

Papillary synovial metaplasia-like change in oral mucoceles: A retrospective institutional study of 105 cases

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Abstract

Background: Mucoceles are mucus-filled cavities and are broadly of two types: mucus retention cysts and mucus extravasation phenomenon. A wide variety of histological features have been documented in the literature. The present study was an attempt to study these histological features: papillary synovial metaplasia-like changes (PSM-like changes) in particular.

Materials and Methods: One hundred and five tissue samples of mucoceles were retrieved and evaluated for age, gender, type, site, color, etiology, symptoms, dimension of the lesion and presence or absence of PSM-like changes. The results were documented on Microsoft Excel spreadsheet and analyzed by using SPSS.

Results: All 105 cases were of mucus extravasation phenomenon with a definitive male preponderance. The mean age of occurrence was 25.82 ± 11.65 years and a predilection for the lower lip. PSM-like changes were seen in 31 cases (Group II), and the remaining 74 cases did not show a definite presence of these features (Group I). The cases in Group II were statistically larger in dimension than Group I cases. No difference was noted in age, gender and laterality.

Conclusion: PSM-like changes appear to be an underrecognized histological alteration seen in oral mucoceles and must be recognized to differentiate from other salivary gland entities showing papillary architecture.

Keywords: Mucocele, mucus extravasation phenomenon, papillary synovial metaplasia, papillary synovial metaplasia-like changes

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INTRODUCTION

Mucoceles (muco – mucus and coele – cavity) are cavities filled with mucus and are among the most common benign soft-tissue lesions in the oral cavity.^[1,2] Apart from the oral cavity, mucoceles can occur in the paranasal sinuses, lacrimal sac, bladder and appendix.^[3] Intraorally, these lesions appear mostly as painless swelling, bluish to normal (pink) in color and measure 0.1–2 cm in diameter.^[4-6]

The most frequently affected site is the lower lip in contrast to salivary gland tumors which show more predilection for the upper lip.^[3,7] These are broadly categorized into two types: mucous retention cyst and mucous extravasation phenomenon, latter being more commonly encountered.

Histologically, these are characterized by extravasation of

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mucin into a nonepithelialized cavity which is surrounded by granulation reaction,^[3] hence considered as a pseudocyst. Granulation tissue involves proliferation of new blood vessels, plump fibroblasts and collagen deposition along with other extracellular matrices accompanied by inflammatory reaction.^[6] Extravasation/spillage of mucin occurs by rupture of minor salivary gland ducts, mostly posttraumatic injuries. The literature documents a wide deviation from these common histological features including myxoglobulosis, clear cell changes, superficial mucocoeles and papillary synovial metaplasia-like changes (PSM-like changes).^[2,6,8,9]

Synovial metaplasia has been reported in association with breast implants, mandibular reconstruction plates, tendon and testicular implants, bone–cement interface of hip prostheses and scarred/traumatized skin.^[2,10] PSM-like changes were initially detailed in the literature in two cases of oral mucocoeles by Chi *et al.* who also reported an incidence of 0.1% over a 10-year period.^[2,11] In a clinic-histopathological and immunohistochemical analysis of 100 oral mucocoeles, Conceição *et al.*^[6] did not find PSM in any cases; in contrast, the incidence in another series of 667 cases was 8.09%.^[3] Recognition of such a phenomenon may be important for a pathologist so as to avoid confusion with other lesions, in particular salivary gland neoplasms with a papillary cystic growth pattern^[2] such as ductal papilloma, cystadenoma, and papillary cystadenoma lymphomatosum.

Since PSM-like changes are not widely studied and often underrecognized in mucous extravasation cysts, the aim of the present paper was to find the incidence of PSM-like changes in oral mucocoeles.

MATERIALS AND METHODS

From the archives of the Department of Oral Pathology and Microbiology, cases of mucocoele received between 2015 and January 2020 were retrospectively retrieved and reviewed. A total of 105 samples of mucocoeles were retrieved for histopathological analysis. The descriptive data of these patients were evaluated and compared with previously documented data in the literature. The study variables included age, gender, type, site, color, etiology, symptoms, dimension of the lesion and presence or absence of PSM-like changes. Two observers analyzed the slides (DP and RA). The criteria for PSM-like changes included (a) the presence of obvious papillary or villous folds, (b) microscopic presence of membrane irrespective of stage of development, (c) marked cellularity and less organized granulation tissue in early lesion, (d) intermediate

cellularity with more definite palisading in mature lesions with a smooth surface and (e) hyalinization and reduced cellularity in long-standing lesions.^[2]

Slides were further examined for other unusual variants such as myxoglobulosis, clear cell change, superficial mucocoeles, calcifications, associated giant cell reaction and solitary/multiple compartmentalization. Special staining and imprint cytology details were also recorded wherever done.

The results were presented on Microsoft Excel spreadsheet and analyzed by using IBM SPSS software (IBM Analytics, Armonk, New York, USA). Descriptive statistics was done for frequency counts. Comparison between two groups was made using Chi-square test, Levene's test for equality of variances and *t*-test for equality of means. $P < 0.05$ was considered statistically significant.

RESULTS

Clinicodemographic profile

Out of total 2358 biopsies received in the department, 105 cases of oral mucous extravasation cysts were included in the study. The overall mean age of occurrence was found to be 25.82 ± 11.65 years (range: 6–68 years). The peak was seen in the third decade [Figure 1]. Males outnumbered females by a ratio of 2.5:1. Swelling was the chief complaint in all but one case where pain was an additional symptom. Fifty-one cases did not reveal any history of trauma/biting oral habits. Thirty-four cases presented with a history of lip/cheek biting, while twenty cases gave a history of trauma including fall, interpersonal violence or accident. The most common site of occurrence in descending order was lower lip ($n = 91$, 86.67%), buccal mucosa and floor of mouth ($n = 5$ each, 9.52%), ventral surface of tongue ($n = 3$, 2.86%) and upper lip ($n = 1$, 0.95%). The highest number of cases was seen on the left side ($n = 58$, 55.2%) followed by right side ($n = 43$, 41%), whereas only

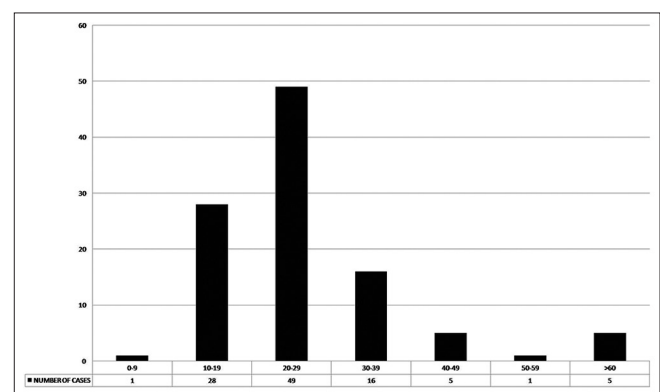


Figure 1: Age distribution of 105 oral mucocoeles in decades of life (age in years)

four cases were seen in the midline.

Clinically, normal color was displayed in 63 cases, while 34 cases exhibited bluish to bluish red color. The remaining eight cases were explained either as red ($n = 3$) or white/keratotic ($n = 5$). The mean diameter measured clinically was 1.298 ± 0.79 cm (range: 0.3–4 cm).

Histological examination

All 105 cases were mucous extravasation cysts. No true mucous retention cyst was found in the present study. The cases were broadly divided into two groups: Group I (without PSM-like changes) and Group II (with PSM-like changes). There were 74 cases which showed a cyst-like space surrounded by compressed granulation tissue including proliferating fibroblasts, capillaries and histiocytes. The cavity was filled entirely or at least partially with mucin and contained abundant mucinophages [Figure 2a-c]. Additional uncommon features were multiple cyst (1 case), giant cell reaction (1 case) and calcification within the cyst cavity (1 case) [Figure 3a-d].

Thirty-one cases (29.5%) showed PSM-like changes in different stages of lesion development [Figure 4]. The early

lesions exhibited marked cellularity with a less organized arrangement, as the lesions matured cellularity decreased and late lesions exhibited hyalinization. The hyaline membrane did not show PAS positivity [Figure 5].

There was no statistically significant difference seen in age, gender, site and laterality ($P > 0.05$). The size of mucocoeles that showed PSM-like changes was significantly larger than those that did not show this feature ($P = 0.031$). The detailed results are shown in Table 1.

DISCUSSION

Broadly, salivary gland pathologies are classified into neoplastic and nonneoplastic diseases. The latter poses diagnostic challenges to pathologists owing to their clinical behavior and varied histological features. Thus, understanding the associated pathophysiological features is vital to distinguish between lesions and better insight into the behavior in order to provide nobler therapeutics. The pathogenesis of oral mucocoeles has been ascribed to the damage of excretory ducts of minor salivary glands following traumatic injuries (including para-oral habits such as lip and cheek biting) which leads to extravasation of mucin into the stroma triggering an inflammatory reaction. Alternatively, it was suggested that mucous extravasation may arise from the traumatic destruction of a large amount of glandular acini followed by continuous secretion from the remaining acini and pooling of mucin.^[12] However, the exact explanation of pathogenesis of mucocoeles remains inchoate.

The mean age of oral mucocoeles in the present retrospective

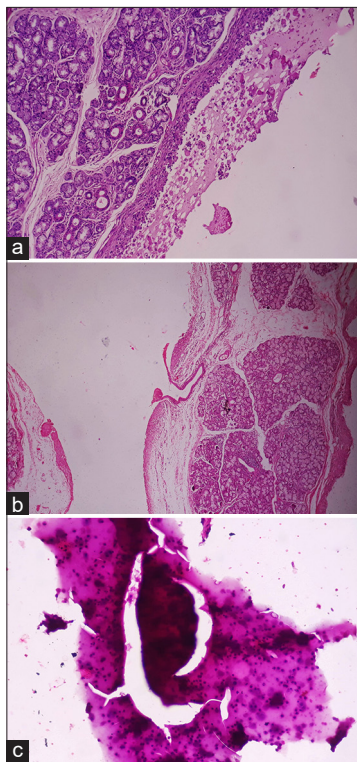


Figure 2: Photomicrograph of H&E sections showing (a) a part of mucous extravasation cyst composed of compressed connective tissue cyst wall, mucin in cavity with abundant mucinophages (right) and minor salivary gland acini (left); (b) lobules of minor salivary gland acini and ruptured duct opening into the cavity ($\times 40$) and (c) imprint cytology showing multiple mucinophages in mucinous background

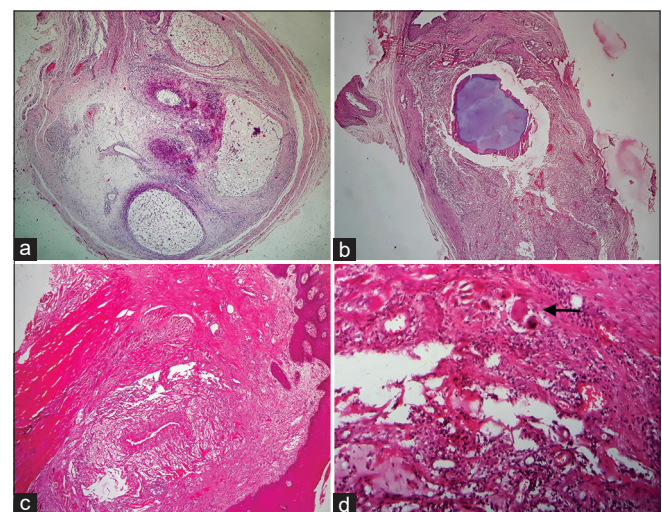


Figure 3: Photomicrograph of H&E sections showing (a) multiple cystic spaces filled with mucin; (b) calcification within the cyst cavity; (c) subepithelial mucous extravasation cyst with a giant cell reaction ($\times 40$) and (d) giant cells at higher magnification ($\times 100$)

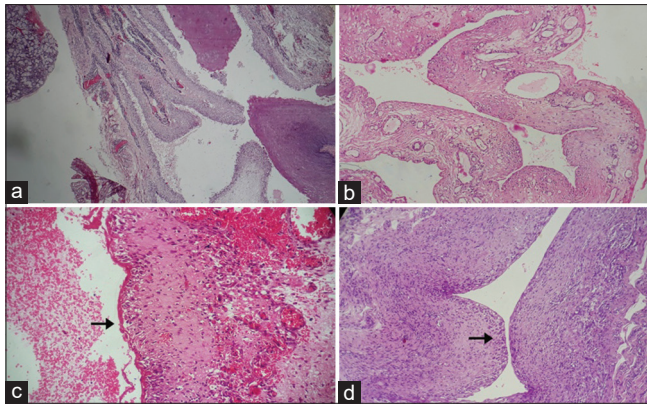


Figure 4: Photomicrograph of H&E sections early to late stages in development of papillary synovial metaplasia (a-c), the late lesions show hyalinization of the membrane and (d) palisading arrange of cells perpendicular to the surface

Table 1: A comparison of parameters between Group I and Group II ($P < 0.05$ is considered as statistically significant)

Parameter	Total (n=105)	P
Age (years)	Overall - 25.8±11.653 Group I - 25.92±11.216 Group II - 25.58±12.829	0.893
Gender	Overall: Male:female - 75:30 (2.5:1) Group I: Male:female - 51:23 (1.64:1) Group II: Male:female - 24:7 (3.43:1)	0.379
Size (cm)	Overall - 1.298±0.79 Group I - 1.173±0.686 Group II - 1.597±0.96	0.031*
Laterality	Overall: Left - 58; right - 43, midline - 4 Group I: Left - 39; right - 32, midline - 3 Group II: Left - 19; right - 11, midline - 1	0.722

* $P < 0.05$ is considered as statistically significant

analysis of 105 cases was 25.82 ± 11.65 years, and the highest percentage was seen in the third decade. This mean age is in concordance with the previous studies despite discordance in the number of cases.^[1,6,11,13] The lowest mean age of 11.18 years has been reported by Shetty *et al.*^[14] and highest (31.9 years) by Re Cecconi *et al.*^[4] No statistical difference was found among two groups, depicting that PSM-like changes are not related to the age of the patient.

Regarding the size of the lesion, the overall mean size of oral mucocoeles in the present review was 1.298 ± 0.79 cm which is slightly higher the mean reported before.^[6,11,15] We further compared the average size in cases showing PSM-like changes (Group II) and cases which did not show this feature (Group I). The size was significantly larger in Group II (1.597 ± 0.96 cm) as compared to Group I (1.173 ± 0.686 cm). Synovial metaplastic changes have been ascribed to gliding forces around tendon implants, further papillary changes were seen around the textured breast implants.^[2,16] The authors opined that gliding action may stimulate PSM-like changes in mucocoeles. The larger size of mucocoeles might allow for relatively greater frictional

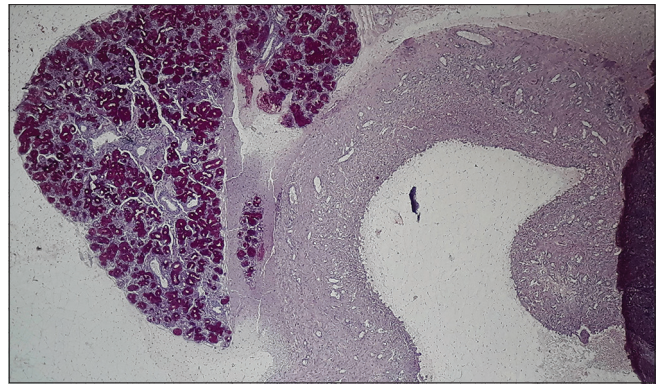


Figure 5: Photomicrograph of periodic acid-Schiff-stained section showing negative staining in membrane (the minor salivary glands acted as positive internal control)

forces, while mucin being the lubricant. The frictional activity along the constant insult to the mucosa by functional and parafunctional habits could act as a stimulus and cause reactionary changes including PSM-like alterations.

A definite male predilection was noted in the present study akin to previous literature,^[1,13] while Chi *et al.*^[11] and Pouloupoulos *et al.*^[15] found a weaker male predominance. Incongruity to this, Hayashida *et al.* reported that females were affected more commonly than males.^[17] A male predominance in young individuals could be attributed to the fact that males are relatively more engaged in outdoor activities and sports, which could be a common source of injuries to the face. Psychological stress and anxiety could be other adjuvant factors that would lead to lip-biting habit and thereby increase the possibility of developing mucocoeles.

In our present study, all mucocoeles were found to be of extravasation type which is consistent with the published literature.^[1,3,6] Interestingly, no cases of mucous retention cyst were found in the present report. Undisputedly, lower lip was the most commonly affected site in our study which is in accordance with the previously published data.^[1,4,6,11,14,15,17] A total of 91 cases (86.77%) occurred on the lower lip and 1 case (0.95%) on the upper lip. It is interesting to note that majority of the cases affected the lip/labial mucosa and most of them were associated with lip-biting habit (36.9%). It is striking that most cases affected the left side (55.2%). It can be argued that psychology could play a vital role in the etiopathogenesis of this lesion, reasoning that people with right-hand dexterity have a subconscious habit of biting their left side of the lip relatively more frequently than the right side as also seen in toothbrushing habit where left side of the dentition is more severely affected in right-handed people and vice versa.

The literature illustrates numerous variants of mucocoeles, including superficial mucocoeles, mucocoeles with

myxoglobulosis and mucoceles with papillary synovial hyperplasia. In the present study of 105 cases, we studied the incidence of these features. PSM-like changes were noted in 31 cases. Many authors have reported not finding these changes in their case studies and case series. Apart from this, we also encountered a case with multiple cysts, another case with giant cell reaction and a single case with calcifications within the cystic cavity. Conceição *et al.* reported giant cell reaction in the cyst wall of mucoceles of a single case which appears different from our cases.^[6] It was noted that in the present case, the giant cell reaction was seen more peripherally and deeper, but irrespective of location, we agree that these foreign body-type giant cells form in reaction to the spilled mucin. These unusual variants are rare in occurrence and their mention in the literature is even scarce. No cases were detected with myxoglobulosis changes, clear cell changes or superficial mucoceles.

Seventy-four out of 105 cases exhibited cyst-like cavity surrounded by granulation tissue including proliferating fibroblasts, histiocytes and capillaries. The cavity was filled with mucin partially or completely and revealed mucinophages in the adjacent stroma. Fascinatingly, 31 cases (29.5%) presented with PSM-like features as opposed to Chi *et al.* who in their review found only 2 cases (0.1%).^[11] De Brito Monterio *et al.*, on the other hand, detected PSM-like features in 54 (8.09%) cases.^[3] In the present study, these changes were confirmed by the presence of villous folds or papillary projections with marked cellularity, palisading arrangement of cells and presence of membrane. All cases displayed these features at some stage of development. Chi *et al.* presented a detailed review of PSM-like changes in mucoceles, Ide *et al.* however argued regarding the nomenclature and pathogenesis of such changes.^[2,18] The latter was of the opinion that PSM-like features are a continuum of spectrum of changes in the regenerative process. They believed that myxoglobulosis and PSM-like changes are closely related phenomena. We support the idea put forward by Chi *et al.*,^[2] as no single case of myxoglobulosis was noted, yet PSM-like changes were explained in 31 good numbers. It is vital to recognize this histopathological feature and differentiate it from other more morbid pathologies and avert misdiagnosis.

CONCLUSION

Considerable variations exist in the prevalence of uncommon histopathological features in mucoceles. In the present study of 105 cases, PSM was observed in 31 (29.5%) cases, depicting that such features are more common than previously thought. Although these histological features bear little to no significance in the clinical presentation of

these cases, in few cases these changes may be conspicuous enough to cause diagnostic difficulties. Knowledge of such histopathological variations is, therefore, crucial.

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Conflicts of interest

There are no conflicts of interest.

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