



Contents lists available at ScienceDirect

Journal of Oral and Maxillofacial Surgery, Medicine, and Pathology

journal homepage: www.elsevier.com/locate/jomsm

Case report

Salivary duct carcinoma of the palate

Yukiko Kusuyama^{a,b,*}, Noritami Takeuchi^{a,b}, Shino Muraoka^{a,b}, Yasuo Fukuda^c, Yoshiaki Yura^b

^a Dentistry and Oral Surgery, Matsubara Tokushukai Hospital, Osaka 580-0032, Japan

^b Department of Oral and Maxillofacial Surgery II, Osaka University Graduate School of Dentistry, Osaka 565-0871, Japan

^c Laboratory for Clinical Investigation, Osaka University Dental Hospital, Osaka 565-0871, Japan

ARTICLE INFO

Article history:

Received 17 March 2011

Received in revised form 13 May 2011

Accepted 29 June 2011

Available online 30 July 2011

Keywords:

Salivary duct carcinoma

Palate

Minor salivary gland

Immunohistochemistry

ABSTRACT

Salivary duct carcinoma (SDC) is a rare and highly aggressive malignancy of the salivary glands. It occurs almost exclusively in the major salivary glands, particularly the parotid, while in much less frequency in the minor salivary glands and the case showing exophytic growth in the oral cavity like the present case is extremely rare. This report is of an 82-year old man with SDC of the palate. A pedunculated discoid mass of 15 mm in diameter was on the right-sided paramedian posterior end of the hard palate. The lesion was excised and the histopathological examination showed the mass composed of various-sized carcinoma cell nests presenting solid to cribriform growth pattern with scanty interlacing stroma and comedonecrosis, and vascular and lymphatic invasion. The diagnosis was SDC. The immunohistochemistry of the tumor cells was positive for proliferating cell nuclear antigen and Her2/neu. The Ki-67 labeling index was approximately 80%. There has been no evidence of local recurrence or metastasis 24 months after surgery. We added a case of SDC arising from the minor salivary gland, which may be representing the early phase of highly aggressive SDC.

© 2011 Asian Association of Oral and Maxillofacial Surgeons. Published by Elsevier Ltd. All rights reserved.

1. Introduction

Salivary duct carcinoma (SDC), which was introduced in 1968 by Kleinsasser [1] and has been adopted into the second WHO classification since 1991 [2], is an extremely aggressive malignancy arising from the duct epithelial cell of the salivary gland. SDCs occur almost exclusively in the major salivary glands, particularly the parotid, while in much less frequency in the minor salivary glands, mainly of the palate [3]. The present paper describes a case of SDC that arose from the minor salivary gland in the palate and was treated at the early phase.

2. Case report

An 82-year-old man was referred to our hospital for closer examination and treatment of a small mass on the palate. The patient had a 2-month history of painless swelling on the palate, the right-sided paramedian posterior end of the hard palate. A smooth-surfaced pedunculated discoid mass of 15 mm in diameter was observed (Fig. 1). X-ray examination revealed no abnormality of the palatal bone. Under a diagnosis of benign salivary gland tumor the

lesion was excised. On operation neither erosion nor local absorption of the underlying bone was noticed. As the pathological report was SDC, wider resection was performed 3 weeks later. Before the second operation, CT, Echo of the neck and PET examinations were carried out for exploring the possible tumor extension including lymph node and distant metastases. The results were completely negative. The postoperative course has been eventless so far at the 24 months follow-up period.

3. Pathological findings

The cut surface of the tumor was whitish medullary and rather well circumscribed in the mucosal loose connective tissue. Histologically the tumor situated in the mucosal propria without any proper minor salivary gland components. The covering mucosal surface was widely eroded and coated with fibrinous exudate instead, namely carcinoma tissue was not exposed to the oral cavity. The tumor mass was composed of various-sized carcinoma cell nests presenting solid to cribriform growth pattern with scanty interlacing stroma, and comedonecrosis was seen in some larger carcinoma nests (Figs. 2 and 3). Most carcinoma cells showed medium-sized and irregular-shaped polygonal cytoplasm, irregular-shaped nuclei, and prominent nucleoli. The mitotic figures are evident, but their distribution was variable site to site, one or none in each field of low power view to one or two in each field of higher power view (Fig. 4). Vascular and lym-

* Corresponding author at: Dentistry and Oral Surgery, Matsubara Tokushukai Hospital, 7-13-26 Amamihigashi Matsubara-shi, Osaka-fu 580-0032, Japan. Tel.: +81 72 334 3400; fax: +81 72 332 3512.

E-mail address: k-yukiko@jf6.so-net.ne.jp (Y. Kusuyama).



Fig. 1. Close-up view of the palatal tumor.

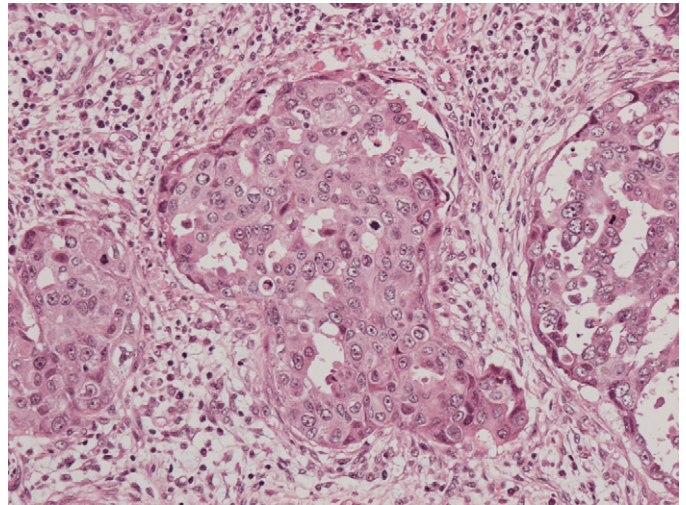


Fig. 4. Moderately atypical carcinoma cells with three atypical mitotic figures (H.E. stain, 100 \times).

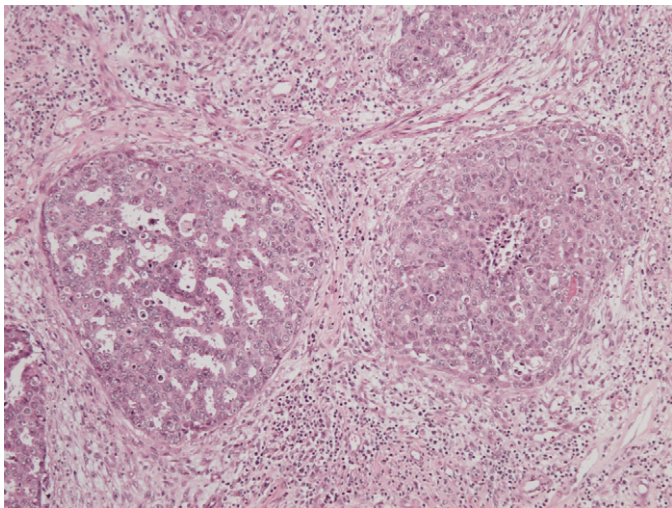


Fig. 2. Carcinoma nests showing solid or cribriform pattern (H.E. stain, 40 \times).

dle cell variant was recognized. The exact greatest dimension of the tumor measured 10 mm. The proper minor salivary glands around the postoperative granulation tissue were partly infiltrated by inflammatory cells, some losing the acinar components. The final diagnosis was moderately differentiated SDC.

The immunohistochemistry of the tumor cells was negative for vimentin (Novocastra Laboratories Ltd., Newcastle, UK, 1:800), S-100 protein (Novocastra Laboratories Ltd., 1:2500), α -smooth muscle actin (α -SMA; Dako, Carpinteria, CA, 1:500) and p53 (Dako, 1:300), while positive for carcinoembryonic antigen (CEA; Novocastra Laboratories Ltd., 1:1000), epithelial membrane antigen (EMA; Dako, 1:800), proliferating cell nuclear antigen (PCNA; Dako, 1:1000) and Her2/neu (Dako, undiluted). The Ki-67 (Dako, 1:500) labeling index was approximately 80% (Figs. 6 and 7).

4. Discussion

SDC is an entity first introduced in 1968 by Kleinsasser as an analogous tumor to duct carcinoma of the breast [1]. This type of carcinoma occupies approximately 1.4–3.9% of all kinds of malignant salivary gland neoplasms, occurring mainly in the parotid, while in much less frequency in the minor salivary glands [3].

phatic invasions were evident (Fig. 5). Peripheral infiltration was not prominent, only a single tiny carcinoma nest being recognized in the additionally excised specimen. Dense fibrosis between the carcinoma nests was not present at all. No mucinous cell or spin-

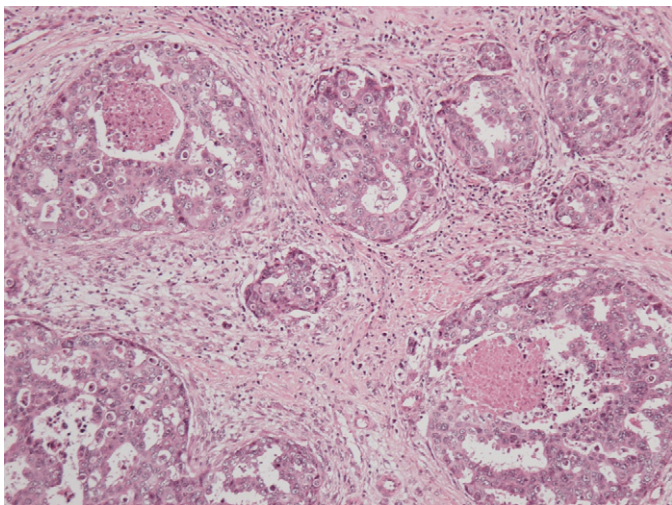


Fig. 3. So-called Roman bridge architecture in the cribriform pattern with some comedonecroses (H.E. stain, 40 \times).

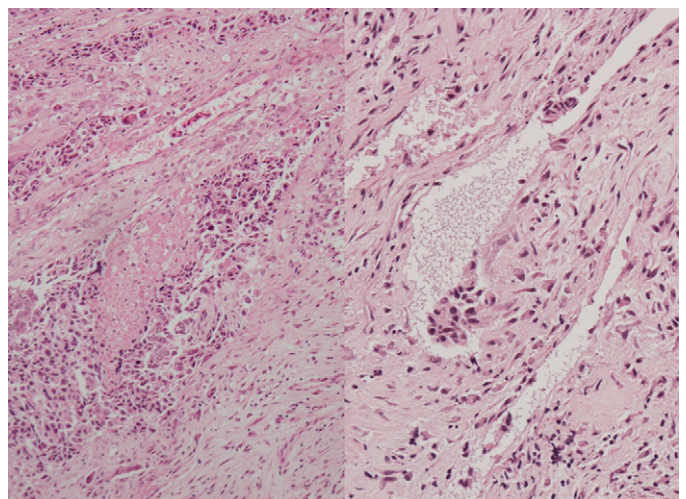


Fig. 5. Vascular (left, 40 \times) and lymphatic (right, 100 \times) invasions by carcinoma cells (H.E. stain).

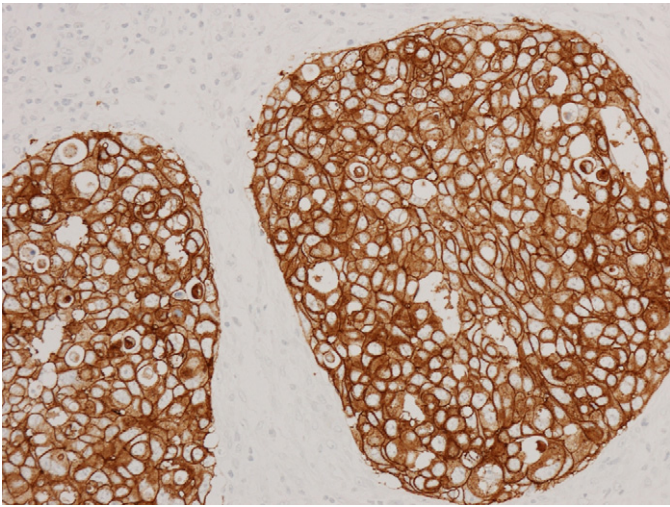


Fig. 6. Strong membranous positivity in Her2/neu immunohistochemistry (200×).

Although 10 palatal cases were reported in the literatures [1,4–10], the macroscopic appearance was not clearly stated in all cases; only semispherical shape or swelling was reported to be the clinical appearance at the first visit. In this regard, the present case showed exophytic growth with a peduncle. This growth pattern may show a peculiar feature of this tumor, leaving the underlying palatal bone intact. The tumors with exophytic growth in the upper respiratory tract or the esophagus are known as rather benign in prognosis, even in case of histological malignancy. However, they are usually low grade malignancies such as carcinoid, adenoid cystic carcinoma or carcinosarcoma. Therefore, the present case should not be considered on the same line.

Histologically, the comedonecrosis in some carcinoma nests has been pointed out as a characteristic feature of SDC as well as cribriform growth pattern of Roman bridge architecture [3,11], both of which come from scanty or no interlacing stroma development within the carcinoma nests. Aggressive invasion is also stressed in SDC. Indeed, we found carcinoma cell nests with cribriform growth pattern and central comedonecrosis, mitotic figures and vascular and lymphatic invasion.

The immunohistochemical results for SDC having been reported are positive for CEA, EMA and gross cystic disease fluid protein (GCDFP)-15 usually applied for duct carcinoma of the breast, and

negative for vimentin, S-100 protein and α -SMA [2,3,7,12]. In the present case, we found the expression of CEA, EMA, PCNA, and Her2/neu, while vimentin, S-100 protein, α -SMA and p53 were undetectable. This clearly supports the conventional histological interpretation that SDC arises from the duct epithelial cell. The expression of PCNA and Ki-67 were useful for the evaluation of the growth potential of tumor cells. Some reports also suggest that tumors with Her2/neu, PCNA and p53 expression are linked to early local recurrence, distant metastasis, and survival rate [2,13–18]. In our case, Her2/neu and PCNA were expressed and the Ki-67 labeling index was 80%, indicating the aggressiveness of the tumor.

The death rate in SDC has been reported to be as high as 60–80% of the patients, and the death in most cases occurred within 5 years after the diagnosis [3]. The clinical feature of SDC has been characterized as remarkably rapid enlargement in size [3], and in our case the tumor size increased approximately 2.5 times during about two months prior to the patient's visit to our hospital. On the other hand, there are some reports of those occurring in the minor salivary glands that the tumor growth was relatively less aggressive and carried a better prognosis [4–6,19–21]. Most of these cases showed intraductal growth pattern or low-grade SDC [5,19–21]. The third WHO classification of salivary gland tumors describes low-grade SDC as low-grade cribriform cystadenocarcinoma [22]. Low-grade SDC show an intraductal proliferation resembling atypical breast ductal hyperplasia or in situ micropapillary ductal carcinoma [23,24]. Kusafuka et al. [25] reported that the tumor originating from the parotid gland expressed cytokeratin 7 and EMA, GCDFP-15 and mucin. Her2/neu was diffusely stained and S-100 protein, a marker of myoepithelial cells, was locally positive. The Ki-67 labeling index was 19.6%. These histological and immunohistochemical findings are distinct from those in our case.

Together, rapid growth in a short term, the histological findings and the result of Ki-67 labeling index suggest that the tumor in our case is highly aggressive. Nonetheless, the tumor extension was T1N0M0 at the time of initial diagnosis and the postoperative course has been eventless so far at the 24 months follow-up period. The location and exophytic growth in the oral cavity must provide a favorable situation for the early detection and surgical treatment. Minimal peripheral invasion suggests having been in the early stage of tumor development. However, a careful long clinical follow-up is essential, because of its inherit property.

Acknowledgements

The authors thank Dr Masanobu Kitagawa for his critical comments and discussion.

References

- [1] Kleinsasser O, Klein HJ, Hübner G. Speichelgangcarcinoms. Ein den Milchgangcarcinomen der Brustdrüse analoge Gruppe von Speicheldrüsentumoren. Arch klin exper Ohren-Nasen- Kehlkopfheilk 1968;192(1):100–5.
- [2] Seifert G, Sobin LH. WHO international histological classification of tumours histological typing of salivary gland tumours. 2nd ed. New York: Springer-Verlag; 1991.
- [3] Ellis GL, Auclair PL. AFIP atlas of tumor pathology tumors of the salivary glands, 4th series, fascicle 9. Washington, DC: American Registry of Pathology; 2008.
- [4] Huh KH, Heo MS, Lee SS, Choi SC. Three new cases of salivary duct carcinoma in the palate: a radiologic investigation and review of the literature. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2003;95(6):752–60.
- [5] Tatemoto Y, Ohno A, Osaki T. Low malignant intraductal carcinoma on the hard palate: a variant of salivary duct carcinoma? Eur J Cancer B Oral Oncol 1996;32(4):275–7.
- [6] Ponniah I, Murali GM, SureshKumar P, Kumaran MG, Shaheen A. Salivary duct carcinoma of the palate. Indian J Dent Res 2005;16(4):167–70.
- [7] Lopes MA, de Abreu Alves F, Levy BA, de Almedia OP, Kowalski LP. Intraoral salivary duct carcinoma: case report with immunohistochemical observations. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2001;91(6):689–92.
- [8] Delgado R, Vuitch F, Albores-Saavedra J. Salivary duct carcinoma. Cancer 1993;72(5):1503–12.

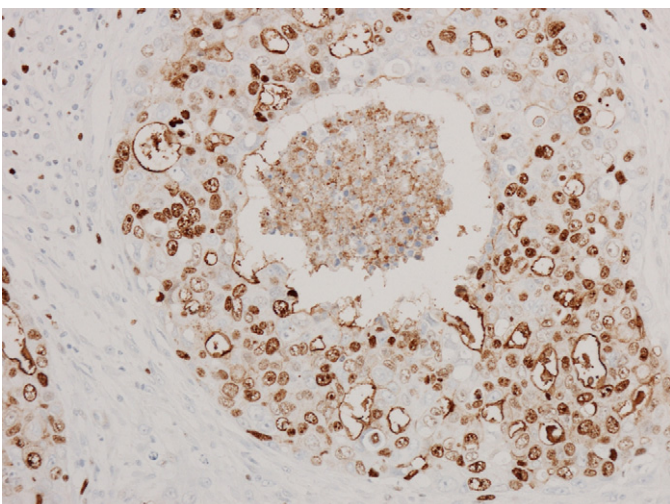


Fig. 7. More than 80% nuclear positivity in Ki-67 immunohistochemistry (200×).

- [9] Epivatianos A, Dimitrakopoulos J, Trigonidis G. Intraoral salivary duct carcinoma: a clinicopathological study of four cases and review of the literature. *Ann Dent* 1995;54(1–2):36–40.
- [10] Kamio N, Tanaka Y, Mukai M, Ikeda E, Kuramochi S, Fujii M, et al. A hybrid carcinoma: adenoid cystic carcinoma and salivary duct carcinoma of the salivary gland. An immunohistochemical study. *Virchows Arch* 1997;430(6):495–500.
- [11] Brandwein-Gensler MS, Skalova A, Nagao T. Salivary duct carcinoma. In: WHO classification of tumours. Pathology and genetics of head and neck tumors. Lyon: IARC Press; 2005. 233.
- [12] Lewis JE, McKinney BC, Weiland LH, Ferreiro JA, Olsen KD. Salivary duct carcinoma. Clinicopathologic and immunohistochemical review of 26 cases. *Cancer* 1996;77(2):223–30, 15.
- [13] Jaehne M, Roeser K, Jaekel T, Schepers JD, Albert N, Löning T. Clinical and immunohistologic typing of salivary duct carcinoma: a report of 50 cases. *Cancer* 2005;103(12):2526–33, 15.
- [14] Felix A, El-Naggar AK, Press MF, Ordonez NG, Fonseca I, Tucker SL, et al. Prognostic significance of biomarkers (c-erbB-2, p53, proliferating cell nuclear antigen, and DNA content) in salivary duct carcinoma. *Hum Pathol* 1996;27(6):561–6.
- [15] Martinez-Barba E, Cortes-Guardiola JA, Minguela-Puras A, Torroba-Caron A, Mendez-Trujillo S, Bermejo-Lopez J. Salivary duct carcinoma: clinicopathological and immunohistochemical studies. *J Craniomaxillofac Surg* 1997;25(6):328–34.
- [16] Etges A, Pinto Jr DS, Kowalski LP, Soares FA, Araújo VC. Salivary duct carcinoma: immunohistochemical profile of an aggressive salivary gland tumour. *J Clin Pathol* 2003;56(12):914–8.
- [17] Kamio N. Coexpression of p53 and c-erbB-2 proteins is associated with histological type, tumour stage, and cell proliferation in malignant salivary gland tumours. *Virchows Arch* 1996;428(2):75–83.
- [18] Hellquist HB, Karlsson MG, Nilsson C. Salivary duct carcinoma—a highly aggressive salivary gland tumour with overexpression of c-erbB-2. *J Pathol* 1994;172(1):35–44.
- [19] Watatani K, Shirasuna K, Aikawa T, Matsuya T. Intraductal carcinoma of the tongue report of a case. *Int J Oral Maxillofac Surg* 1991;20(3):175–6.
- [20] Zohar Y, Shem-Tov Y, Gal R. Salivary duct carcinoma in major and minor salivary glands A clinicopathological analysis of four cases. *J Craniomaxillofac Surg* 1988;16(7):320–3.
- [21] Chen KT. Intraductal carcinoma of the oral cavity. *Am J Surg Pathol* 2005;29(2):279.
- [22] Brandwein-Gensler MS, Grepp DR. Low-grade cribriform cystadenocarcinoma. In: WHO classification of tumours. Pathology and genetics of head and neck tumors. Lyon: IARC Press; 2005. 233.
- [23] Delgado R, Klimstra D, Albores-Saavedra J. Low grade salivary duct carcinoma A distinctive variant with a low grade histology and a predominant intraductal growth pattern. *Cancer* 1996;78(5):958–67.
- [24] Brandwein-Gensler M, Hille J, Wang BY, Urken M, Gordon R, Wang LJ, et al. Low-grade salivary duct carcinoma: description of 16 cases. *Am J Surg Pathol* 2004;28(8):1040–4.
- [25] Kusafuka K, Itoh H, Sugiyama C, Nakajima T. Low-grade salivary duct carcinoma of the parotid gland: report of a case with immunohistochemical analysis. *Med Mol Morphol* 2010;43(3):178–84.