CASE REPORT

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Diagnostic utility of CD117 in an unusual adenoid cystic carcinoma of the upper lip

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ABSTRACT

Adenoid cystic carcinoma (ACC) is a malignant neoplasm of the salivary gland, of slow evolution but aggressive behavior, which frequently occurs in the palate; however, in the upper lip, where more benign neoplasms are usually found, its presence is scarcely reported. We report the case of a 63-year- old woman, referred for presenting a nodule in the right upper lip, with benign appearance, firm consistency, circumscribed, mobile, painful to palpation, with no determined time of evolution and whose histopathological study showed a proliferation of angular and hyperchromatic cells with scarce cytoplasm, organized in a cribriform pattern and predominantly tubular. An immunohistochemical study was performed, which showed positivity for SMA, p63 and CD117 with a Ki-67 of approximately 10%. These results confirm the diagnosis of ACC with tubular pattern, highlighting the role of CD117 for the differential diagnosis with polymorphous adenocarcinoma. The patient was referred for surgical treatment and radiotherapy, and after one year of follow-up she maintained a good clinical behavior.

Keywords: adenoid cystic carcinoma, CD117, salivary gland neoplasm.

INTRODUCTION

With a reported annual incidence of 3 to 4.5 cases per million population, adenoid cystic carcinoma (ACC) is a rare malignant salivary gland neoplasm that accounts for approximately 1% of all malignant head and neck tumors and about 10% of all salivary gland neoplasms (1). This tumor is frequently located in the minor salivary glands (45-68% of cases), especially in the palate (66%), while it is less frequently observed in the upper lip (5-20%) (2).

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Clinically, ACC presents with ulceration and pain, although with slow growing, where almost half of the affected patients develop distant metastases within the first 5 years from diagnosis, while local recurrences tend to develop even later, even after 8 years post-treatment (1, 2), a characteristic that reveals its aggressive behavior and its description as a high-grade malignant tumor (3). Histopathologically, three histological patterns are described in ACC: cribriform, tubular and solid, which can occur simultaneously in the same tumor. Therefore, it is relevant to determine the predominant pattern for its subsequent grading (3, 4).

We report a clinical case of a patient with ACC located in the upper lip, something extremely uncommon and with special emphasis on the clinical presentation, which at the time of surgery suggested the diagnosis of a benign neoplasm. Moreover, the importance of the use of the immunomarker c-kit or CD117 in the confirmation of the diagnosis is described, which allows to rule out frequent differential diagnoses of this pathology.

CASE PRESENTATION

We present the case of a 63-year-old woman with controlled hypothyroidism, referred to the Maxillofacial Dental Service of Hospital de Los Andes, Chile, due to a nodular enlargement of firm consistency, circumscribed, mobile, painful to palpation, located in the thickness of the upper labial mucosa on the right side, of apparent long standing and slow growth, located in the thickness of the labial mucosa on the right side (Figure 1A). At the time of biopsy, a yellowish lesion was observed, lobulated in its deepest portion, and apparently adherent to adjacent planes (Figures 1B and 1C).

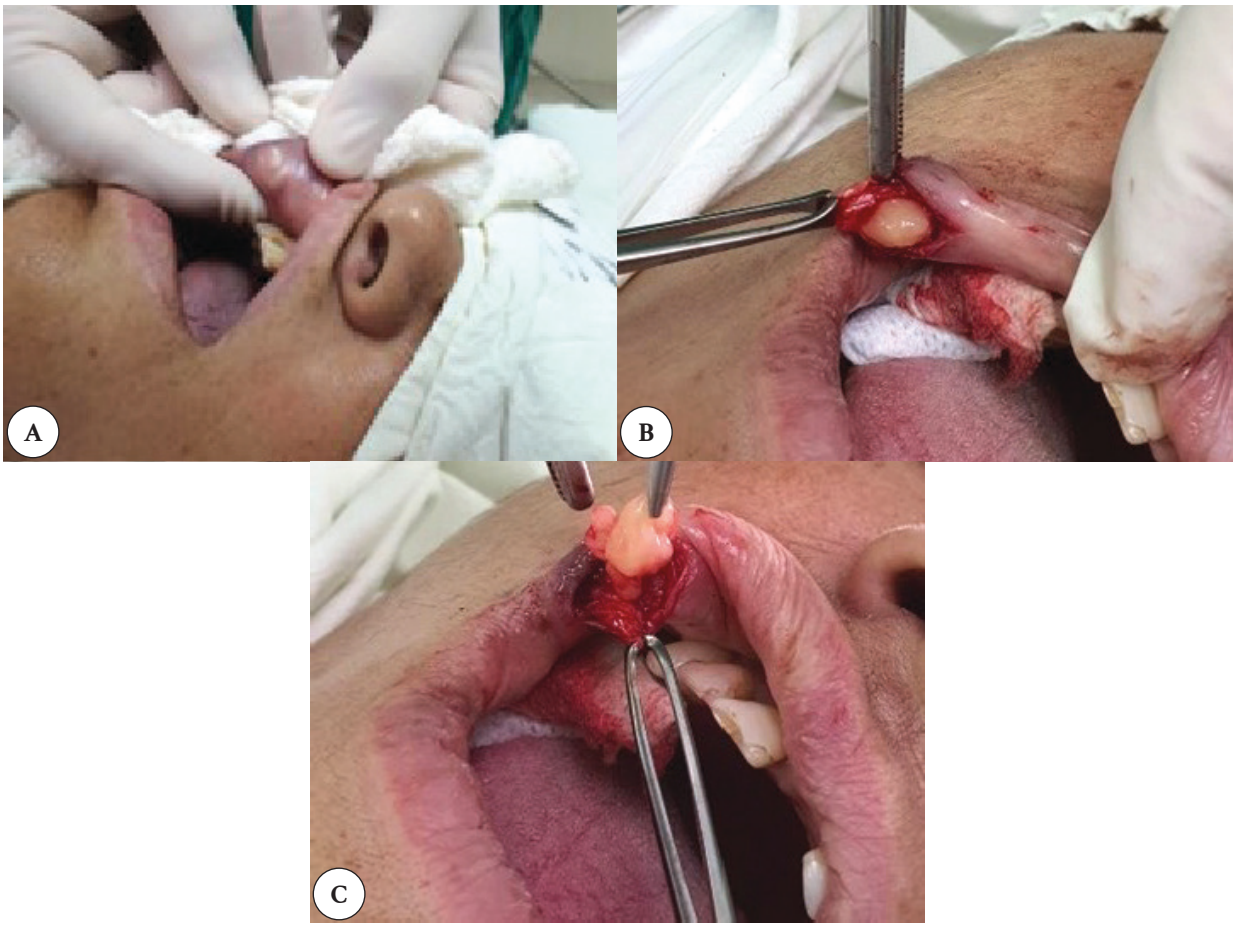

Figure 1. Clinical and surgical aspect of the lesion.
A: Appearance of the lesion before surgery.
B and C: Image of the excisional biopsy of the lesion.

A microscopic analysis performed at the Anatomic Pathology Unit of Hospital San Camilo revealed a partially delimited tumor, in which a proliferation of hyperchromatic and angulated cells with scant cytoplasm stands out, forming multiple microcystic spaces with eosinophilic content of mucinous appearance, organized in a cribriform and predominantly tubular pattern with focal areas of solid islands (Figures 2A and 2B). The stroma is fibrous with few inflammatory cells. No vascular or perineural infiltration is observed. No atypical mitoses or areas of necrosis are identified. Neoplastic proliferation affected all surgical margins. Immunohistochemical staining for CD117, also known as c-kit, was conducted, showing positive cytoplasmic labeling, mainly in the inner cells (Figure 2E). Positive marking is also observed in abluminal cells for p-63 (nuclear) and SMA (cytoplasmic) with increased intensity (Figures 2C and 2D). GFAP immunohistochemical staining was negative and Ki-67 (or cell proliferation index) showed positivity for about 10% of the sample (Figure 2F).

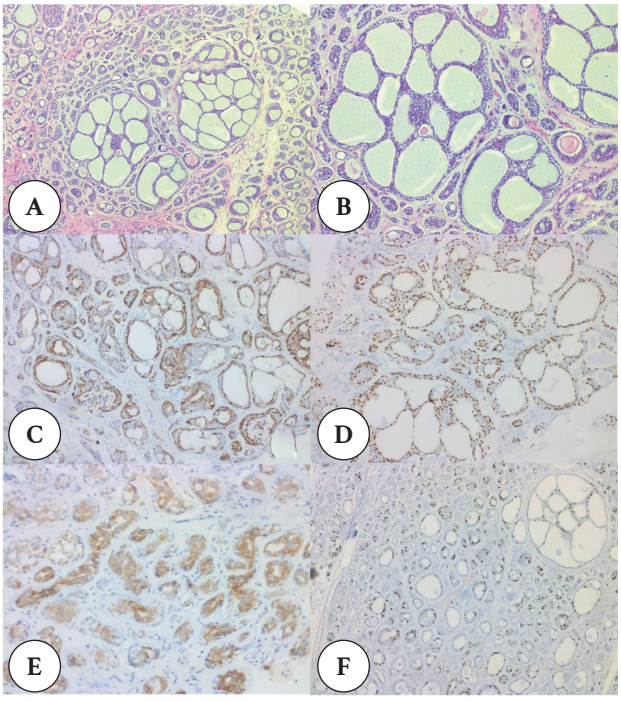

Figure 2. Histopathologic features of the neoplasm. A: Proliferation of tumor cells in a cribriform and tubular pattern. B: Cribriform islands formed by cells of scarce cytoplasm and hyperchromatic nucleus with microcysts of mucinous content. C: Cytoplasmic myoepithelial cells positive for SMA. D: Nuclear positive myoepithelial cells for p63. E: Internal cytoplasmic CD117-positive cells. F: Ki-67 with a rate of 10%.

Finally, a malignant epithelial proliferation compatible with tubular-predominant ACC was diagnosed. The patient was referred to hospital treatment and underwent further surgical treatment, combined with postoperative radiotherapy, showing so far, a good clinical behavior.

DISCUSSION

The value of the present case lies in the importance of establishing differential diagnoses, especially due to its apparent benign clinical appearance, which could suggest diagnoses such as lipoma (5) or some salivary gland neoplasm more frequent in that location, such as pleomorphic adenoma (PA) and canalicular adenoma (CA), whose most common location (in the case of CA) is precisely the upper lip (6). With respect to ACC, approximately only 5% of cases would present in the upper lip (7), while, within malignant tumors affecting the upper lip, ACC accounts for 1.7% of cases (8).

Although histologic appearance is highly suggestive of an ACC, the complement of an appropriate immunohistochemical analysis is relevant, especially to establish prognosis and differentiate from other salivary gland neoplastic entities. It has been reported that immunostaining with CD117 can be useful to differentiate two neoplastic entities, such as ACC and polymorphous adenocarcinoma (PCA), in which their cribriform and tubular patterns can be confused. CD117 shows strong diffuse cytoplasmic reactivity in more than 80% of ACC tumor cells, whereas less than 20% of cells show negative to weak positivity in PCA (8). In our report, the positive immunolabeling for this protein was approximately 90%, which coincides with that described by Mino et al. (9), who observed positive labeling in 89% of tumor cells. Other immunohistochemical stains useful in the diagnosis of ACC include p40 and GFAP, especially when their analysis is combined with p63 immunolabeling (10). In the case presented, immunolabeling was performed for p63, which was positive, while there was no immunolabeling for GFAP, which coincides with what is described in the literature. In this sense, positivity for p63 in abluminal cells and negativity for GFAP are useful to differentiate ACC, especially from PA; and in the case of positive CD117 immunolabeling, this will allow differentiating ACC from PCA (9, 10).

In the upper lip, ACC appeared as a slow-growing nodule that commonly does not appear with significant early symptoms. This not only coincides with what has

been described in the literature, but also reinforces the need for early diagnosis. Due to its slow evolution and apparently benign behavior, the patient's diagnosis is usually delayed (11, 12).

Regarding prognosis, histologic features have been correlated with prognosis with inconsistent results (13). It has been suggested that the solid pattern appears to be more aggressive and may be associated with an adverse clinical course and poor prognosis (14). On the other hand, other studies have not identified any correlation between histological subtype and clinical behavior (15).

Infiltrative growth and perineural invasion present in ACC are other features associated with prognosis, considered as the worst prognosis when they are present (16). This would explain the high risk of recurrence of this neoplasm, which could be interpreted as an incomplete surgical excision or invasion of structures that favor metastatic processes. However, other authors have not identified any correlation between perineural invasion and prognosis (14), which marks a controversy regarding the prognosis of this pathology. In turn, a positive microscopic surgical margin is associated with a worse prognosis (17). Currently, surgical resection of the tumor in combination with adjuvant radiotherapy is practically the most effective method of choice (1, 18), treatment that coincides with what was done in the present case, where good behavior has been observed so far.

It is extremely important to do a permanent follow-up of patients who have suffered from this neoplasm, since ACC is a slow growing but relentless and unpredictable cancer, which favors metastatic evolutionary processes (1). Due to its rarity and lack of understanding of its molecular etiology, there is currently no standard chemotherapy for this neoplasm and many patients suffer from recurrent and/or metastatic disease. Therefore, the development of safe and effective therapies is imperative. In addition to conventional chemotherapies and angiogenesis inhibitors, the emergence of new therapies, such as immunotherapy and those targeting cancer trunks are expected to bring clinical benefits to patients in the future (19). On the other hand, in terms of diagnosis, it is possible to use immunomarkers such as CD117 when the normal morphology is similar to other pathologies (such as PA or PCA) in order to obtain confirmation of the diagnosis of ACC.

CONCLUSIONS

The diagnostic utility of CD117 immunohistochemistry for the differential diagnosis of ACC with PCA and even with PA is good and beneficial, especially in unusual locations such as the minor salivary glands of the upper lip, where benign glandular tumors are more frequent, allowing the establishment of adequate therapeutic protocols that favor the prognosis of patients and their adequate follow-up.

REFERENCES

1. Coca-Pelaz A, Rodrigo JP, Bradley PJ, Vander Poorten V, Triantafyllou A, Hunt JL, et al. Adenoid cystic carcinoma of the head and neck – An update. Oral Oncol [Internet]. 2015; 51(7): 652-661. Available from: https://doi.org/10.1016/j.oraloncology.2015.04.005
2. Dogra BB, Batra G, Wahegaonkar C, Patil B. Adenoid cystic carcinoma of the upper lip: a case report and review of literature. Int J Oral Health Sci [Internet]. 2016; 6(1): 40-43. Available from: https://journals.lww.com/ijoh/fulltext/2016/06010/adenoid_cystic_carcinoma_of_the_upper_lip_a_case.10.aspx
3. Van Weert S, Bloemena E, Van der Waal I, De Bree R, Rietveld DH, Kuik JD, et al. Adenoid cystic carcinoma of the head and neck: a single-center analysis of 105 consecutive cases over a 30-year period. Oral Oncol [Internet]. 2013; 49(8): 824-829. Available from: https://doi.org/10.1016/j.oraloncology.2013.05.004
4. Morita N, Murase T, Ueda K, Nagao T, Kusafuka K, Nakaguro M, et al. Pathological evaluation of tumor grade for salivary adenoid cystic carcinoma: a proposal of an objective grading system. Cancer Sci [Internet]. 2021; 112(3): 1184-1195. Available from: https://doi.org/10.1111%2Fcas.14790
5. Aita TG, Bonardi JP, Stabile GAV, Pereira-Stabile CL, Faverani LP, Hochuli-Vieira E. Lipoma on the lower lip. J Craniofac Surg [Internet]. 2017; 28(8): e750-e751. Available from: https://doi.org/10.1097/scs.0000000000003908
6. Peraza AJ, Wright J, Gómez R. Canalicular adenoma: a systematic review. J Craniomaxillofac Surg [Internet]. 2017; 45(10): 1754-1758. Available from: https://doi.org/10.1016/j.jcms.2017.07.020
7. Waldron CA, El-Mofty SK, Gnepp DR. Tumors of the intraoral minor salivary glands: a demographic and histologic study of 426 cases. Oral Surg Oral Med Oral Pathol [Internet]. 1988; 66(3): 323-333.

Available from: https://doi.org/10.1016/0030-4220(88)90240-x
8. Tariq H, Anjum S, Din HU, Akhtar F. Diagnostic utility of C-kit protein (CD117) expression in differentiating adenoid cystic carcinoma and polymorphous low grade adenocarcinoma. Pak J Med Sci [Internet]. 2017; 33(6): 1376-1380. Available from: https://doi.org/10.12669%2Fpjms.336.13373
9. Mino M, Pilch BZ, Faquin WC. Expression of KIT (CD117) in neoplasms of the head and neck: an ancillary marker for adenoid cystic carcinoma. Mod Pathol [Internet]. 2003; 16(12): 1224-1231. Available from: https://doi.org/10.1097/01.mp.0000096046.42833.c7
10. Atiq A, Mushtaq S, Hassan U, Loya A, Hussain M, Akhter N. Utility of p63 and p40 in distinguishing polymorphous adenocarcinoma and adenoid cystic carcinoma. Asian Pac J Cancer Prev [Internet]. 2019; 20(10): 2917-2921. Available from: https://doi.org/10.31557%2FAPJCP.2019.20.10.2917
11. Huang M, Ma D, Sun K, Yu G, Guo C, Gao F. Factors influencing survival rate in adenoid cystic carcinoma of the salivary glands. Int J Oral Maxillofac Surg [Internet]. 1997; 26(6): 435-439. Available from: https://doi.org/10.1016/s0901-5027(97)80008-2
12. Sanchez-Sanchez M, Infante-Cossio P, Lozano-Rosado R, Gonzalez-Perez LM, Japon-Rodriguez MA, Gonzalez-Padilla JD, et al. Resection of upper lip adenoid cystic carcinoma and reconstruction with reverse Yu flap: report of three cases and a literature review molecular and clinical oncology. Mol Clin Oncol [Internet]. 2017; 6(3): 444-450. Available from: https://doi.org/10.3892/mco.2017.1150
13. Nascimento AG, Amaral AL, Prado LA, Kligerman J, Silveira TR. Adenoid cystic carcinoma of salivary glands. A study of 61 cases with clinicopathologic correlation. Cancer [Internet]. 1986; 57(2): 312-319. Available from: https://doi.org/10.1002/1097-0142(19860115)57:2< 312::AID-CNCR2820570220>3.0.CO;2-A
14. Spiro RH, Huvos AG, Strong EW. Adenoid cystic carcinoma: factors influencing survival. Am J Surg [Internet]. 1979; 138(4): 579-583. Available from: https://doi.org/10.1016/0002-9610(79)90423-9
15. Hemprich A, Schmidseder R. The adenoid cystic carcinoma: special aspects of its growth and therapy. J Craniomaxillofac Surg [Internet]. 1988; 16: 136-139. Available from: https://doi.org/10.1016/S1010-5182(88)80034-9
16. Brown JS. Prognostic factors in oral, oropharyngeal and salivary gland cancer. En: Booth PW, Schendel SA, Hausamen JE, editores. Maxillofacial Surgery. Vol. 1. New York: Churchill Livingstone; 1999. pp. 291-308.
17. Šteiner P, Pavelka J, Vaneček T, Miesbauerová M, Skálová A. Molecular methods for detection of prognostic and predictive markers in diagnosis of adenoid cystic carcinoma of the salivary gland origin. Cesk Patol [Internet]. 2018; 54(3): 132-136. Available from: https://pubmed.ncbi.nlm.nih.gov/30445817/
18. Sahara S, Herzog AE, Nör JE. Systemic therapies for salivary gland adenoid cystic carcinoma. Am J Cancer Res [Internet]. 2021; 11(9): 4092-4110. Available from: https://pubmed.ncbi.nlm.nih.gov/34659878/
19. Luna-Ortiz K, Güemes-Meza A, Villavicencio-Valencia V, Mosqueda-Taylor A. Upper lip malignant neoplasms. A study of 59 cases. Med Oral Patol Oral Cir Bucal [Internet]. 2012; 17(3): e371-e376. Available from: https://doi.org/10.4317%2Fmedoral.17501