Definitive treatment of androgen receptor–positive salivary duct carcinoma with androgen deprivation therapy and external beam radiotherapy

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Accepted 15 May 2013
Published online 00 Month 2013 in Wiley Online Library (wileyonlinelibrary.com). DOI 10.1002/hed.23383

ABSTRACT: *Background.* Salivary duct carcinoma (SDC) is an aggressive malignancy with high recurrence rates. Standard management includes surgical resection followed by adjuvant radiation. Androgen receptor positivity has been described to be present in 40% to 90% of SDCs, and a recent case series showed a benefit to androgen deprivation therapy (ADT) in recurrent or metastatic disease.

Methods and Results. We present the case of an 87-year-old woman with a locally advanced androgen receptor–positive parotid SDC treated definitively with ADT and external beam radiotherapy, a regimen modeled after the treatment of prostate cancer. She had a complete response on positron emission tomography (PET)/CT scan and had no evidence of disease 24 months after the completion of treatment.

Conclusion. To our knowledge, this case report is the first to describe the use of ADT plus radiation to definitively treat SDC. This regimen could be considered in patients with androgen receptor–positive SDCs who are considered unresectable or who refuse surgery. © 2013 Wiley Periodicals, Inc. *Head Neck.* 00: 000–000, 2013

KEY WORDS: salivary duct carcinoma, salivary gland, androgen receptor, radiation, androgen deprivation therapy

INTRODUCTION

Salivary duct carcinoma (SDC) is an aggressive malignancy with high rates of locoregional recurrence and distant metastasis. Standard management includes surgical resection followed by postoperative radiation. Androgen receptor positivity has been described to be present in 40% to 90% of SDCs, and a recent case series showed a benefit to androgen deprivation therapy (ADT) in the setting of recurrent or metastatic disease.[1–3] We present the case of an 87-year-old woman with a locally advanced SDC of the parotid treated definitively with ADT and external beam radiotherapy with a complete response.

CASE REPORT

An 87-year-old woman presented with a painful left facial mass. Physical examination revealed a 9-cm firm, fixed mass in the left parotid gland extending from the zygoma to the mandible. MRI showed a 7-cm parotid mass with suspected facial nerve and zygoma invasion. There was no lymphadenopathy on examination or imaging. A CT-guided core needle biopsy showed SDC, androgen receptor–positive, and Her2 negative. The patient's American Joint Committee on Cancer (2010) classification was cT4a N0, group stage IVA. She was offered surgical resection but declined.

The patient was treated with neoadjuvant and concurrent ADT and external beam radiotherapy. She was initially started on oral bicalutamide 150 mg daily and after 2 weeks noted decreased pain and shrinkage of the mass. She then received intramuscular leuprolide 22.5 mg, and this was repeated 3 months later. Radiotherapy was begun 5 weeks after the initiation of bicalutamide and consisted of 70 Gy to the mass delivered via intensity-modulated radiation therapy with 6 MV photons. The ipsilateral neck was treated electively.

MRI performed 1 month after the completion of radiotherapy showed a 2.5 cm residual left parotid mass. Positron emission tomography (PET)/CT scan 2 months later showed mild hypermetabolic activity in this region. Repeat PET/CT performed 6 months after the completion of radiotherapy showed no residual hypermetabolic activity. The patient's latest PET/CT, performed 23 months after treatment, continued to show no hypermetabolic activity.

Clinically, the patient noted complete resolution of her pain with treatment. She denied side effects from ADT. The dose of bicalutamide was decreased to 50 mg daily 4 months after the completion of radiotherapy, and she remains on this dose. She was last seen 24 months after the completion of treatment and had no clinical evidence of disease. Figures 1 and 2 show the patient before and 20 months after treatment. Figures 3 and 4 are representative slices from her CT scan before and 12 months after treatment.

DISCUSSION

Salivary gland malignancies account for less than 5% of head and neck cancers and encompass a wide range

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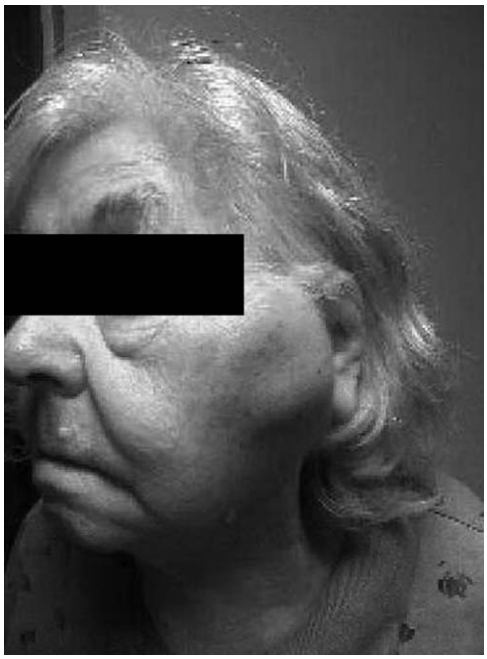

FIGURE 1. Before treatment.

of histologic subtypes.[4] Among these, SDC is a rare and aggressive tumor type. SDC typically arises in the parotid gland and has high rates of nodal and metastatic spread.[5] Median survival is approximately 3 years.[6] Standard management includes surgical resection followed by postoperative radiation. Patients whose disease is unresectable or who refuse surgery are typically managed with radiation alone, but outcomes are poor. Ten-year overall survival in a heterogeneous population of patients with inoperable or unresectable salivary gland malignancies treated with radiation alone has been reported to be 15% to 25%.[7]

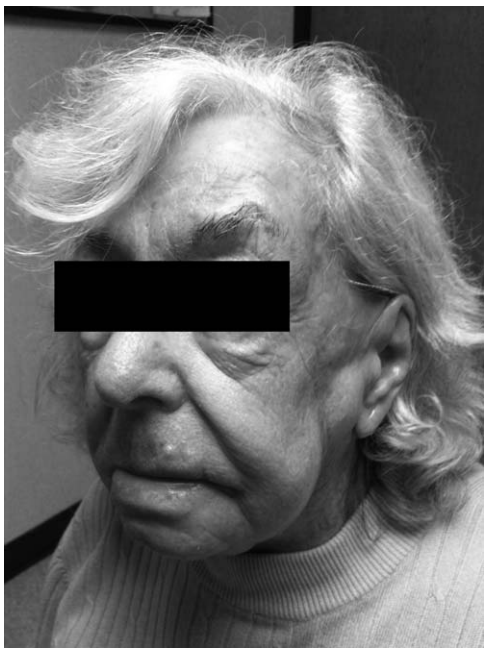

FIGURE 2. Twenty months after treatment.

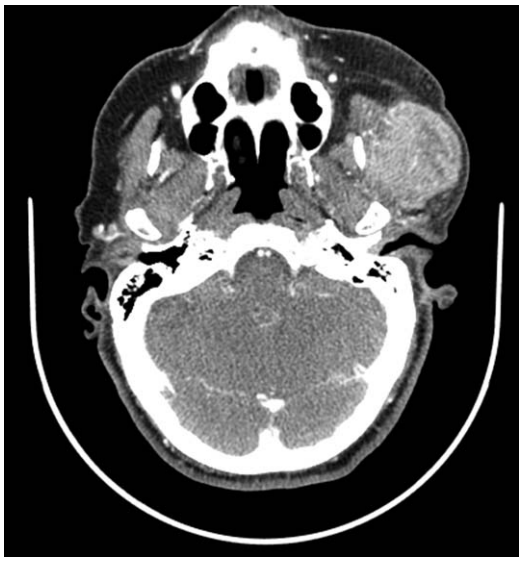

FIGURE 3. CT scan obtained at diagnosis showing an enhancing left parotid mass.

Morphologically, SDC resembles invasive ductal carcinoma of the breast (Figure 5). Estrogen and progesterone receptor expression is rare. However, androgen receptor expression has been described to be present in 40% to 90% of cases (Figure 6).[1,2] This has led to interest in including ADT in the management of these tumors. In 2005, Locati et al[8] described 7 patients with recurrent or metastatic androgen receptor-positive salivary gland cancer who achieved a 33% response rate with complete anti-androgen blockade; 2 of these patients had SDC. In 2011, Jaspers et al[3] published a case series of 10 patients with androgen receptor-positive SDC, 9 of whom had

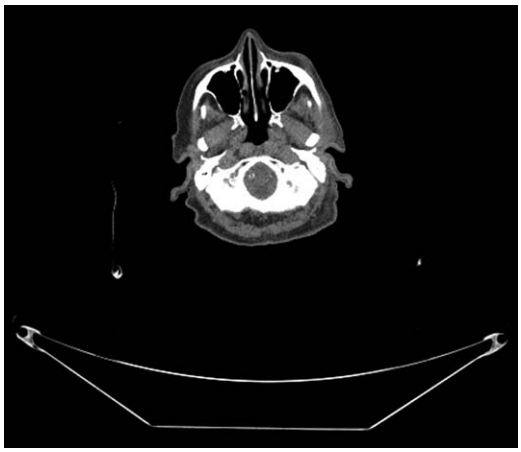

FIGURE 4. CT scan obtained 12 months after the completion of radiotherapy showing resolution of disease.

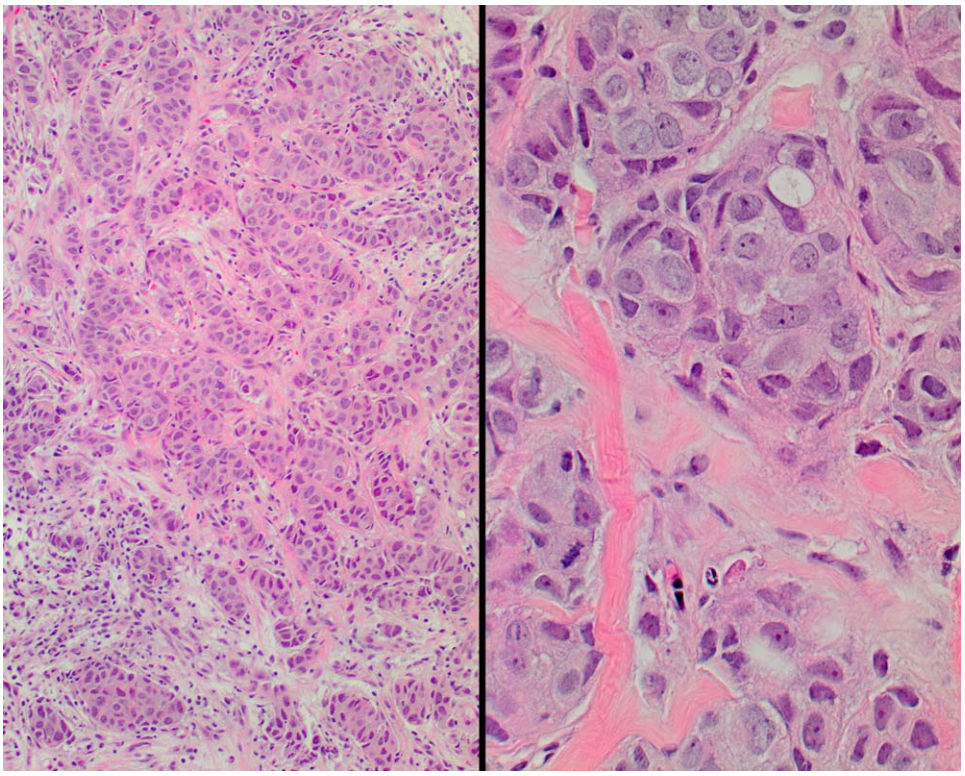

FIGURE 5. Left: Salivary duct carcinoma shows trabecular to glandular architecture in this core needle biopsy hematoxylin-eosin–stained photomicrograph, ×100. Right: High power (×400) shows nuclear pleomorphism, prominent nucleoli, and a mitosis. There is a glandular lumen present.

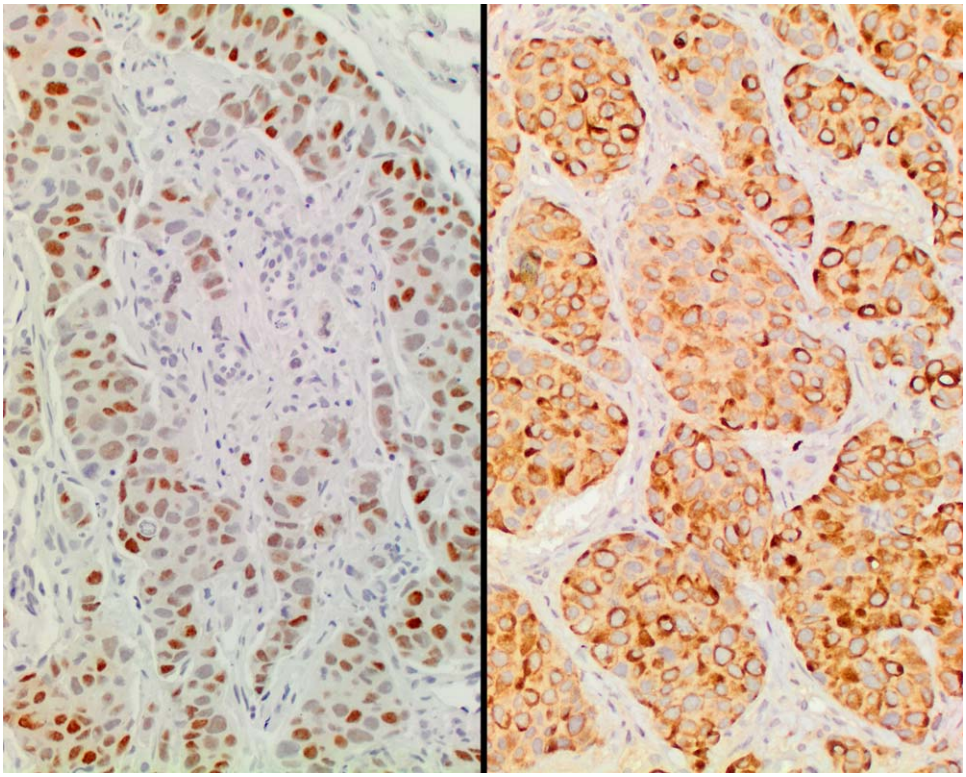

FIGURE 6. Left: Androgen receptor stains most of the tumor cell nuclei strongly and diffusely. Right: CK5/6 is shown in a cytoplasmic and membranous pattern in this salivary duct carcinoma. Both photomicrographs are at ×400.

recurrent or metastatic disease. They showed a clinical benefit to ADT, with a median progression-free survival of 12 months.

To our knowledge, this is the first case report describing ADT plus radiation used to definitively treat SDC. Our approach was modeled after the treatment of the most common androgen receptor-positive cancer, prostate adenocarcinoma. In high-risk prostate cancer, studies such as Radiation Therapy Oncology Group 86-10 have shown a benefit to the addition of neoadjuvant and concurrent ADT over radiation alone.[9] We are encouraged by the preliminary outcome of this approach in our patient, especially given the advanced initial presentation of her disease. This regimen could be considered in patients with androgen receptor-positive SDCs who are not candidates for surgical resection or who refuse surgery. However, only a randomized trial will be able to confirm the benefit of this approach.

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