at this site, and the presence of oncocytes with extensive eosinophilic cytoplasm in Warthin tumor contribute to the differentiation between these lesions. The extent of the lumen was significantly reduced in 4.79% of the cases studied here because of the large proportion of papilla growing toward the cavity.

With respect to superficial mucoceles, 2.9% of the cases were classified as this variant because they exhibited the clinical and histopathological features described by Eveson [7]. Cases of multiple superficial mucoceles have been reported in the literature in association or not with other diseases such as graft-vs-host disease [3,13,14]. Before their first description, superficial mucoceles were often erroneously diagnosed as benign papillomatous of the mucous membranes or bullous lichen planus [3]. However, according to Xu et al [3], the clinical appearance of superficial mucoceles and of these immune-mediated lesions is somehow different. In bullous pemphigoid and oral bullous lichen planus, the blisters are generally larger, flaccid, and opaque. On the other hand, in most superficial mucoceles, the blisters are translucent and have a tense surface [3]. In addition, in bullous pemphigoid, the most common autoimmune blistering disease, IgG autoantibodies are directed against 2 hemidesmosomal components in the dermal-epidermal junction [15,16]. The disease is diagnosed on the basis of clinical, histologic, and immunologic findings by direct and indirect immunofluorescence [15]. In the present sample, all superficial mucoceles were single lesions.

Piña et al [11] described a clinical case of oral mucocele in a 74-year-old patient. Microscopic analysis revealed a dense population of clear cells surrounding an inner cavity which contained scarce mucoid material. The clear cells exhibited cytoplasmic vacuolization with shrunken pyknotic peripheral nuclei and a signet ring appearance, intermingled with a delicate network of small vessels. According to the authors, these cases are difficult to diagnose because of the similarity with clear cell tumors and signet ring cell lesions, such as salivary gland tumors or metastatic neoplasms. Although most exhibit distinctive microscopic characteristics, histochemistry and immunohistochemistry can be required as well as relevant clinical information to achieve the correct diagnosis [11]. In the present study, clear cell change was observed in only 1.64% of the sample. However, the structural organization of the lesion, the presence of a cavity sometimes filled with mucus, and the morphological identification of clear cells as foamy macrophages led to the diagnosis of mucus extravasation phenomena.

As mentioned earlier, considerable variation exists in the prevalence of uncommon histopathological findings in oral mucoceles. In the present sample of 667 cases, 1 or more of these variations described in the literature were observed in 19.1% of cases. Except for myxoglobulosis, there are no explanations for the morphological appearance of most of these alterations. These histological features are incidental findings, and the clinical presentation of these lesions does not differ from oral mucoceles exhibiting the usual histology [5,11], except for superficial mucoceles. However, in some cases, these changes may be prominent enough to cause important diagnostic difficulties. Knowledge of the possible histopathological variations of oral mucoceles is therefore essential.

References