Journal of Oral and Maxillofacial Surgery, Medicine, and Pathology xxx (2016) xxx–xxx

Contents lists available at ScienceDirect

Journal of Oral and Maxillofacial Surgery, Medicine, and Pathology

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

Case Report

# A case of very elderly patient with multiple cervical metastases of salivary duct carcinoma successfully treated by anti-androgen and proton beam therapies

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ARTICLE INFO

*Article history:*
Received 16 November 2015
Received in revised form 2 June 2016
Accepted 22 August 2016
Available online xxx

*Keywords:*
Salivary duct carcinoma
Androgen deprivation therapy
Proton beam therapy
Androgen receptor
Salivary gland carcinoma

ABSTRACT

*Objective:* The prognosis of salivary duct carcinoma (SDC) is reported to be very poor, worse than those of other salivary gland cancers. Previous immunohistochemical studies have demonstrated high expression of androgen receptor (AR) in SDC cases, suggesting that androgen deprivation therapy (ADT) may be effective for this disease.
*Methods & results:* A 90-year-old man with SDC from left buccal mucosa and multiple cervical lymph node metastases was treated with ADT. After 6 months of therapy, the tumor was markedly reduced on visual inspection, palpation, and positron emission tomography. No adverse events were noted. Subsequently, proton therapy was added, and a complete response was obtained. There has been no recurrence for 1.5 years since proton therapy was completed.
*Conclusions:* ADT should be considered as a therapeutic option for unresectable advanced SDC.


## 1. Introduction

Salivary duct carcinoma (SDC) is a highly aggressive malignant form of salivary gland cancer that occurs predominantly in men of elder male. SDC reportedly has a very poor prognosis, with a 5-year survival rate of 20–40% [1]. Distant metastasis occurs in almost half of all patients, contributing to the poor outcomes of patients with this cancer.

Although the basic treatment for SDC is surgical resection, systemic drug therapy combined with radiation therapy is carried out for recurrent and metastatic lesions. However, there has been no clinical study in which treatment was restricted to SDC. Systemic drug therapy for adenocarcinomas presumably including SDC has occasionally been reported. As for chemotherapy, monotherapy with cisplatin, vinorelbine, or paclitaxel, and polychemotherapy with CAP (cyclophosphamide/doxorubicin/cisplatin), CAPF (cyclophosphamide/doxorubicin/cisplatin/5FU), CPPr (cyclophosphamide/cisplatin/pirabucin), PV (cisplatin/vinorelbine), PT (carboplatin/paclitaxel), or GP (gemcitabine/cisplatin) have been reported. Generally, systemic chemotherapy for metastatic salivary gland cancers has considered as palliative treatment [2]. In recent years, targeted therapies have been attempted. Such therapies include trastuzumab monotherapy, as well as therapy combining trastuzumab and a taxanes [3], lapatinib, gefitinib, cetuximab, or temsirolimus/bevacizumab. Although these therapies were examined in a limited number of patients, considerable responses have been reported in several patients. Thus, this field is currently attracting considerable attention.

On the other hand, endocrine therapy (androgen deprivation therapy: ADT) has also been attempted in SDC cases. In general, hormone receptors are not expressed in other salivary gland cancers, but it is known that androgen receptors (AR) are frequently positive in SDC cases [1]. In prostate cancer cases, the AR is a receptor that is involved in the development, progression, and relapse of cancer [4]. AR serves as the target of ADT when treating prostate cancer, and the efficacy and safety of this therapy have already been established. Because ARs are also expressed in SDC, ADT has been used for the treatment of SDC, and successfully treated cases have

☆ AsianAOMS: Asian Association of Oral and Maxillofacial Surgeons; ASOMP: Asian Society of Oral and Maxillofacial Pathology; JSOP: Japanese Society of Oral Pathology; JSOMS: Japanese Society of Oral and Maxillofacial Surgeons; JSOM: Japanese Society of Oral Medicine; JAMI: Japanese Academy of Maxillofacial Implants.

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http://dx.doi.org/10.1016/j.ajoms.2016.08.003
2212-5558/

been reported in the literature [5–7]. We report our experience with a very elderly patient with advanced SDC who responded well to ADT.

## 2. Case report

The patient was a 90-year-old man who had harbored a left buccal mass for 1 year, with submental swelling and pain lasting for 1 month. Because biopsy of the buccal mucosa tumor led to a diagnosis of SDC, the patient came to our department. At presentation, he had mass lesions extending from the left buccal mucosa to the buccal skin. Multiple metastatic lymph nodes were palpable in the submental and left cervical regions, and lymph nodes in the submental region showed dermal infiltration, producing a small amount of continuous bleeding daily (Fig. 1a and b).

Magnetic resonance imaging (MRI) (Fig. 2a–c) and positron emission tomography-computed tomography (PET-CT) (Fig. 3a) revealed a primary lesion in the buccal mucosa, and metastatic lymph nodes in the submental region, the inferior pole of the parotid gland, and the left cervical region. PET-CT showed neither evidence of distant metastasis nor fluorodeoxyglucose accumulation in the mammary gland. The neoplasm classified as T4aN2bM0 (stage IV), based on mouth cancer TNM classification criteria of the UICC (Union for International Cancer Control).

Pathological findings: hemotoxilin-eosin preparations showed histological findings similar to those of mammary ductal carcinoma, consisting of glandular formation and a trabecular pattern. Tumor cells were characterized by abundant eosinophilic cytoplasm, prominent nuclear atypicality, and sporadic division of nuclei (Fig. 4a). Immunohistochemically, the nuclei of tumor cells were diffusely positive for AR (Fig. 4b). The Ki67 value was about 25%. Expressions of HER2, EGFR, CK5/6, CK20, p63 and PAS were negative. GCDFP15 was slightly positive and CK7 was positive. Because there were no breast tumors, a diagnosis of SDC arising from the minor salivary gland of the oral buccal mucosa was established.

The patient's performance status (PS) was 0. He showed good cardiopulmonary function and good organ functions. Serum prostate specific antigen was within normal limits. Given his advanced age of 90 years, the patient declined surgical treatment, chemotherapy, or radiation therapy. Therefore, ADT was started on the basis of the AR-positive results, after obtaining his informed consent.

In March 2012, the regimen of oral bicalutamide (Casodex Tablet 80 mg®), 1 tablet/day, and subcutaneous injection of injectable leuprorelin acetate (Leuplin®) 11.25 mg (every 3 months) was initiated.

Patient provided written informed consent and this treatment was approved by the Institutional Ethics Review Board of Mita Hospital.

The tumor began to decrease after 2 months of therapy, and there was marked reduction in August 2012, after 6 months of therapy (Fig. 1c and d). The therapeutic effect was rated as a partial response (PR) by MRI (Fig. 2d–f), and complete response (CR) by PET-CT (Fig. 3b).

At the patient's request, proton therapy at 66 GyE/30 Fr was carried out, aiming at radical cure, and the patient's response was eventually judged to be a CR. Grade1 dermatitis radiation and mucositis oral were occurred each in accordance with Common Terminology Criteria for Adverse Events (CTCAE) version 4.0.

He is currently free of recurrence, 1.5 years after the beginning of treatment.

## 3. Discussion

SDC is histopathologically defined as "an aggressive adenocarcinoma which resembles high-grade breast ductal carcinoma" [1]. Immunohistochemically, SDC has features in common with breast cancer such as the expressions of HER2 and EGFR, but is different from breast cancer in that SDC rarely shows estrogen and progesterone receptor expressions. It has been reported that SDC frequently expresses AR [1], and thus biologically resembles prostate cancer. Because effective systemic therapies have already been developed for prostate cancer and breast cancer, it is possible that new systemic therapies for SDC will be developed with reference to these drug treatment strategies.

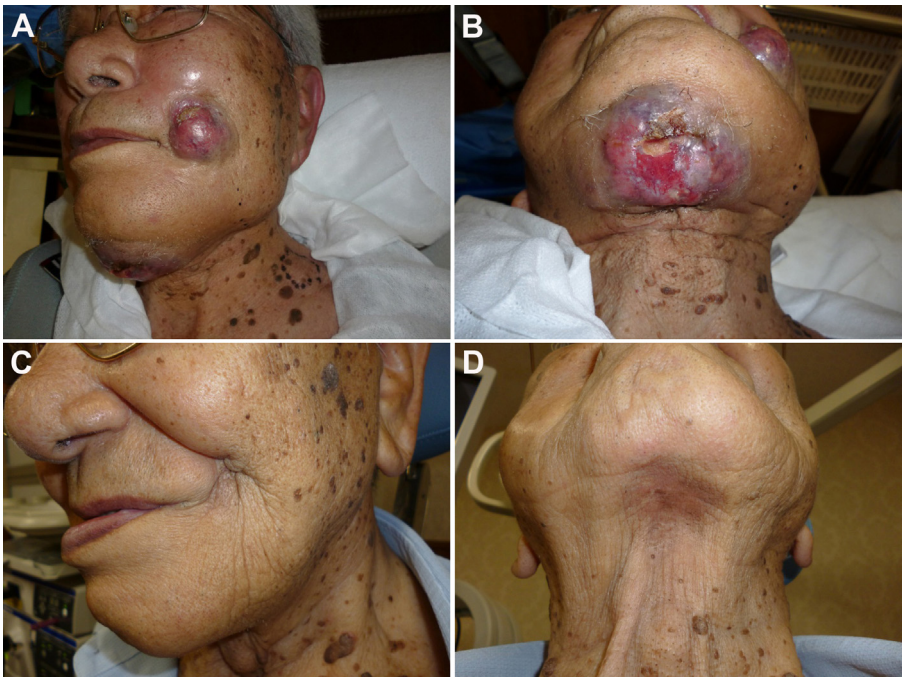


**Fig. 1.** (a and b) Primary tumor and submental metastasis before treatment. (c and d) After 6 months with androgen-deprivation therapy.

Please cite this article in press as: Fushimi C, et al. A case of very elderly patient with multiple cervical metastases of salivary duct carcinoma successfully treated by anti-androgen and proton beam therapies. J Oral Maxillofac Surg Med Pathol (2016), http://dx.doi.org/10.1016/j.ajoms.2016.08.003