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Surgery and Adjuvant Radiation for High-Risk Skin Adnexal Carcinoma of the Head and Neck

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Abstract

OBJECTIVES—Skin adnexal carcinoma (SAC) is a rare cutaneous malignancy that arises from sebaceous and sweat glands. These carcinomas are believed to behave more aggressively than cutaneous squamous cell carcinomas (SCC) with a propensity for local recurrence. The role of adjuvant radiotherapy in SAC is undefined.

METHODS—We retrospectively reviewed all cases of head and neck SAC treated with surgery and adjuvant radiation from 2000-2012 at a single institution.

RESULTS—Nine cases were identified. Median age was 67 (range 52-88). The histologies were: adnexal carcinoma (n=1), adnexal carcinoma with sebaceous differentiation (n=1), adnexal carcinoma with squamous differentiation (n=1), skin appendage carcinoma (n=1), sclerosing sweat duct carcinoma (n=1), mucinous carcinoma (n=1), ductal eccrine adenocarcinoma (n=1), porocarcinoma (n=1), and trichilemmal carcinoma (n=1). All tumors were reviewed by a dermatopathologist to confirm the SAC diagnosis.

All patients had surgery. Indications for adjuvant radiation included involved lymph nodes (n=4), perineural invasion (n=2), nodal extracapsular extension (n=2), positive margin (n=1), high-grade histology (n=6), multi-focal disease (n=2), and/or recurrent disease (n=5). Radiation was delivered to the primary site alone (n=3), to the draining lymphatics alone (n=2), or to both (n=4). One patient received concurrent cisplatin. Median dose to the primary site was 60Gy and to the neck was 50Gy.

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Median follow-up was 4.0 years (0.6-11.4 years). Locoregional control was 100%. Five-year progression free survival was 89%. There was one acute grade 3 toxicity and no grade 2 late toxicities were recorded.

CONCLUSIONS—Surgery and adjuvant radiation for high-risk SAC offers excellent locoregional control with acceptable toxicity.

Keywords

Skin adnexal carcinoma; cutaneous appendage carcinoma; sebaceous carcinoma; radiation; eccrine carcinoma

INTRODUCTION

Skin adnexal carcinomas (SACs) are rare cutaneous malignancies that arise from skin appendages located within the dermis.¹⁻³ Varied patterns and differentiations have been identified with more than 15 different histologies.³⁻⁵ They are derived from three different structures: the pilosebaceous unit, the eccrine sweat glands, and the apocrine glands.³ It is most often diagnosed in long standing lesions of the head and neck.^{1, 2, 6} The lesions occur primarily in the Caucasian population but have been reported in other ethnicities such as African American, Asian, or Pacific Islander.^{1,2} There is increasing incidence with age, with peak frequency in the eighth decade.^{2, 7} Predominance in the head and neck region, higher prevalence in white individuals, and higher incidence on the left side of the body suggest ultraviolet light exposure to be a risk factor.⁸ Immunosuppressed patients are thought to be at higher risk of developing malignant appendageal tumors and previous exposure to ionizing radiation is thought to be a risk factor.^{9, 10} There are also case reports that describe lesions associated with previously noted benign skin tumors.⁶

Although published experience in the treatment of these tumors is sparse, they seem to have a propensity for local invasion and recurrence.^{1, 3, 11} Regional or distant metastases are less common but have been reported to occur in up to 30% of cases.⁷ Current staging of adnexal carcinoma is included in the American Joint Committee on Cancer (AJCC) cutaneous squamous cell carcinoma (SCC) staging.¹² Like many rare tumors, there is no standard of care management.^{2, 13} Surgical extirpation with or without regional lymph node dissection followed by adjuvant radiotherapy in select cases is often performed, although definitive therapy with RT in lieu of an operation has been reported.^{14, 15} Locoregional recurrence has been reported up to 60% after surgical excision alone.¹⁶⁻¹⁸

At our institution, skin adnexal carcinomas are initially managed with primary surgery, followed by consideration for adjuvant radiation based on presence of high risk characteristics such as perineural invasion, extracapsular extension, positive margin, high grade, multi-focal disease, involved lymph nodes (LNs), and/or recurrent disease. This series details the outcomes after treatment with combined modality therapy for skin adnexal carcinomas at a single institution.

MATERIALS AND METHODS

Patients with non-melanoma skin cancer (NMSC) who were treated with primary surgery and adjuvant radiation from 2000 to 2012 at our institution were retrospectively identified (n = 108). Squamous cell carcinoma, basosquamous cell carcinoma, basal cell carcinoma (BCC), and merkel cell carcinoma were excluded from the analysis. All cases were subsequently reviewed by a dermatopathologist to confirm that tumors were SACs and not poorly differentiated variants of more common tumors. Patients were excluded if they had less than 6 months of follow-up or were treated with palliative intent. A total of nine patients met the inclusion criteria. In patients with nodal disease and no obvious cutaneous lesion, a full workup was undertaken to attempt to identify a cutaneous or mucosal primary. All patients were staged using the AJCC 7th edition staging system.¹² Patient demographics, relevant clinical history, tumor information, treatment, and follow-up were abstracted from the relevant medical records in accordance with an Institutional Review Board approved protocol and the Health Insurance Portability and Accountability Act (HIPAA). All toxicity was graded based on CTCAE v4.0.

The primary endpoints for analysis included locoregional control (LRC) and overall survival (OS). The sites of relapse were categorized as follows: 1) local if it occurred in surgical bed; 2) regional if tumor was detected in nearby lymph nodes or surrounding structures; and 3) distant if metastases were seen in a non-adjacent organ or lymph node. LRC was defined as lack of local or regional relapse. OS was calculated using the Kaplan-Meier survival curves and was calculated from the end date of radiation to the date of death or last follow-up.

RESULTS

Median age was 67 (range 51 – 88) with five females and four males. The histologies reported on the pathology report were as follows: adnexal carcinoma (n = 1), adnexal carcinoma with sebaceous differentiation (n = 1), adnexal carcinoma with squamous differentiation (n = 1), skin appendage carcinoma (n = 1), sclerosing sweat duct carcinoma (n = 1), mucinous carcinoma (n = 1), ductal eccrine adenocarcinoma (n = 1), porocarcinoma (n = 1), and trichilemmal carcinoma (n = 1). 67% of patients (n = 6) were determined to be either high grade or poorly differentiated (Table 1). Due to the high grade/poorly differentiated nature of some of the tumors, further characterization beyond “adnexal carcinoma” could not be performed. A PET/CT scan was obtained for the patient with mucinous carcinoma to confirm that the cutaneous tumor was not a metastasis. All lesions occurred in the head and neck region. Staging based on AJCC 7th edition for non-melanoma skin cancer were as follows: I (n = 1), II (n = 4), III (n = 2), IVA (n = 1), and IVB (n = 1).¹²

All patients had primary surgery: 56% (n = 5) of patients had a neck dissection, 22% (n = 2) had sampling of LNs adjacent to the primary site, and 22% (n = 2) had clinically negative necks observed. Pathologically involved lymph nodes were common (n = 4, 44%). Adjuvant therapy consisted of RT to the primary site alone (n = 3), to the draining lymphatics alone (n = 2), or to the primary site and draining lymphatics (n = 4). One patient received concurrent chemotherapy (weekly cisplatin).

Median follow-up among living patients was 4.0 years (0.6 – 11.4 years). Locoregional control was 100%. Progression free survival was 89% at 5 years, with distant failure in a single patient (brain metastasis). (Figure 1) The brain metastasis was seen on imaging one week after cessation of radiation treatment, which was stopped one fraction early due to patient's poor performance status and other chronic issues. No biopsy of the brain lesions was obtained. The patient passed away shortly after the diagnosis of brain metastasis. Overall survival at 5 years was 67%.

Median dose of radiation to the primary site was 60 Gy (range, 50 – 60). Median dose to the neck was 50 Gy (range, 46 – 58). Photons (6 MV) were most commonly used, followed by electrons (6 MeV), with or without bolus (0.5cm – 1cm). Indication for adjuvant RT was high risk features such as involved LNs (n = 4), perineural invasion (n = 2), extracapsular extension (n = 2), positive margin (n = 1), high grade (n = 6), multi-focal disease (n = 2), and/or recurrent disease (n = 5). Median time to recurrent disease was 2 years (range, 9 months – 8 years).

Two radiation fractionations were used: 50Gy in 20 fractions or 60Gy in 30 fractions. There was no difference in the tolerability of the two regimens and both offered 100% locoregional control. The primary site was treated in most cases. In two cases where the recurrent lesion occurred as a neck mass with no recurrence in the area of the previously treated cutaneous lesion, the primary site was not treated. Treatment of the draining lymphatics was performed at the discretion of the treating physician with six of the nine patients receiving regional lymph node irradiation. All patients with pathologically involved lymph nodes received regional lymph node irradiation. Two additional patients received irradiation to the regional lymph nodes but were node negative. One patient had a large, neglected primary lesion and the risk of local-regional recurrence was felt to be high despite having 2 negative lymph nodes. The other patient had a primary cutaneous lesion on the neck and the draining lymphatics would already be partially in the field if only the primary lesion was treated so the decision was made to treat the regional lymph nodes as well. Radiation treatment was well tolerated. There was one acute grade 3 nausea necessitating placement of a gastrostomy tube in a patient who also received amifostine. This is the only patient who received amifostine. The gastrostomy tube was not permanent.

DISCUSSION

Cutaneous adnexal carcinomas are extremely rare, reported to represent 0.005% of all skin tumors.¹⁹ Due to the paucity of skin adnexal carcinomas, there is no consensus on management of these tumors and treatment is often based on small case series. The majority of cases have been treated with surgery either with wide local excision or Mohs surgery.^{2, 7, 8, 20} Local or regional recurrence has been reported in up to 60% of lesion treated with surgical excision alone of cutaneous adnexal carcinomas.⁸ The often infiltrative nature of these lesions can make it difficult to obtain adequate margins without large surgical defects.¹⁴ Surgical series have reported a re-excision rate of up to 30% of patients with wide local excision alone due to persistently positive margins.⁸ As a result, surgical series have shown the final defect area can be up to six times that of the original lesion.^{8, 21} Pathologic features such as perineural invasion, recurrent tumor, and positive margin have shown to be

factors predictive of local recurrence in more common non-melanoma skin carcinomas^{22, 23}; however, the presence of these features is unclear in the management of cutaneous adnexal carcinomas.

A Recent SEER analysis of this disease suggests that more aggressive grade is associated with significantly decreased survival.² In addition, patients who have metastatic disease, either regional or distant, have been shown to have decreased survival compared to patients who present with localized tumors.^{2, 5} In our analysis, the majority of patients had high grade or poorly differentiated histologies, had recurrent tumors, or were lymph node positive. With adjuvant RT, LRC was excellent amongst the patients with high grade or poorly differentiated pathologies as well as those with more indolent grade. More than half of the patients in this series presented with recurrent tumors up to 8 years after treatment of the initial lesion with excellent local control rates of the recurrent lesion. This suggests that patients should be followed routinely after initial surgical treatment especially in the presence of high risk features and no additional treatment.

In our series, most patients had one or more high risk factors and were therefore treated with adjuvant RT. Local and/or regional control was achieved in 100% of patients using one of two fractionations: 50Gy in 20 fractions or 60Gy in 30 fractions. Other single institution, small case series have demonstrated similar local control rates with adjuvant RT ranging from 93-100%.^{14, 24} In those two small series, varied radiation techniques were used and indications for radiation were primarily PNI and positive margin. No patients in these series had lymph node positive disease, whereas almost 50% of our patients did. Adjuvant RT demonstrated equally excellent local control in all three series.

Use of radiation as monotherapy has been reported in the literature with varied results. One report used radiation monotherapy for a lesion of the lower lip and clinically positive submental lymph node.²⁵ This patient had no evidence of disease at six months follow-up. Transformation into a more aggressive histology using radiation alone has been reported.¹⁵ Based on a population-based study from the Netherlands, patients who received radiation therapy alone had a higher risk of death, likely secondary to selection bias.⁵

Limitations of the study include its retrospective nature, small number of patients, long interval of treatment, and lack of comparison between similar patients treated with surgery alone. Although it is difficult to draw definitive conclusions from a small number of patients, post-operative radiation therapy offered excellent local control in patients with cutaneous adnexal carcinoma (with and without lymph node metastasis) with acceptable associated toxicity in our patient population.

Skin adnexal carcinomas are aggressive cutaneous malignancies with a propensity for local recurrence especially those with high risk features including perineural invasion, involved lymph nodes, positive margin, high grade, multi-focal disease, recurrent disease, or extracapsular extension. Initial surgical excision followed by adjuvant radiation offers excellent local-regional control for patients with skin adnexal carcinomas and risk factors for local-regional recurrence.

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Figure 1.
Locoregional Control and Progression Free Survival

Table 1

Patient Characteristics

Age/Gender	Location	Histology	Stage	Grade/differentiation	Recurrence?	Time to recurrence	PNI?	Pos margin?	Mutil-focal?	Region treated
52F	Neck mass	skin appendage carcinoma	III	poorly differentiated	Y	2 years	N	N	N	LN only
60M	Preauricular skin lesion	adnexal carcinoma with squamous differentiation	II	high grade	N	N/A	N	N	N	Primary + LN
68M	Preauricular skin lesion	adnexal carcinoma with sebaceous differentiation	III	poorly differentiated	Y	1 year	N	N	N	Primary + LN
88M	Neck mass	adnexal carcinoma	IVB	poorly differentiated	Y	9 months	N	N	N	LN only
72F	Lower lip	sclerosing sweat duct carcinoma	II	unknown	Y	8 years	Y	Y	N	Primary
57F	Scalp	mucinous	II	low grade	N	N/A	N	N	Y	Primary
74F	Scalp	porocarcinoma	IVA	high grade	Y	4 years	Y	N	N	Primary + LN
67F	Scalp	trichilemmal carcinoma	II	intermediate grade	N	N/A	N	N	Y	Primary
51M	Neck skin nodule	ductal eccrine adenocarcinoma	I	poorly differentiated	N	N/A	N	N	N	Primary + LN