Extent of Parotid Disease Influences Outcome in Patients With Metastatic Cutaneous Squamous Cell Carcinoma

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**Objectives:** To test a new clinical staging system in patients with metastatic cutaneous squamous cell carcinoma involving the parotid gland or lymph nodes of the neck.

**Design:** Retrospective analysis of clinicopathological data from patients with a minimum of 2 years’ follow-up.

**Setting:** Multidisciplinary head and neck unit in a tertiary referral center.

**Patients:** Between 1987 and 1999, 126 patients (104 men and 22 women; median age, 69 years) were treated for metastatic cutaneous squamous cell carcinoma involving the parotid and/or neck.

**Main Outcome Measures:** Locoregional recurrence and disease-specific survival.

**Results:** Of the 126 patients, disease involved the parotid gland in 81 patients, of whom 14 also had clinical neck disease, while 45 patients had neck involvement only. Parotid stages were as follows: P0, 45 patients; P1, 55; P2, 20; and P3, 6. Neck stages were: N0, 67 patients; N1, 31; and N2, 28. Treatment involved combined surgery and radiotherapy in 93 patients, surgery alone in 12, and radiotherapy alone in 18. Three patients received palliative treatment only. There were 47 therapeutic and 40 elective neck dissections. Pathologic evaluation demonstrated parotid involvement in 70 patients and neck involvement in 51, representing 44 therapeutic and 7 elective neck dissections. Disease involved both the parotid and neck in 19 patients. The 5-year local (parotid) control rate was 80% and this varied statistically significantly with P stage. Parotid stages 2 and 3 were independent risk factors for a decrease in local control rate using multivariate analysis. The 5-year disease-specific survival rate for the entire group was 68% and P stage significantly influenced survival: P0, 60%; P1, 81%; P2, 51%; and P3, 33% (*P* < .001). Pathological involvement of neck nodes did not worsen survival of patients with parotid disease. Overall multivariate analysis demonstrated that single-modality therapy, P3 stage, and presence of immunosuppression independently predicted a decrease in survival.

**Conclusions:** These results confirm that the extent of metastatic disease in the parotid gland significantly influences outcome and suggests that staging the parotid separately in metastatic cutaneous squamous cell carcinoma may be useful. Further evaluation of the recommended staging changes with a larger patient cohort will be required to clarify the influence of neck node involvement.


A recent study from Royal Prince Alfred Hospital in Sydney analyzed the treatment results in 87 patients with metastatic SCC involving the parotid gland and drew attention to the limitations of the current American Joint Committee on Cancer staging for metastatic cutaneous malignancy. Results demonstrated that the extent of parotid disease and the presence of neck metastases may independently influence outcome in this group of patients.

A new staging system that separated parotid (P stage) from neck involvement (N stage) was recommended. The proposed staging system is shown in Table 1.

The aim of the present study was to test this new staging system in a group of patients with metastatic cutaneous SCC involving the parotid gland and neck from another institution (Westmead Hospital, Sydney).
Patients were eligible for this study if they had clinical metastatic cutaneous SCC involving the parotid and/or neck, no previous treatment, and a minimum follow-up period of 2 years. All the patients were treated in a multidisciplinary head and neck oncology unit (Westmead Hospital).

The relevant patient data had been prospectively recorded onto the database of the institution; however, the patients were restaged according to the proposed new staging system for the present study.

Treatment of the parotid and/or neck was based on the extent of the metastatic disease. Localized, mobile tumors with normal facial nerve function were treated by a conservative parotidectomy, sparing the facial nerve. Patients with massive disease or clinical facial nerve palsy had a radical parotidectomy. Clinical neck disease was treated by a modified radical neck dissection. Clinically negative necks were treated by radiotherapy or a selective neck dissection encompassing either levels I-III or I-IV. Adjuvant radiotherapy was recommended if there were close or involved surgical margins within the parotid specimen or more than 1 node or extracapsular spread in the neck.

Patients who were unfit or refused surgery were treated with definitive radiotherapy.

Statistical analysis of proportions was carried out using the $\chi^2$ test. Cumulative recurrence and survival data were calculated using the Kaplan-Meier method and curves were compared using the log-rank test. Multivariate analysis of factors influencing local control and survival was carried out using the Cox method of proportional hazards.

RESULTS

A total of 128 patients were treated for metastatic cutaneous SCC involving the parotid gland and/or neck between 1987 and 1999. The records of 126 patients were analyzed after the exclusion of 2 patients who were lost to follow-up. There were 104 men and 22 women, with a mean age of 69 years (range, 24-100 years). The minimum follow-up period was 2 years. Immunosuppression was a comorbidity in 18 patients, with hematological malignancies being the cause in 6, renal transplant in 4, and corticosteroid therapy in 8.

Disease involved only the parotid gland in 67 patients, the parotid and neck in 14, and only the neck in 45. Tumors involving the parotid gland were staged P0 in 45 patients, P1 in 55, P2 in 20, and P3 in 6. Patients with neck disease were staged N0 in 67 cases, N1 in 31, and N2 in 28. The 45 patients with disease only in the neck were staged P0. These findings are summarized in Table 2.

Clinical neck disease was present in 18% of patients staged P1, 20% of those staged P2, and none of those staged P3. Overall, only 14 (17%) of 81 patients with clinical parotid disease had clinical disease in the neck.

Among 67 patients with disease only in the parotid gland, 58 had a parotidectomy, 40 also had an elective neck dissection, 53 had postoperative radiotherapy, and 8 were treated with radiotherapy alone.

Among 45 patients with disease only in the neck, 35 had a neck dissection and 8 of these also had a parotid resection. Adjuvant radiotherapy was given to 30 of the 35 patients who had a neck dissection. Nine patients in this group were treated with radiotherapy alone. All 8 “ elective” parotidectomies were histologically negative.

In the group of 14 patients with disease in both the parotid gland and the neck, 12 were treated by parotidectomy and neck dissection. Postoperative radiotherapy was delivered to the neck in 10 of these cases and the parotid in 9. Three patients, one from each group, were treated with palliative intent only.

In summary, 105 of 126 patients had surgical treatment and 93 of these (89%) received adjuvant radiotherapy. A total of 18 patients were treated with radiotherapy alone and 3 received palliative treatment. All 70 clinically parotid glands were pathologically positive for SCC.

Clinically positive neck nodes were pathologically positive in 44 (94%) of 47 therapeutic dissections, while 7 (18%) of 40 electively dissected necks contained positive lymph nodes. The incidence of positive neck pathology among patients with parotid disease was 36%, comprising 12 patients with clinically positive parotids and necks who had dissection and the 7 electively dissected (19 of 52 patients).

Disease recurred in the parotid region in 17 patients, the neck in 18, and at distant sites in 6. Local control decreased as parotid disease increased from P0 to P3 and this was statistically significant (Figure 1). Multivariate analysis using the Cox proportional hazards method indicated that P2 and P3 stage independently predicted for a reduced local control in the parotid region. P stage also significantly influenced survival in patients who had parotid disease (Figure 2). Cumulative 5-year disease-specific survival rates were 60% for P0 (ie, those with neck disease only at presentation), 81% for P1, 51% for P2, and the 2-year disease-specific survival for patients with P3 was 33% (P<.001). Neck disease in patients who had metastatic involvement of the parotid did not influence sur-

**Table 2. Clinical Stage of Parotid and Neck Disease in 126 Patients**

<table>
<thead>
<tr>
<th></th>
<th>N0</th>
<th>N1</th>
<th>N2</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>P0</td>
<td>0</td>
<td>22</td>
<td>23</td>
<td>45</td>
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<td>P1</td>
<td>45</td>
<td>7</td>
<td>3</td>
<td>55</td>
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<tr>
<td>P2</td>
<td>16</td>
<td>2</td>
<td>2</td>
<td>20</td>
</tr>
<tr>
<td>P3</td>
<td>6</td>
<td>0</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>Total</td>
<td>67</td>
<td>31</td>
<td>28</td>
<td>126</td>
</tr>
</tbody>
</table>

**Table 1. Clinical Staging System for Metastatic Cutaneous Squamous Cell Carcinoma of the Parotid and/or Neck**

<table>
<thead>
<tr>
<th></th>
<th>Parotid</th>
<th>Neck</th>
</tr>
</thead>
<tbody>
<tr>
<td>P0</td>
<td>No clinical disease in the parotid</td>
<td>No clinical disease</td>
</tr>
<tr>
<td>P1</td>
<td>Metastatic node up to 3 cm in diameter</td>
<td>Single ipsilateral neck node up to 3 cm in diameter</td>
</tr>
<tr>
<td>P2</td>
<td>Metastatic node &gt;3 cm and up to 6 cm in diameter or multiple nodes</td>
<td>Single node &gt;3 cm in diameter or multiple nodes or contralateral nodes</td>
</tr>
<tr>
<td>P3</td>
<td>Metastatic node &gt;6 cm in diameter or disease involving the facial nerve or skull base</td>
<td>N0: No clinical disease</td>
</tr>
</tbody>
</table>

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vival (Figure 3). Also in these patients with neck disease, there was no survival difference between the proposed stages, although there was a trend toward a reduced survival in the N2 group (Figure 4). Treatment by surgery with or without and adjuvant radiotherapy resulted in statistically better survival compared with radiotherapy alone. There was no difference in survival among patients treated with surgery alone compared with dual-modality therapy (Figure 5).

Immunosuppressed patients had a significantly worse outcome (Figure 6). Overall, when multivariate analysis was performed, single-modality treatment, P3 stage, and the presence of immunosuppression independently predicted for a reduced survival.

The overall recurrence rate was 33% (41 of 126), with a mean time to recurrence of 9 months and the 5-year disease-specific survival after treatment for recurrent SCC was only 17%. A total of 34 of patients who developed recurrence died of their disease, with a mean survival after treatment of 15 months.

The overall disease-specific survival rate for the 126 patients was 68% at 5 years.

**COMMENT**

Patients with metastatic cutaneous cancer involving the lymph nodes of the parotid gland or neck present a significant management problem. The American Joint Com-
mittee on Cancer staging system classifies these patients as having N1 disease irrespective of the extent of regional involvement. A recent study from Royal Prince Alfred Hospital has highlighted the inadequacy of the current staging classification by proposing a new staging system, which separates parotid disease (P stage) from neck disease (N stage) and subdivides each region according to clinical extent of disease. The outcome of that pilot study indicated that patients with metastatic SCC in the parotid gland had a significantly better survival than patients with disease in both parotid and neck. In addition, local control rates in the parotid region correlated significantly with P stage.

In the present study we set out to test this new system on a sample of patients treated at another institution. A total of 74% of patients in this series were treated with combined surgery and radiotherapy, fewer than the 86% who had combined therapy in the Royal Prince Alfred Hospital series. Single-modality therapy was given in 30 patients (24%) while 3 patients were offered palliation only due to significant comorbidities. Recent reports have suggested that local control and survival are improved with combined modality treatment and in the present study survival was superior in patients who had combined therapy (or surgery alone) compared with patients who were treated with radiotherapy only. Patients treated with surgery alone, however, had lesser disease than those treated with combined therapy. These results concur with those in other series and it remains our policy to recommend combined surgery and postoperative radiotherapy.

Local extent of disease is the most important prognostic factor in primary parotid cancer and the importance of the extent of metastatic disease in the parotid gland was confirmed in the present study. Both survival and locoregional recurrence varied significantly with P stage. In patients with disease in the parotid gland, 35% also had disease in the neck either clinically or subclinically; however, patients with neck disease did not have a worse outcome than those with disease just in the parotid. This is in contrast to the very significant negative influence of neck metastases demonstrated in our previous study. In that series, the occult metastatic rate was 34% and, overall, 52% of patients treated with a neck dissection had positive pathologic findings.

The cause for this difference is not clear and we suggest the need for evaluation of a larger cohort of patients to clarify this issue. Also, separating neck disease into N0, N1, and N2 stages did not prove significant in this sample of patients, although there was a clear trend to a worse outcome for patients with N2 involvement (Figure 4).

Immunosuppression was associated with a worse survival in this group of patients. This has been well supported in the literature and recently described in a study by Veness et al, who found that 4% of patients after organ transplantation developed an aggressive cutaneous malignancy and 44% died of their disease.

Our study concludes that local extent of parotid disease (P stage) is an important prognostic factor among patients with metastatic cutaneous SCC. A multi-institutional, and preferably international, study is required to clarify the significance of cervical node involvement in this disease. When sufficient validated data have been accrued, a change to the current TNM staging system for cutaneous malignancy, in the head and neck at least, may be appropriate.

Accepted for publication March 14, 2003.

This study was presented at the annual meeting of the American Head and Neck Society, Boca Raton, Fla, May 12, 2002.

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