CASE REPORT

Clear cell change in a lower lip mucocele

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ABSTRACT

Oral mucocele is a common reactive lesion of the oral mucosa, which microscopically exhibits mucus extravasation surrounded by a wall of granulation tissue containing abundant foamy macrophages. Unusual variants, such as superficial mucoceles, mucoceles with myxoglobulosis-like change and mucoceles with synovial metaplasia-like change have been reported. We report a 74-year-old man who presented an asymptomatic translucent swelling on the lower labial mucosa diagnosed as mucocele showing a macrophage proliferation with extensive clear cytoplasmic vacuolation and signet-ring formation. This unusual presentation expands the microscopic spectrum of the oral mucoceles and can eventually lead to differential diagnosis with primary or metastatic clear cell neoplasms. In these cases, relevant clinical information, histochemistry and especially immunohistochemistry, are helpful for arriving at an accurate diagnosis.

Key words: Clear cell change, immunohistochemistry, lip, mucocele, signet-ring cell change

INTRODUCTION

Most oral mucoceles tend to occur in children or young adults, with preferential affectation of the lower lip. The typical microscopic appearance includes mucus extravasation surrounded by a wall of granulation tissue containing abundant foamy macrophages.[1] Unusual variants, such as superficial mucoceles, mucoceles with myxoglobulosis-like change and mucoceles with papillary synovial metaplasia-like change, have been reported.[2,3] Recently, we have seen an unusual presentation of oral mucocele being exclusively composed by macrophages showing extensive clear cytoplasmic and signet-ring cell (SRC) changes. The current case can potentially lead to diagnostic difficulties with clear cell and/or SRC lesions of the oral mucosa such as salivary gland or metastatic origin neoplasms.

CASE REPORT

A 74-year-old man was referred presenting an asymptomatic nodular lesion on his lower lip with 1 month duration. The clinical diagnosis was oral mucocele. The medical history was noncontributory and the extra-oral examination did not show alterations. Microscopic sections, at lower magnification, showed a dense population of clear cells surrounding an inner cavity [Figure 1a and b], which contained sparse to absent mucoid material. At the periphery, the clear cells displayed irregular infiltration into adjacent minor salivary gland parenchyma as broad sheets and cords, being supported by a dense fibrous stroma. In high-power, the cells showed clear cytoplasmic vacuolation with shrunken, pyknotic peripheral nuclei [Figure 1c] and a SRC appearance, intermingled with a delicate network of small vessels [Figure 1d]. Periodic acid-Schiff and mucicarmine stains revealed focal areas with homogeneous mild positivity, consistent with intracellular mucin [Figure 2a]. Despite these diagnostic approaches, definitive diagnosis still could not be achieved, because both epithelial cells and macrophages may contain cytoplasmic mucin. Therefore, immunohistochemical analysis was indicated, which showed strong positivity for CD68 (KP1) and CD163 [Figure 2b], whereas AE1/AE3 pan-cytokeratin, S100, HMB-45 and CD1a were negative, supporting a macrophage lineage cell. The post-surgical evaluation did not reveal any abnormality and after 3 years of follow-up the patient is well without complications.

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DISCUSSION

Interestingly, unusual mucocele variants have been reported. Superficial mucoceles are solitary or multiple,

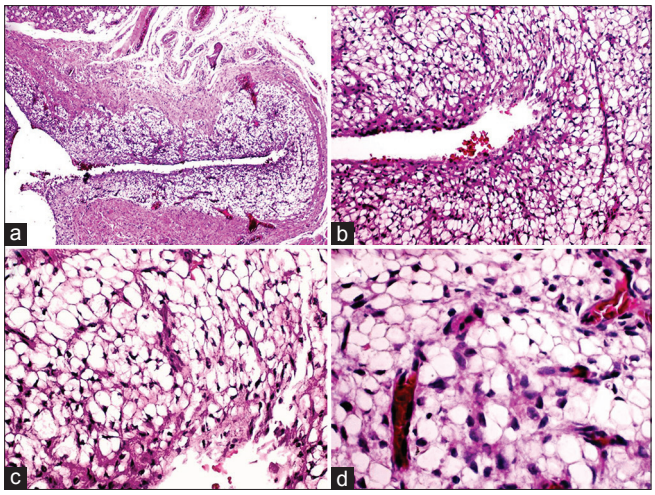

Figure 1: Histopathological features of the oral mucocele showing extensive clear cytoplasmic vacuolation and signet-ring formation (H&E stain). Notice a dense population of clear cells surrounding a central cavity (a, ×50; b, ×200). In high-power view (×400), observe the clear cytoplasmic vacuolation (c) and signet-ring cell change surrounded by a delicate capillary network (d)

which microscopically show mucus extravasation at the epithelial-connective tissue interface.[1] Myxoglobulosis-like change have been reported in some oral mucoceles, in which globular hyalinized structures interspersed with mucin and mucin-laden macrophages are present into the lumen or in the extraluminal connective tissue.[2] Another unusual pattern characterized by a metaplastic transformation from granulation tissue that circumscribes the mucin pool to papillary folds exhibiting in their surface synovial-like changes has also been described.[1] Myxoglobulosis-like and papillary synovial metaplasia-like changes appear to represent incidental findings among oral mucoceles and similar with the current case, the clinical presentation for these variants did not differ significantly from the common variant of oral mucoceles.

As above commented, mucus extravasation surrounded by abundant foamy macrophages is the typical microscopic appearance of the oral mucocele, being that rare variants have been reported. Differently, the current case displayed numerous macrophages with extensive clear cytoplasmic vacuolation and SRC configuration and exhibited a diffuse distribution pattern at the peripheral areas, prompting initially a difficult differential diagnosis with clear cell/SRC neoplasms. Accordingly, there are some studies indicating that pale foamy macrophage aggregates can mimic SRC adenocarcinoma[4] and metastatic clear cell renal cell carcinoma.[5]

Differential diagnosis of tumors with a predominant clear cell and/or SRC components in the head and neck region can be challenging. Usually, clear cell/SRC change results from fixation artifacts, intracellular storage of glycogen, mucin or lipid, or due to paucity of organelles.[6] The differential diagnosis of clear cell lesions of the oral mucosa includes

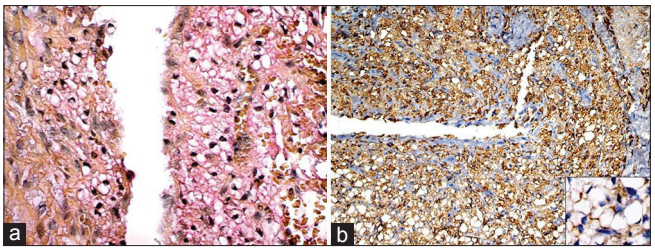

Figure 2: Sialomucin content is demonstrated by mucicarmine staining (a, ×400). By immunohistochemistry, a strong CD68 expression, as well as CD163 positivity (inset), supported a macrophage lineage cells (b, ×200)

salivary gland, sebaceous gland, melanocytic and metastatic tumors.[6] Although most exhibit distinctive microscopic characteristics, histochemistry and immunohistochemistry can be required as well as relevant clinical information in order to achieve the correct diagnosis.

Mucocele with clear cell features as the presented here should be distinguished from clear cell variant of salivary gland tumors such as myoepithelioma, oncocytoma, mucoepidermoid carcinoma, myoepithelial carcinoma, acinic cell carcinoma and clear cell carcinoma, not otherwise specified. The malignant salivary gland tumors exhibit the propensity for regional or distant metastasis and low recurrence.[6,7] In addition, SRC adenocarcinoma of the minor salivary glands is other extremely rare neoplasm, which typically exhibit invasive growth pattern. By immunohistochemistry, all these salivary gland tumors are cytokeratin positive while that mucoceles are uniformly negative.[7] Moreover, it should be noted that SRC morphology is not always a sign of malignancy. In the oral cavity, recently it has been described an unusual lesion affecting the minor salivary glands of the lower lip and composed largely of benign epithelial SRCs.[8]

Melanocytic tumors containing clear cells such as balloon cell nevus and balloon cell malignant melanoma usually affect the skin of the head and neck, being rarely found in the oral cavity. Only two intraoral balloon cell nevi, affecting the soft palate and buccal mucosa, have been reported.[9,10] Microscopically, they show densely packed proliferation of cells showing large clear, foamy or fine vacuolated cytoplasm. Nevertheless, different from the current case, occasional pigmentation and/or typical melanocytes can be observed, which helps to establish the diagnosis. Balloon cell change within malignant melanoma is unusual; in these cases, malignancy is supported by cytologic pleomorphism, atypia and mitoses. By immunohistochemistry, balloon melanocytic cells show positivity for melan-A, Human Melanoma Black (HMB)-45 and S-100.[9,10] Melanocytic markers were negative in the current case. On the other hand, although rare, clear cell variant of sebaceous tumors should also be considered; nevertheless, most of them present typical areas containing sebaceous cells, which suggest the diagnosis.[11] In the oral cavity, sebaceous hyperplasia, sebaceous adenoma and

sebaceous carcinoma are found uncommonly and rarely present clear cell differentiation. Moreover, sebaceous cells are cytokeratin positive.[12]

Primary clear cell neoplasms from kidney, prostate, thyroid, small intestine and lung, are also able to metastasize to the oral mucosa.[6] The most common metastatic clear cell tumor to the oral mucosa is renal cell carcinoma.[6] This neoplasm shows an alveolar or solid architecture with varying degrees of cystic change and numerous capillaries and thin-walled blood vessels in the supporting stroma, the cytoplasm of the tumor cells is rich in lipids and glycogen.[6] In the current case, we have found focal subepithelial areas mimicking low-grade clear cell renal cell carcinoma [Figure 1d]. Supporting this view, it has been previously reported that foamy macrophages can mimic metastatic renal cell carcinoma cells.[5]

In summary, clear cell aggregates can lead to confusion and challenge the Pathologist to be able to differentiate a reactive indolent lesion from an aggressive malignant neoplasm. In these cases, the use of CD68, CD163 and AE1/AE3 pan-cytokeratin immunomarkers is a valuable tool to avoid a misdiagnosis and arrive at an accurate diagnosis.

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