Invited Review

Diagnostic challenges of superficial mucoceles: An update

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Abstract

A superficial mucocele is a unique variant of a mucocele of the oral cavity that was described by Eveson for the first time in 1988. It occurs due to subepithelial extravasation of sialomucin at the epithelial–connective tissue interface and is related to damage of the minor salivary gland ducts. Clinically, they appear as small, asymptomatic, clear, tense vesicles with a predilection for the soft palate, retromolar pads, and posterior buccal mucosa. They are reported to occur more frequently in women than in men. Before Eveson endeavoured to describe these rather peculiar lesions, they were often misdiagnosed as vesiculobullous lesions such as bullous lichen planus, mucous membrane pemphigoid, and the like. It is incumbent on the present-day pathologist to be cognizant of the presence of these entities as it could present a formidable diagnostic challenge otherwise. This review gives an updated account on the etiology, prevalence, clinical features, differential diagnosis, and management of superficial mucoceles.

Keywords: Bullous lichen planus, differential diagnosis, mucocele variants, mucous membrane pemphigoid, recurrent oral ulcers, superficial mucocele

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INTRODUCTION

Mucoceles are relatively common, benign lesions of the oral region that ensue from minor trauma causing lacerations of the excretory ducts and subsequent discharge of saliva into the surrounding tissues. These mucus extravasation phenomena are merely surrounding tissue responses to the spilled mucin, which eventually get walled off by granulation tissues. Hence, there is no true epithelial lining, unlike the mucus retention cysts, which occur within the salivary gland ducts and are surrounded by the ductal epithelium.[1] An intriguing and unique variant of the mucus extravasation phenomena was reported by Eveson in 1988, which he subsequently christened as the superficial mucocele.[2] This peculiar type of mucocele occurs immediately below the epithelium, causing a blister-like appearance on the mucosal surface. Although superficial mucoceles exhibit distinctive clinical and histopathologic features, they can cause diagnostic problems if present amidst an existing mucosal pathology or if the diagnosing clinician or the pathologist is ignorant of their existence.[2,3] This article gives a brief update on the prevalence, etiopathogenesis, clinical features, and management of the superficial mucocele with a brief note on the diagnostic challenges that it may pose.

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Prevalence

Until Eveson's report in 1988, followed by Jensen's additional re-affirmation in 1990, superficial mucoceles

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were often misdiagnosed as vesiculobullous lesions such as pemphigoid, bullous lichen planus, or herpes.[2,3] As superficial mucoceles often resolve spontaneously or cause little inconvenience, the affected patients may not seek treatment, and hence, the lesions do not get biopsied and submitted for histopathological examination. It is believed that for these propounded reasons, the true prevalence of superficial mucoceles could be underreported[4]. In one of the largest case series of oral mucoceles, Chi *et al.* reported measly three cases (0.2%) of superficial mucoceles that fulfilled the clinical and histopathological criteria among a cohort of 1824 oral mucoceles.[4] In a multi-centric study of 1901 mucocele cases from Brazil, only a meager 0.5% fulfilled the clinical and histopathological criteria for superficial mucoceles.[5] The relative incidence and distribution of mucous extravasation phenomena or mucoceles were described in another retrospective Brazilian study which examined 719 oral mucoceles over a 43-year period. However, although the study mentions the superficial sub-type, it does not specifically state the prevalence of this entity.[6]

According to the compiled data from erstwhile reports, superficial mucoceles most commonly were seen in women aged 30 years and above and the predilected sites are the soft palate, retromolar pad, buccal mucosa, lower labial mucosa, and floor of mouth.[2-4,7-10]

Etiopathogenesis

In general, the most common etiology implicated in the development of mucoceles is trauma. However, Demarosi F *et al.*, 2007, deem the traumatic etiology unlikely in the case of superficial mucoceles based on the sites of predilection which are not exposed to trauma, and therefore, the traumatic mechanism of conventional mucoceles seems unlikely in superficial mucoceles.[11] However, minor mechanical trauma caused during the mastication of hard food substances cannot be ignored. Although the etiopathogenesis of these distinct entities is still unclear, it has been suggested that superficial mucoceles could be formed from ductal rupture and spillage of sialomucin into the surrounding tissues, secondary to increased pressure caused by the mucous plugs within the squamous-cell-lined portion of the excretory duct.[12] However, some authors claim that the lesion is intra-epithelial rather than sub-epithelial and therefore may be caused by local mucosal irritation. Several trigger factors for the irritation have been proffered, such as smoking, using alcoholic mouth rinses, and tartar control toothpastes.[13] Interestingly, Eveson had noticed partial epithelial regeneration across the floor of the superficial mucocele in most of his cases, which he reported could give a pseudo-epithelial appearance if the regeneration were to be complete and around the lesion,[2] an observation which disputes the true intra-epithelial nature of the vesicles. The intra-epithelial appearance of these lesions could be due to a 3D effect, with the mucous material concomitantly seeping its way through the surface epithelium at a superficial level and extending beneath the basement membrane at a deeper level and separating the overlying surface epithelium in the process.[8]

Clinical features

Superficial mucoceles present clinically as small, translucent, tense vesicles in the oral mucosa and could be either single or at times multiple [Figure 1]. Some patients relate the development of the lesions to mealtimes.[14] These short-lived vesicles rupture spontaneously and leave shallow eroded ulcers, which tend to cause discomfort to the patients more often than not. Although these ulcers heal rapidly within a couple of days, in some cases, there could be persistent recurrence in the same region for many years,[8] in which case, patients may complain of small recurrent ulcers that appear every a few days, which heal in a day or two. Some patients may experience the appearance of the vesicles at mealtimes for obvious reasons.[2] The sites for predilection are the areas where minor salivary glands are present and hence include the soft and hard palate, labial mucosa, buccal mucosa, lingual mucosa, and floor of the mouth.[15]

Due to the vesicular clinical presentation of superficial mucoceles, they often pose diagnostic challenges and tend to be misdiagnosed as mucocutaneous lesions such as bullous lichen planus, pemphigus, and mucous membrane pemphigoid, or herpetic lesions.[2,3,5,16] However, the lesions in vesiculobullous disorders tend to be larger, more fragile, and opaquer than superficial mucoceles and are often associated with epithelial desquamation

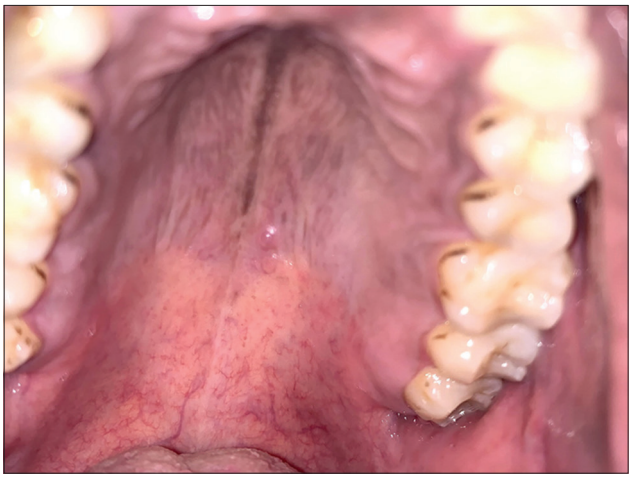

Figure 1: Clinical intraoral picture showing two dome-shaped vesicles (3 × 3 mm) along the palatal midline

clinically and deposits of immunoglobulins on direct immunofluorescence. These features are not appreciated in superficial mucoceles.[17,18] Table 1 depicts the various clinical features of the conventional mucous extravasation phenomenon and superficial mucoceles.

Differential diagnosis

Differential diagnoses of superficial mucoceles would include a myriad of conditions, and among them, vesicular lesions such as bullous lichen planus, pemphigus, mucous membrane pemphigoid, recurrent herpes, and recurrent aphthous stomatitis would top the list.[2,19] Other lesions that could be considered in the clinical differential diagnoses are lymphangioma, fibroma, lipoma, suppurative stomatitis glandularis, benign and malignant salivary gland tumours, multiple hamartoma syndrome associated fibroepithelial hyperplasia, and multiple endocrine neoplasia type 2 B-associated neuromas.[19] To aid the attending pathologist, a detailed clinical description and lesional behaviour of any suspected superficial mucocele should be submitted with the surgical specimen. Diagnostic difficulties may be encountered clinically when superficial mucoceles appear simultaneously with a mucosal disorder or when the reporting pathologist does not identify the unique entity histopathologically.

Histopathology

Histologically, there is a dome-shaped cavity, caused by the spillage and accumulation of sialomucin, in the superficial connective tissue. The resultant effect is the formation of a cleft at the interface of the underlying connective tissue and the overlying mucosal epithelium [Figure 2a]. The epithelium forms the roof of the vesicle and appears normal albeit attenuated in most instances.[2,7,13] The amorphous mucin-filled cavity is well defined, and epithelial regeneration across the floor is a common finding [Figures 2b and c]. If the epithelial regeneration is extensive across the vesicle, then a pseudo-epithelial appearance is apparent. The cavity itself may be usually strewn with neutrophils amidst the mucous content, and underneath the floor of the cavity in the sub-epithelial connective tissue, mild inflammatory cell infiltrates may be appreciated. The presence of sialomucin within the cavity is diagnostic, and an accessory salivary gland or duct in the vicinity of the cavity sways favourably towards the diagnosis of superficial mucoceles.[2,3,7]

Association with other conditions

The concomitant occurrence of superficial mucoceles with oral lichen planus (OLP),[2,3,20,21] lichenoid reactions of chronic graft versus host disease (GVHD),[10,18,22,23] allergic stomatitis,[12] mycoplasma-induced mucositis,[24] and radiation-induced mucositis[25] has been reported by several authors. Among these reports, the most commonly associated oral disease is OLP, the erosive type

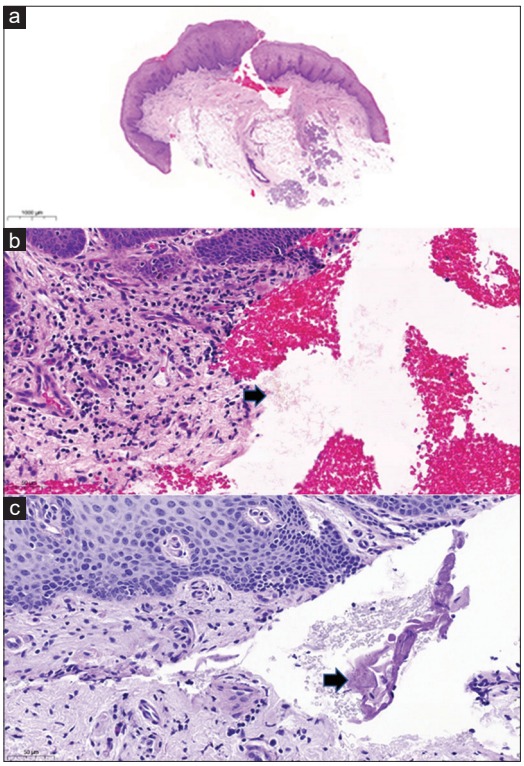

Figure 2: (a) H & E section showing an area of sub-epithelial cleft containing extravasated mucin and haemorrhage (b) Extravasated mucin (black arrow) and hemorrhage in a higher magnification view (c) Extravasated mucin (black arrow) stained positively with Periodic acid Schiff (PAS) stain after diastase digestion

Table 1: Clinical features of superficial mucocele and conventional mucous extravasation phenomenon (mucocele)

Clinical features	Superficial mucocele	Conventional mucocele
Gender Predilection	Older middle-aged females	Children and young adults
Site Predilection	Soft palate, retromolar pad, buccal mucosa, lower labial mucosa, and floor of mouth	Lower lip, floor of mouth (ranulas), anterior ventral tongue (from the glands of Blandin-Nuhn), buccal mucosa, palate, and retromolar pad
Size	1 to 4 mm	1 or 2 mm to several centimetres
Appearance	Vesicles or blisters	Dome-shaped swellings
Colour	Translucent	Bluish or clear. Deeper mucoceles may be normal in colour.
Consistency	Tense	Fluctuant, firm
Location	Intra/subepithelial	Submucosal
Association with Muco-cutaneous Disorders	Yes	No

in particular. Some investigators have hypothesized that the continuous erosion and re-epithelialization seen in erosive lichen planus-affected oral mucosa could facilitate the rupture of minor salivary gland ducts, resulting in the mucus build-up below the epithelium. Similarly, the etiopathogenesis of recurrent mucoceles may also be influenced by inflammation since lymphocytic infiltrations can block the ducts of the accessory glands, causing them to become disrupted and extravasate mucus beneath the epithelium.[7]

Multiple superficial oral mucoceles on the labial mucosa after Mycoplasma pneumoniae mucositis were observed in a child.[24] A retrospective study, which examined the clinical, etiologic, and histologic features of Stevens–Johnson syndrome in a child, reported the development of superficial mucoceles after drug-induced Steven–Johnson syndrome.[26] Many cases of superficial mucoceles have been observed in other inflammatory conditions, such as allergic stomatitis.[12] There have been speculations that severe inflammation brought on by lichenoid, infectious, or inflammatory aetiologies may lead to disruption of the ductal epithelia of minor salivary glands and mucin extravasation. In these instances, superficial mucoceles can mimic persistent or recurrent stomatitis and lead to erroneous diagnosis.[24] The aetiopathogenesis of this occurrence has been proposed to be the result of the lichenoid inflammation damaging the salivary gland ducts by causing either blockage or rupture.[7,10,20]

Complications following oral cancer radiotherapy have been studied extensively over the years, and among them, the most commonly reported ones are oral mucositis, hyposalivation, osteoradionecrosis, oral and peri-oral fibrosis, oral infections, dental caries, and sensory and taste disturbances.[25,27] To the list of complications, the occurrence of superficial mucoceles in oral cancer patients who underwent radiation therapy was reported by some authors who concluded that the occurrence of superficial mucoceles may be regarded as an acute oral toxicity of head and neck radiotherapy.[28] Keshet *et al.* observed similar superficial mucoceles in patients undergoing radiotherapy with concomitant cisplatin therapy.[29] They opined that the concomitant radiotherapy and cisplatin administration may possibly cause damage to the minor salivary gland ducts, which in turn cause mucin leakage into the surrounding soft tissue. They also proposed another possible underlying mechanism, which involves the functional damage of aquaporins (AQPs). AQPs are proteins that transport water and are expressed at the plasma membranes in epithelial, endothelial, and other cell types as well as in salivary glands cells. Experimental research has shown that cisplatin can significantly reduce the expression of membrane AQPs in the renal cells of rats and together with the radiation-induced damage of minor salivary gland tissues and their AQPs may result in superficial mucoceles.[30,31]

Management

The transitory nature of superficial mucoceles allows them to elude biopsies in the clinical setting. Unless they are associated with another condition such as mucous membrane pemphigoid or bullous lichen planus, they are usually not biopsied.[27] Across the existing literature, no effective treatment has been provided.[8] Reassurance and periodic follow-up are the primary management protocols for asymptomatic superficial mucoceles.[32] However, when persistent functional impairment or irritation is present, the causative minor gland may need to be removed. The gland can be removed by conservative surgical excision,[2,33] laser vaporisation with Nd: YAG lasers,[9,20] or cryosurgery.[34] Concerns regarding scar and tissue deformation following surgical management of multiple lesions has been raised.[20] However, Jinbu *et al.* reported that laser vaporisation for recurrent multiple superficial mucocele treatment showed no such complications.[9]

CONCLUSION

It is indeed rather intriguing that although 35 years have passed since Eveson's seminal description of the superficial mucoceles, diagnosis of this innocuous lesion still remains a challenge for a sizable number of dental practitioners. The sheer lack of knowledge of its existence has led to erroneous diagnosis of the superficial mucocele as sub-epithelial vesiculating disorders like mucous membrane pemphigoid or bullous lichen planus often compelled by misleading clinical presentation. The transient nature of superficial mucoceles often quickly leads to their rupture, whereby they appear as ulcerative lesions. This enables them to evade detection by the clinician and often go undiagnosed or misdiagnosed on patients exhibiting mucositis in adjacent areas. An accurate understanding of these often self-limiting and transitory lesions is mandatory in ensuring an appropriate patient treatment protocol. Hence, it is also pivotal in not only preventing misdiagnosis of more sinister vesiculobullous diseases but also avoiding invasive biopsies, especially in medically compromised patients, which can have a significantly negative impact on the quality of their lives.

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The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

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