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Clinicopathologic study of salivary duct carcinoma and the efficacy of androgen deprivation therapy☆,☆☆

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ARTICLE INFO

Article history:
Received 16 May 2014

ABSTRACT

Objective: Salivary duct carcinoma is a rare and aggressive tumor of the salivary glands. The objectives of this study were to investigate the clinicopathological features of salivary duct carcinoma and to determine whether androgen deprivation therapy should be recommended.

Study design and Methods: The clinical records of seven patients diagnosed with salivary duct carcinoma between 2002 and 2012 were retrospectively assessed. Tumor specimens were examined for overexpression of human epidermal growth factor receptor 2 (HER2) and androgen receptor by immunohistochemistry. A case of androgen receptor-positive salivary duct carcinoma who received androgen deprivation therapy is presented.

Results: Of the seven patients, 43% had recurrences and metastases, and the 5-year survival rate was 68.6%. All patients were androgen receptor-positive, and 71% were HER2-positive. One patient, a 66-year-old man with androgen receptor-positive salivary duct carcinoma, received oral bicalutimide for 14 months and practically all lung metastases disappeared.

Conclusion: Androgen receptor is often overexpressed in salivary duct carcinoma. Androgen deprivation therapy is safe and should be considered for patients with androgen receptor-positive salivary duct carcinoma.

1. Introduction

Salivary duct carcinoma (SDC) is a rare tumor of the salivary glands, representing 1%–3% of all malignant salivary tumors [1]. SDC progresses rapidly and is frequently diagnosed at an advanced stage, with a 5-year survival rate of 11.5%–26.9% [2,3]. While surgical resection with postoperative radiotherapy is the standard treatment, there is a high risk of both local (48%) and distant (48%) recurrence [1]. In view of the poor survival rate, a structured therapeutic approach should be developed to improve disease outcome.

SDC is pathologically similar to ductal carcinoma of the breast [4]. Recent studies showed human epidermal growth factor receptor 2 (HER2) overexpression in SDC and its association with poor prognosis [1,5,6], similar to HER2-positive ductal carcinoma of the breast. Trastuzumab, a monoclonal

☆ Financial support or funding: None.
☆☆ Conflict of interest: None.

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http://dx.doi.org/10.1016/j.amjoto.2014.07.007
0196-0709/

antibody that interferes with the HER2 receptor, is one treatment option for HER2-positive SDC [6–9]; however, its efficacy remains uncertain. On the other hand, androgen receptor (AR) overexpression is more common in SDC (43%–92.3%) [3,10,11], and androgen deprivation therapy (ADT) is beneficial in patients with recurrent or disseminated disease [12–14].

The objectives of this study were to determine the proportion of HER2- or AR-positive SDC patients and to evaluate the association between HER2 and AR positivity with prognosis. Moreover, we report findings for one patient with AR-positive SDC who was prescribed ADT.

2. Patients and methods

Seven patients with a diagnosis of SDC were treated in the Department of Otolaryngology at the National Tokyo Medical Center between 2002 and 2012. Only patients with histologically proven SDC were enrolled. We retrospectively reviewed clinical records and pathology archives to analyze age, gender, site of tumor, presenting symptoms, duration of symptoms, clinical stage, initial treatment, pathological characteristics, recurrence, and clinical outcome. Clinical stage was described according to the 6th Edition of Salivary Gland Neoplasms published by the American Joint Committee on Cancer. The survival rate was calculated using the Kaplan–Meier method. AR and HER2 immunohistochemistry was also performed on fixed tumor specimens. According to established criteria [15], HER2 immunoreactivity was scored for membrane localization as follows: 0, negative staining or staining in <10% of cells; 1+, faint/barely perceptive staining in >10% of cells; 2+, weak to moderate staining in >10% of cells or strong staining in <30% of cells; and 3+, strong staining in >30% of cells. With regard to AR, tumors with ≥10% nuclear-stained cells were considered positive [16].

One patient was diagnosed with AR-positive SDC. He experienced relapse after surgery and postoperative radiotherapy, and his tumor was difficult to control surgically. The patient was prescribed ADT with the permission of the ethics committee of our hospital. We report this case and evaluate the usefulness of ADT.

3. Results

3.1. Clinical findings

Table 1 summarizes the clinical findings. This study consisted of six men and one woman, with ages ranging from 49 to 77 years (mean, 62 years). Parotid and submandibular glands were affected in four (57%) and three (43%) patients, respectively. During the initial visit, five (71%) patients presented with painless nodes and two (29%) presented with facial nerve paralysis. The time interval from the onset of symptoms until diagnosis was 3 months–26 years. Cervical lymph node metastases were detected in three patients at the time of diagnosis. Five patients had stage IV tumors, one had a stage III tumor, and one had a stage I tumor.

All patients underwent surgery. Three patients underwent total parotidectomy with partial or complete facial nerve resection. The initial neck dissection was performed with therapeutic intent in three patients and with prophylactic intent in two patients. Four out of seven patients received postoperative localized radiotherapy (60–66 Gy).

Two patients experienced local relapses and one (14%) developed cervical lymph node metastasis in the non-dissected area. Three patients developed distant metastases in the skin, bone, or lung. Recurrences were evident at 7–17 months (mean, 11 months) after the initial surgery. A combination of surgery and radiotherapy resulted in local–regional control of the disease in two out of four patients (50%). The follow-up time ranged from 16 months to 5 years (mean, 34 months). Two patients died from the disease. Four patients were alive with no evidence of disease at the time of the last follow-up, and one was alive with disease. The 5-year survival rate was 68.6%.

3.2. Histopathological findings

Table 2 summarizes the histopathological findings. The surgical specimens from three patients (43%) showed morphological evidence of remnants of pleomorphic adenoma (case nos. 3, 4, and 7). Case no. 4 exhibited the longest clinical history, and case no. 7 previously underwent surgical resection of a benign tumor

Table 1 – Clinical results from the seven patients with SDC.

Case no.	Age, y (sex)	Tumor site	Symptoms	Duration of symptoms	Clinical status	Treatment	Surgical margin	Recurrence	Follow-up (months)
1	71 (M)	PG	Painless node, facial paralysis	8 months	T4aN0M0	Tot parotid, ND	–	T, M (lung)	DOD (30)
2	77 (M)	PG	Painless node	7 months	T2N2bM0	Tot parotid, ND, RT	+	T, M (skin, bone)	DOD (16)
3	53 (M)	PG	Painless node	4 months	T1N0M0	Superf parotid	–	–	NED (60)
4	49 (F)	SMG	Painless node	26 years	T3N0M0	SMG resection	–	–	NED (36)
5	49 (M)	SMG	Painless node	10 years	T2N2bM0	SMG resection, ND, RT	–	–	NED (60)
6	66 (M)	PG	Painless node, facial paralysis	3 months	T4aN0M0	Tot parotid, ND, RT, ADT	+	N, M (lung)	AWD (34)
7	72 (M)	SMG	Painless node	6 months	T2N2bM0	SMG resection, ND, RT	–	–	NED (28)

SDC, salivary duct carcinoma; M, male; F, female; PG, parotid gland; SMG, submandibular gland; Tot parotid, total parotidectomy; Superf parotid, superficial parotidectomy; ND, neck dissection; RT, radiotherapy; ADT, androgen deprivation therapy; DOD, died of disease; NED, no evidence of disease; and AWD, alive with disease.