CUTANEOUS METASTATIC SQUAMOUS CELL CARCINOMA TO THE PAROTID GLAND: ANALYSIS AND OUTCOME

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Abstract: Background: Our aim was to review the presentation, treatment, and outcome of patients with metastatic cutaneous squamous cell carcinoma involving the parotid gland at a tertiary referral center.

Methods: We performed a retrospective chart review of the cancer registry at the Princess Margaret Hospital, Toronto, from 1970 to 2001. All patients had a previously untreated metastatic cutaneous head and neck squamous cell carcinoma involving the parotid gland. A minimal follow-up of 1 year was mandatory for inclusion in the study.

Results: Fifty-six white patients (43 men and 13 women), with a median age of 76 years (range, 49–97 years), were eligible for inclusion. The disease in all patients was retrospectively staged according to a new system. Twenty patients had P1 disease, 14 had P2, and 22 had P3. Therapy included surgery and adjuvant external beam radiation in 37 patients, single-modality external beam radiation in 12, and surgery alone in seven patients. The overall recurrence rate was 29%. The disease-specific survival was significantly worse in patients treated with external beam radiation alone ($p < .05$). Tumor size $>6$ cm ($p < .01$) and the presence of facial nerve involvement ($p < .01$) were poor prognostic factors.

Conclusions: Metastatic cutaneous squamous cell carcinoma to the parotid gland is an aggressive neoplasm that requires combination therapy. The presence of a lesion in excess of 6 cm or with facial nerve involvement is associated with a poor prognosis. © 2004 Wiley Periodicals, Inc. Head Neck 26: 727–732, 2004

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Cutaneous malignancy is a common occurrence in the head and neck region. The most frequent histologic subtype encountered is basal cell carcinoma, followed by squamous cell carcinoma (SCC) (approximately 30%) and melanoma. The incidence of cutaneous SCC is increasing throughout the world. For example, in the southern hemisphere, the annual incidence in Australia has risen from 185 per 100,000 in 1985 to the current level of 300 per 100,000.¹ Physicians in the northern hemisphere (ie, North America) must be aware of this problem and its consequences, given the increase in migration and ease of travel. Characteristically, the patients are elderly white men of northern European descent with a history of lifelong exposure to ultraviolet radiation. In 95% of cases, the lesion presents within the head and neck region. Regional metastasis occurs

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in approximately 2% to 5% of patients. Parotid and cervical lymphatics represent the first echelon of lymph nodes affected by cutaneous SCC of the head and neck region.

The current American Joint Committee on Cancer (AJCC) staging system for cutaneous SCC metastatic to regional lymph nodes fails to adequately describe the extent of disease (Table 1). Therefore, O'Brien et al have recently proposed a new staging system that separates parotid gland from cervical lymph node involvement (Table 2). This has prompted us to review our experience with the treatment of cutaneous SCC metastatic to the parotid gland and report on disease-specific outcome with this new staging system.

**MATERIALS AND METHODS**

A retrospective chart review of the Princess Margaret Hospital cancer registry was carried out to identify those patients with a diagnosis of metastatic cutaneous SCC involving the parotid gland (1970–2001). All patients were treated with curative intent and a minimum follow-up of 1 year. Treatment of metastatic disease involving the parotid gland and/or neck lymphatics was based on disease extent. Patients in whom facial nerve function was normal preoperatively were treated with a conservative (ie, nerve sparing) parotidectomy. Patients with clinically positive neck lymphatics were treated with a modified radical neck dissection. Those patients whose disease was deemed surgically unresectable or who had significant comorbidities (ie, advanced age, intercurrent medical disease) that precluded prolonged anesthesia were treated with primary external beam radiotherapy (EBR).

Patient demographics (ie, age, sex), tumor characteristics (ie, size, facial nerve function, skin involvement, cervical lymph node involvement), treatment (ie, conservative vs radical parotidectomy, extent of neck dissection, primary vs adjuvant), and outcome data (ie, recurrence, disease status at final follow-up, length of follow-up) were collected. The extent of parotid disease was retrospectively classified according to O'Brien's new staging system (Table 2).

Disease outcome after primary treatment was defined as either alive with no disease, alive with disease, dead of disease, or dead of other causes. Follow-up was calculated from the date of primary treatment. Parametric data were evaluated with Student's t test. Nonparametric data were analyzed with the chi-square method. Survival was plotted with use of the Kaplan-Meier method, and actuarial survival curves were compared by use of the log-rank test. A Cox proportional hazards stepwise regression model was applied for factors significant for disease-specific outcome on univariate analysis (entry \( p < .05 \), removal \( p > .1 \)) All statistics were analyzed with SPSS Software version 11.0 (SAS Institute, Cary, NC). A \( p \) value of less than .05 was considered to be statistically significant.

**RESULTS**

**Patient and Tumor Characteristics.** Fifty-six white patients were eligible for inclusion in this review.
There were 13 women and 43 men, with a median age at presentation of 76 years (range, 49–97 years). All patients had a prior history of cutaneous SCC in the head and neck region. The median size of the parotid metastases was 4 cm (range, 1–12 cm). The facial nerve and overlying skin were involved in 13 patients. Clinically palpable neck nodes were identified in an additional six (11%) of 56 cases. Parotid disease was staged as P1 in 20 patients (36%), P2 in 14 patients (25%), and P3 in 22 patients (39%). Concomitant neck disease was classified as N1 in six of 56 patients (Table 3).

Treatment. Surgery was the mainstay of treatment in 47 patients (79%). Twenty-five patients (57%) received a conservative parotidectomy (nerve sparing), and 20 (43%) underwent a radical parotidectomy with sacrifice of the facial nerve, the overlying skin, or both. Adjuvant EBR encompassing the parotid gland and ipsilateral neck was used to treat 37 patients (79%) (Table 3). Twenty-eight patients (60%) underwent neck dissection; 24 (86%) of these dissections were elective and four (14%) were therapeutic. All patients who underwent a therapeutic neck dissection and four patients who underwent an elective neck dissection had pathologically proven metastatic SCC within cervical nodal tissue (ie, occult rate of 16%, four of 24). EBR alone was the treatment modality in 12 patients (20%) with parotid gland and/or neck disease.

Outcome. The overall recurrence rate was 29% (16 of 56). Tumors recurred at the primary site in six patients, in regional lymphatics in six patients, and at a distant site in four patients. Patients treated with combination therapy had a recurrence rate of 27% (10 of 37), those treated with surgery alone had a recurrence rate of 57% (four of seven), and patients who received EBR only had a recurrence rate of 17% (two of 12) (Table 4).

The 3-year disease-specific survival (DSS) as predicted by the Kaplan-Meier actuarial method was 70% for stage P1 (median follow-up, 2.9 years),
83% for P2 (median follow-up, 1.5 years), and 47% for P3 (median follow-up 1.1 years) \((p < .01)\) (Figure 1 and Table 5). The addition of neck disease at the time of treatment was not statistically significantly associated with a worse prognosis. The overall survival rate was 53% (median follow-up, 1.5 years). DSS rate by treatment approach was 72% for combination therapy, 80% for surgery alone, and 47% for those treated with EBR only \((p = .05)\) (Figure 2 and Table 4). Facial nerve paralysis at the time of presentation was an independent predictor of poor prognosis on multivariate regression \((p = .01)\).

**DISCUSSION**

Physicians from different specialties with varying experience often underestimate the pernicious behavior of cutaneous SCC affecting the head and neck region. Rowe et al\(^2\) reported an extensive review of the literature on cutaneous SCC of the face, ear, and lip. They identified certain risk factors associated with an increase in local recurrence and regional metastasis, such as index lesion \(>2\) cm in diameter, depth of invasion \(>4\) mm, poorly differentiated histopathologic findings, previous treatment, location (ie, ear, lip, scar or non–sun-exposed skin), and perineural invasion. In addition, other patient factors such as immunosuppression play a significant role in the development of an aggressive variant of cutaneous SCC.\(^2,5\) The implications of these disease factors for treatment selection and disease-specific outcome are frequently unrecognized by the treating surgeon. It is important, therefore, to understand the mechanism of spread in head and neck cutaneous SCC and to be cognizant of potential metastatic sites.

The parotid gland is known to contain lymph nodes within both the superficial and the deep lobes.\(^6–9\) These are the first echelons of nodes draining the skin of the ipsilateral eyelids, fronto-temporal region, posterior cheek, and anterior ear. Cutaneous SCC lying posterior to the ear, including the scalp, drain primarily to level V. Pathak et al\(^10\) clearly demonstrated these potential sites of lymph node metastases in patients with cutaneous melanoma. Lymph nodes associated with the external jugular vein are at risk from cutaneous SCC arising from both the retroauricular and the preauricular regions. A thorough evaluation of these sites is therefore imperative in all patients with primary cutaneous SCC involving the head and neck region. Despite the low metastatic rate of cutaneous SCC, however, close and careful observation of the clinically negative neck is mandatory in the follow-up of these patients.

Regional metastatic disease for carcinoma of the skin is currently classified by the AJCC as N1 (Table 1).\(^3\) This does not reflect the extent of both parotid gland and cervical lymph node involvement. O’Brien et al\(^4\) recognized this inadequacy when proposing a new classification for metastatic cutaneous SCC (Table 2). The goal of this new system is to separate parotid gland from cervical nodal involvement in an attempt to allow meaningful comparison of both disease extent and modes of treatment. This new classification was retrospectively applied to 87 patients with parotid and/or neck involvement from metastatic cutaneous SCC, and the addition of cervical nodal disease statistically significantly worsened the prognosis. In a similar review that used this staging system, Palme et al\(^11\) demonstrated that the extent of parotid gland disease (P1, P2, or P3) did affect DSS. Patients with small \((\leq 3\) cm) single parotid nodes had a higher DSS at 5 years (81%) than did those with extensive parotid disease \((>6\) cm) or with facial nerve or skull base involvement (33%). Our review similarly demonstrates a significantly worse prognosis in patients with stage P3 disease compared with patients with P1 and P2 lesions \((p < .01)\). Nearly 50% of patients with P3 lesions were dead of disease within 1 year of treatment. This confirms the importance of the extent of parotid gland involvement in patients with metastatic cutaneous SCC of the head and neck. Similarly, clinical involve-
ment of the facial nerve was associated with a worse prognosis ($p = .002$). The presence of facial nerve involvement suggests a more aggressive neoplasm, and O’Brien et al$^4$ recognized this fact by including facial nerve involvement as part of the P3 stage. The treatment approach in patients with metastatic cutaneous SCC to the parotid gland is a nerve-sparing parotidectomy when possible. However, in cases in which clinical, radiologic, and intraoperative evidence of facial nerve involvement is identified, a radical parotidectomy with facial nerve sacrifice is usually necessary. Continual controversy exists in the management of perineural spread involving the intratemporal component of the facial nerve. Evaluation of the extent of proximal facial nerve involvement by performing a cortical mastoidectomy may assist in the planning of postoperative EBR (eg, intensity-modulated radiotherapy).

In our series, most patients were treated with both surgery and adjuvant EBR. Ten patients had recurrences after dual-modality therapy; six had recurrences after single-modality treatment. This was not statistically significant ($p = .88$). When comparing DSS by treatment approach, we identified a significantly worse outcome in patients treated with EBR alone ($p < .05$) (Figure 2). Clearly, this confirms results by Palme et al$^{11}$ and others$^{12–14}$ that the best outcome in this disease is achieved with combination therapy. However, we do recognize that there are significant limitations to our analysis. This is a retrospective review spanning some 30 years and therefore includes various treatment philosophies held by physicians at the time of presentation in addition to significant variations in both imaging modalities and EBR. The poor result achieved by radiotherapy alone is clearly indicative of advanced disease extent, because the disease in most patients treated in our group was deemed unresectable at the time of presentation. Similarly, the good DSS enjoyed by patients who underwent surgical resection alone can be explained by the early stage of their disease at presentation.

The standard management of the clinically positive neck is to perform a modified radical neck dissection.$^{15}$ Recent data, however, suggest performing a selective neck dissection with adjuvant EBR in patients with limited neck disease (single, ipsilateral, upper level node <3 cm).$^{16}$ Veness et al$^{17}$ recently reported on 74 patients seen with metastatic cutaneous SCC of the head and neck involving only the cervical lymph node (levels I–V). In patients treated with surgery and adjuvant EBR, the extent of neck surgery (modified radical vs selective neck dissection) did not significantly alter locoregional recurrence or DSS. These findings suggest that a more conservative approach to the clinically positive neck may be appropriate in patients with limited neck disease. Clearly, the number of patients with neck disease was low in this study and therefore was not statistically relevant for DSS. However, we are currently assessing the efficacy of performing selective neck dissections for low-volume and upper level neck disease. We believe that this approach reduces morbidity experienced by the patient and has disease-specific outcome comparable with that of more radical neck surgery when combined with adjuvant EBR.

**CONCLUSION**

Metastatic cutaneous SCC to the parotid gland, neck lymphatics, or both is an aggressive malignancy with a poor prognosis that ranges between 30% and 75%.$^{2,4,12}$ Our results demonstrate a similarly poor outcome with an overall DSS of 52% at 2 years. Disease extent is a significant predictor of disease-specific outcome, and we identified stage P3 and the presence of facial nerve involvement as statistically significant poor prognostic factors ($p < .01, p < .01$).

For all patients with metastatic cutaneous SCC of the parotid gland, neck lymphatics, or both, we recommend a comprehensive treatment approach consisting of surgery and adjuvant EBR. In addition, we advocate a change to the current staging system of metastatic cutaneous SCC of the head and neck in an attempt to better stage disease extent. This will allow better prognostication and comparison of treatment regimens, both within and between institutions managing this complex disease. Further multiinstitutional and international trials are required to test staging systems (such as the one proposed by O’Brien et al$^4$) before these can be uniformly applied for the routine management of patients with metastatic cutaneous SCC of the head and neck.

**REFERENCES**

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