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Case Report

Adenosquamous Carcinoma of the Floor of the Mouth Mimicking an Oral Erythroleukoplakia: Case Report and Review of Literature

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Abstract

Adenosquamous carcinoma (ASC) is an uncommon and controversial epithelial neoplasm characterized by simultaneous and distinct areas of squamous cell carcinoma and adenocarcinoma. Only few cases of oral adenosquamous carcinoma have been previously reported in the literature. It has been described as a squamous cell carcinoma subtype with a high infiltrative capacity. The majority of the patients suffer with early recurrence, local and distant metastases, and low survival rate. In this article, a case of ASC which was clinically similar to an oral leukoplakia is reported and the literature is reviewed. We underline the main histological features and the importance of the oral pathologist in the recognition of the squamous cell carcinoma subtypes.

Keywords: Adenocarcinoma; Clear Cell; Early diagnosis; Erythroleukoplakia; Mouth

Introduction

Adenosquamous carcinoma (ASC) is an uncommon tumor in the oral cavity and is histologically characterized by the presence of both glandular and squamous components. Reports of ASC cases arising from oral mucosa stated it as a squamous cells carcinoma variant with adenocarcinoma's features.[1-4]

In the upper aerodigestive tract, ASC frequently affects the supraglotic region of larynx, and the oral cavity, particularly the tongue.[5-6] Although its histogenesis is not completely understood, the tumor probably originates from the basal cells of surface epithelium, which may be capable of divergent differentiation.[2,7] The clinical course of ASC is markedly aggressive, characterized by numerous local recurrences, regional and distant metastases,[5] and low survival rate.[1,6,8,9]

The purpose of the current article was to report a patient which was referred to our Diagnostic Center presenting an oral leukoplakia of the floor of the mouth that was ultimately diagnosed as an adenosquamous carcinoma.

Case Report

A 74-year-old male patient was referred to the Oral Diagnostic Clinic with a history of discomfort due to chronic trauma associated with inadequate inferior denture. His medical history indicated hypertension, adequately controlled with medication (atenolol 25mg once a day). Intraoral examination reveled a grade I denture stomatitis, without clinical signs of chronic trauma. An erythematous elevated lesion with keratotic margins was observed on the floor of the mouth (Figure 1).

Lesion was fibroelastic on palpation, and 2.0 x 1.0

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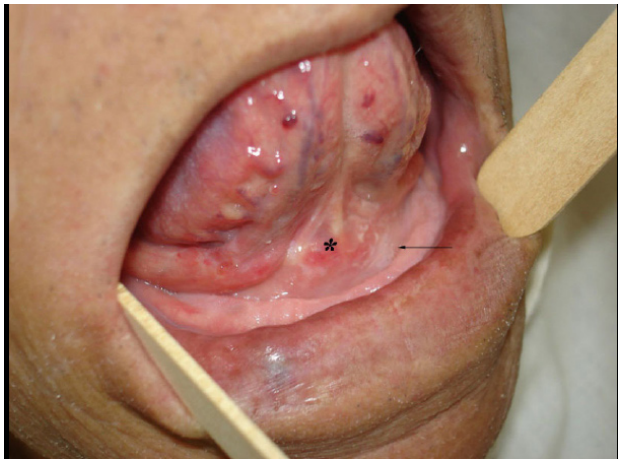

Figure 1 - Erythematous (*) lesion with keratotic white borders (arrow) of the floor of the mouth.

cm in size. Levels of white blood cells, red blood cells and platelets indices were within normal range. Clinical diagnosis of oral leucoplakia or an oral SCC was established, and an incisional biopsy was performed. No palpable node or distant metastases were detected. The Oral Pathology Center diagnosed the lesion as oral adenosquamous carcinoma.

Microscopic Findings

The specimen was paraffin embedded, and haematoxilyn & eosin stained. Microscopic examination of the sections revealed a malignant neoplasm arising from epithelial surface, which exhibited areas of severe epithelial dysplasia with intense nuclear pleomorphism and suprabasal mitotic figures. The subepithelial connective tissue was widely infiltrated by the neoplastic squamous cell forming island and strands with prominent pleomorphism and occasional areas of keratin production (Figures 2-4).

Another area of the tumor showed a glandular component associated with dysplastic ductal epithelium. Ductal structures were commonly present exhibiting columnar mucous cells surrounding inflammatory exsudato or mucinous substance. In addiction, duct-like, reticular, or acantholitic features were visualized in the center of some cancer nests (Figure 4). These two components were found to occur in close proximity becoming confluent in some areas. The minor salivary glands adjacent to the tumor showed chronic inflammatory infiltrate and ectasic ducts, but were not invaded by tumoral cells.

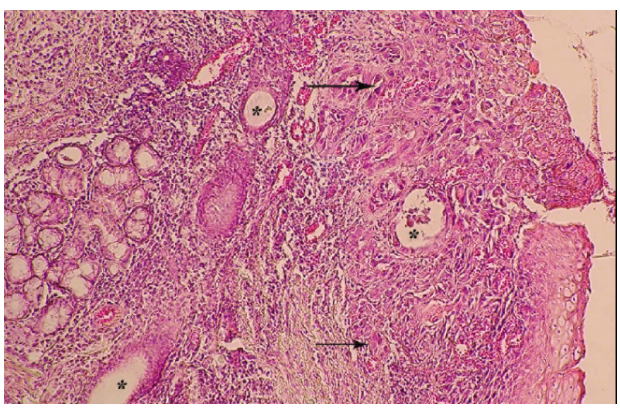

Figure 2 - Superficial aspect of the lesion composed by severe dysplasia and invasive SCC. Arrows show high pleomorphim in the epithelial neoplastic cells and individual keratinization (HE, 100X). The asterisk indicates ductal structures.

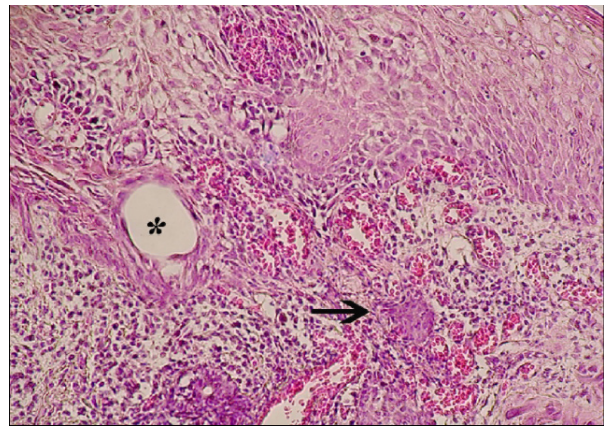

Figure 3 - Higher magnification of the neoplastic islands of invasive SCC (arrow) (HE, 200X). The asterisk indicates ductal structures.

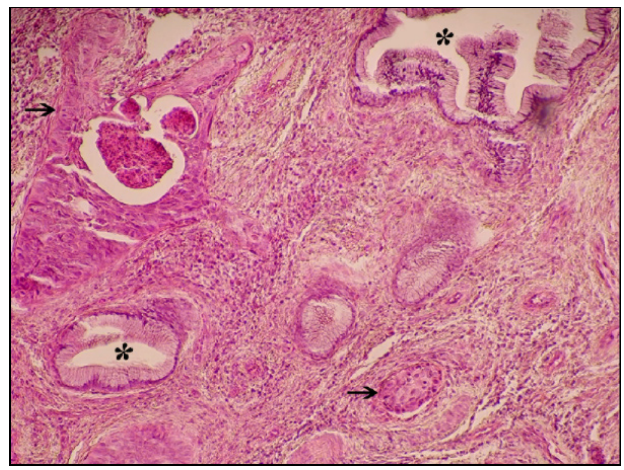

Figure 4 – Submucosal aspect of the lesion exhibiting both epithelial component (arrow) and glandular component (asterisk). Note the central degeneration of the largest squamous island. Ductal structures show columnar cells with mucous aspect (HE, 200X).

Representative paraffin sections were selected in order to perform PAS stained (Figures 5 and 6).

Ductal structures were PAS negative as well as neoplastic superficial epithelium. PAS positive

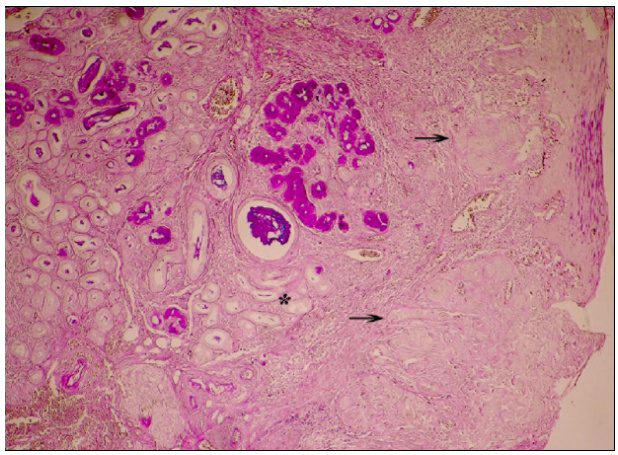

Figure 5 – Photomicrography exhibiting superficial aspect of the lesion composed by severe dysplasia and invasive SCC. Arrows show basement membrane disruption and neoplastic invasion. The asterisk shows PAS negative ductal structures (PAS, 40X).

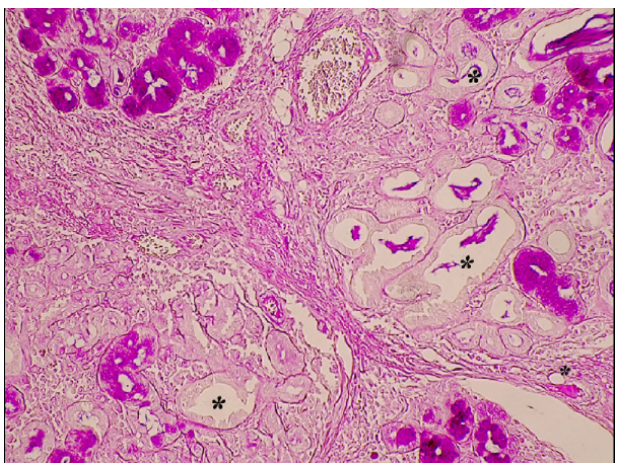

Figure 6 – Higher magnification image shows PAS negative ductal structures (PAS, 100X).

amorphous material could be seen inside the ducts and in some adjacent glandular structures.

Discussion

The first description of ASC occurring in oral mucosa was published in 1968 by Gerughty.[1] Knowledge concerning the rare variants of oral SCC is required to establish the histopathologic diagnosis of adenosquamous carcinoma.[6]

A little more than 50 cases of ASC affecting the head and neck have been reported, confirming the rarity of this tumor. This unusual tumor may occur at many body sites including sun exposed skin. Although, in the head and neck, most cases occur in the larynx and paranasal sinusis.[1,5-7,10-11]

Although uncommon, it is important to note that some clinical features may help with differential diagnosis. A marked gender predication for males seem to occur (3.5:1; male-to-female ratio) including the presented case, and similar to SCC, an age incidence which ranges from 22 to 80 years of age. In the oral cavity, the most common location is the floor of the mouth and the tongue, followed by alveolus, palate and upper lip. The tumor-related symptoms are greatly variable, but pain is a common feature. Approximately 40% of the patients reported pain at the initial consultation, probably because of the tendency of spreading by perineural invasion.[11-17] Odinophagia, otalgia, tongue numbness, bleeding and weight loss were also tumor-related symptoms.[12-26]

To the best of our knowledge, the presented case is the first whose presentation mimics an oral leukoplakia. This finding is not common for glandular neoplasms, and may help with differential diagnosis. The clinical presentation of the previously published ASCs varies from the keratotic ulcer to nodular, exophytic, indurated or undulated masse.[1,5-7,10-11]

The histopathological features of the presented case are according to those described previously. Alos et al. [6] observed severe dysplasia or carcinoma *in situ* of surface mucosa in all 12 head and neck cases of their series, and considered glandular involvement as secondary to tumor infiltration.[17,21] The adenocarcinomatous and squamous components were found to occur in close proximity and become confluent in some areas in all of published works. This may lead to ambiguous histogenesis hypothesis.[4,26] It is essential to note the presence of abundant keratinization in squamous cell components of ASC and sites of regular oral squamous cell carcinoma.[6] The adenocarcinoma component is always composed by ductular structures and variable presence of mucous cells.[7] The precise origin of the neoplasm was unclear once both glandular ducts and surface epithelium had been advocated as a reasonable source of malignancy.[7] Moreover, in the last World Health Organization publication for head and neck tumor classification, ASC was described as originated from surface epithelium.[4,6]

Special staining techniques have been used in order to clarify tumor histogenesis and establish the diagnostic criteria, although inconclusive. Mucicarmin stain is often positive evidencing mucin production in a luminal and intracellular pattern in the adenocarcinoma component. However, this is not a fundamental aspect to

the diagnosis and some tumors may not present it, despite the true neoplastic glanduloductal formation.[6,16,24]

An immunohistochemical study was not performed for the presented case since incisional biopsy collected insufficient material for further experiments. Immunohistochemically, most papers show the glandular differentiated areas are positive for pancytokeratin, epithelial membrane antigen, CK7/8, CAM 5.2 and CEA, and negative for CK20.[6,13,16-17,23-24] Squamous cell component is positive for high molecular weigh cytokeratin (MNF116) and CEA, being negative for CK7/8, CK 20 and low molecular weigh cytokeratin (Cam5.2).[6,13,16-17,23-24] Other significant findings concerned immunpositivity of ASC include p53, Ki67 and β-catenin proteins, which could indicate deregulation of cell cycle, high proliferation index, and loss of cellular adhesion related to acantholytic cells, respectively.[6,22,24] The immunoprofile of ASC, although not specific, may aid differentiation from other neoplasms.[5-6]

Differential diagnosis between mucoepidermoid carcinoma (MEC) and ASC is of major importance because of their distinct biological behavior. The best prognosis of MEC is a fundamental issue to be considered by the pathologist. MEC also displays biphasic morphology, consisting of glandular and epidermoid neoplastic components. High grade MED is composed of intermediate or epidermoid cells but without keratin formation. On the other hand, ASC shows an infiltrative pattern, similar to usual SCCs, with nuclear pleomorphism, high mitotic rate and frequent keratin pearls.[5] In addition, MEC does not show dysplastic changes in the surface epithelium without evidence of carcinoma in situ of the squamous epithelium.

Other differential histopathological diagnoses include carcinomas with adenoid features, including acantholytic squamous cell carcinoma, basaloid squamous cell carcinoma (BSC) and usual SCC. Distinction is mandatory since prognosis of ASC is much more limited.[8-9,21]

ASCs are strongly associated with poor prognosis.[8-9,16] A high metastatic rate (about 80%) and low 5-year survival rate (20-25%) is expected, as well as frequent local recurrences and distant metastases.[1,5,8-9] This aggressive behavior is strongly associated with aneuploidy and high proliferative activity, assessed by immunohistochemical positivity for Ki67.[6]

In the cases of inadequate surgical treatment, locoregional and distant recurrences, as well as spread to cervical lymph nodes, frequently occurs regardless of adjuvant therapy.[17] On the other hand, Yoshimura et al.,[11] reported a better prognosis in 19 Japanese head and neck ASC patients treated similarly to those of Gerughty et al.,[2] and Scully et al.[7] Other prognostic features may be involved besides the treatment protocol.

There is no consensus regarding the treatment of ASC of the head and neck. Surgery alone, as well as the association with radiation therapy and/or chemotherapy has been used in the treatment of these patients, obtaining similar frustrating results. In addition, most authors were unable to find a statistical relationship between biomarkers parameters (CEA, CAM5.2, CK7, CK20, 34BE12, Ki67, p53) and tumor stage or patient outcome in ASCs of their series.[6]

Therefore, there is no consensus about the best radiation and chemotherapy schemes for ASC treatment, difficulting to establish the best treatment modality. Thus, it seems that surgical intervention with radical cervical resection is the treatment of choice, once no improvement of the overall survival rates is observed when radiation therapy and/or chemotherapy are associated with surgery.[5] Further controlled studies should be performed in larger groups of patients with ASC in order to clarify the most effective management strategy.

References

1. Gerughty RM, Hennigar GR, Brown FM. Adenosquamous carcinoma of the nasal, oral, and laryngeal cavities: a clinicopathological survey of ten cases. Cancer 1968;22:1140-55.
2. Sanner JR. Combined adenosquamous carcinoma and ductal adenoma of the hard and soft palate: report of case. J Oral Surg. 1979;37:331-4.
3. Marcucci G, Birman EG, de Araujo VC, de Araujo NS. Adenosquamous carcinoma of the oral cavity: report of two cases. Rev Fac Odontol Sao Jose Dos Campos. 1976;5:87-92.
4. Cardesa A, Zidar N, Alos A. Adenosquamous carcinoma. In: Barnes L, Eveson JW, Reichart P, Sidransky D, editors. Pathology & genetics – head and neck tumors. Lyon: IARC Press; 2005. p.130-1.
5. Keelawat S, Liu CZ, Roehm PC, Barnes L. Adenosquamous carcinoma of the upper aerodigestive tract: a clinicopathologic study of 12 cases and review of the literature. Am J Otolaryngol. 2002;23:160-8.
6. Alos L, Castillo M, Nadal A, Caballero M, Mallofre C, Palacin A, et al. Adenosquamous carcinoma of the head and neck: criteria for diagnosis in a study of 12 cases. Histopathology. 2004;44:570-9.
7. Scully C, Porter SR, Speight PM, Eveson D, Gale D. Adenosquamous carcinoma of the mouth: a rare variant of squamous cell carcinoma. Int J Oral Maxillofac Surg. 1999;28: 125-8.
8. Thompson LDR. Squamous cell carcinoma variants of the head and neck. Curr Diag Pathol. 2003;9:384-96.
9. Cassarino DS, Damian PD, Barr RJ. Cutaneous squamous cell carcinoma: a comprehensive clinicopathologic classification. Part two. J Cutan Pathol. 2006;33:191-206.
10. Martinez-Madrigal F, Baden E, Casiraghi O, Micheau C. Oral and pharyngeal adenosquamous carcinoma: a report of four cases with immunohistochemical studies. Eur Arch Otorhinolaryngol.

1991;248:255-8.

11. Yoshimura Y, Mishima K, Obara S, Yoshimura H, Marayama R. Clinical characteristics of oral adenosquamous carcinoma: report of a case and an analysis of the reported Japanese cases. Oral Oncol. 2003;39:309-15.
12. Siar CH, Ng KH. Adenosquamous carcinoma of the floor of the mouth and lower alveolus: A radiation-induced lesion? Oral Surg Oral Med Oral Pathol. 1987;63:216-20.
13. Napier SS, Gormley JS, Newlands C, Ramsay-Baggs P. Adenosquamous carcinoma: a rare neoplasm with aggressive course. Oral Surg Oral Med Oral Pathol. 1995;79:607-11.
14. Abdelsayed RA, Sangueza OR, MD, Newhouse RE, Singh BS. Adenosquamous carcinoma; a case report with immunohistochemjical evaluation. Oral Surg Oral Med Oral Pathol Oral Radio Endod. 1998;85:173-7.
15. Guerrero J, Alvarez V, Novo O, Garcia A, Romero L, Melchor MA, Ballestin C. Carcinoma adenoescamoso de glandulas salivares menores: exposicion de un caso de localizacion lingual. An Otorrinolaringol Ibero Am. 1995;3:299-309.
16. Izumi K, Nakajima T, Maeda T, Cheng J, Saku T. Adenosquamous carcinoma of the tongue. report of a case with histochemical, immunohistochemical, and ultrastructural study and review of the literature. Oral Surg Oral Med Oral Path Oral Radio Endod. 1998;85:178-84.
17. Sheahan P, Fitzgibbon J, Lee G, O´Leary G. Adenosquamous carcinoma of the tongue in a 22-year-old female: report of a case with immunohistochemistry. Eur Arch Otorhinolaryngol. 2003;206:509-12.
18. Jones AC, Freedman PD, Kerpel SM. Oral adenoid squamous cell carcinoma: a report of three cases and review of the literature. J Oral Maxillofac Surg. 1993;51:676-81.
19. Minic AJ, Stajcic Z. Adenosquamous carcinoma of the inferior turbinate: a cse report. J Oral Maxillofac Surg. 1994;52:764-7.
20. Fujino K, Ito J, Kanaji M, Shiomi Y, Saiga T. Adenosquamous carcinoma of the larynx. Am J Otolaryngol 1995;16:115-8.
21. Abdelsayed RA, Sangueza OP, Newhouse RF, Singh BS. Adenosquamous carcinoma: a case report with immunohistochemical evaluation. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 1998; 85:173-7.
22. Mancusi G, Susani M, Kornfehl J, Girsch W, Kautzky M. Adenosquamous carcinoma of the palate. Laryngorhinootologie. 2002;81:568-72.
23. Driemel O, Braxein K, Pistner H, Kosmehl H. Oral adenoid squamous carcinoma. tumor markers and prognosis. Mund Kiefer GesichtsChir. 2004;8:118-22.
24. Kusafuka K, Ebihara M, Ishiki H, Takizawa Y, Iida Y, Onitsuka T, et al. Primary adenoid squamous cell carcinoma of the oral cavity. Pathol Int. 2006;56:78-83.
25. Zidar N, Gale N, Zupevc A, Dovsak D. Pseudovascular adenoid squamous-cell carcinoma of the oral cavity: a report of two cases. J Clin Pathol. 2006;59:1206-8.
26. González-Vela MC, Val-Bernal JF, Mayorga M, Zaldumbide L, Báscones M. Adenoid squamous cell carcinoma of the larynx: an uncommon histological variant of squamous cell carcinoma: case report. APMIS. 2006;114:470–3.