The Role of Total Parotidectomy for Metastatic Cutaneous Squamous Cell Carcinoma and Malignant Melanoma

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IMPORTANCE Metastatic cutaneous malignancies of the head and neck, including cutaneous squamous cell carcinoma (cSCC) and malignant melanoma (MM), are aggressive cancers frequently involving the parotid-area lymph nodes (LNs). In such cases, controversy exists about the extent of surgical resection, with many centers choosing not to remove the parotid deep lobe LNs.

OBJECTIVES To determine patterns of intraparotid and neck metastasis, to identify risk factors, and to report outcomes in patients with parotid superficial lobe LN metastasis from cSCC and MM.

DESIGN, SETTING, AND PARTICIPANTS We retrospectively reviewed 65 adults from Mayo Clinic in Minnesota who underwent total parotidectomy and neck dissection for metastatic cSCC (n = 42) or MM (n = 23) involving the parotid superficial lobe.

INTERVENTIONS Total parotidectomy and neck dissection.

MAIN OUTCOMES AND MEASURES The presence and number of parotid deep lobe and neck LNs involved with metastatic disease were assessed. Risk factors associated with metastatic spread to the parotid deep lobe were identified, and patient outcomes are reported.

RESULTS Eleven of 42 patients with cSCC (26%) and 3 of 23 patients with MM (13%) metastatic to the parotid superficial lobe also had parotid deep lobe metastasis. Thirteen of 42 patients with cSCC (31%) and 6 of 23 patients with MM (26%) had positive cervical LN metastasis. Among all patients, 22% (14 of 65) had metastasis to the parotid deep lobe, and 29% (19 of 65) had metastasis to cervical LNs. By univariate analysis, neck metastasis and N2 neck disease were risk factors for metastatic cSCC spread to the parotid deep lobe. Parotid-area local control was excellent in patients with metastatic cSCC (93% [39 of 42]) and MM (100% [23 of 23]). Long-term survival remains poor because distant metastases are common.

CONCLUSIONS AND RELEVANCE Metastatic cSCC and MM to the parotid superficial lobe also involve LNs in the parotid deep lobe and neck in a significant and almost equal number of patients. Parotid deep lobe metastasis from cutaneous malignancies portends a poor prognosis. Therefore, patients with superficial parotid gland metastasis should be considered for management with not only neck dissection and adjuvant therapy but also deep lobe parotidectomy.
The embryological development of the parotid gland and its relationship with the facial nerve (FN) pose important considerations and challenges in parotid surgery. During development, the FN migrates anteriorly from the stylo-mastoid foramen and becomes surrounded by the parotid gland. The separation of the parotid gland into superficial and deep lobes by the FN is a surgical division and not an embryological or fascial one. Therefore, no barrier exists to malignant spread between the superficial and deep lobes directly or via lymphatic channels traversing the gland. In addition, as the parotid gland becomes encapsulated by fascia, a variable but significant number of lymph nodes (LNs) are incorporated into the gland superficial and deep to the FN. Studies have reported mean totals of 6 to 9 (range, 2-22) parotid superficial lobe LNs and 1 to 2 (range, 0-9) parotid deep lobe LNs.

The parotid-area LNs are a common location for the development of metastasis from high-risk cutaneous malignancies of the head and neck originating from the frontotemporal scalp, face, and ear. Patients with palpable or confirmed parotid-area LN metastasis from cutaneous squamous cell carcinoma (cSCC) or malignant melanoma (MM) generally undergo a superficial parotidectomy and often an accompanied neck dissection. Controversy exists about the need to remove the parotid gland tissue deep to the FN. Despite aggressive multimodality treatment, including surgery and irradiation with or without chemotherapy, patients with metastatic cSCC or MM to the parotid gland have high rates of parotid-area local recurrence, distant metastasis, and poor outcomes.

The aim of this study was to determine the presence and quantity of parotid deep lobe LNs and ipsilateral cervical LNs involved with metastatic cSCC or MM when metastasis has developed in the parotid superficial lobe LNs. Risk factors associated with metastatic spread of cSCC and MM to the parotid deep lobe and patient outcomes are discussed.

Methods

Institutional review board approval was obtained from Mayo Clinic in Minnesota. Written informed consent was obtained from all participants through Mayo Clinic’s tumor registry. A retrospective review from January 1, 1994, through December 31, 2010, was performed among all adult patients undergoing a superficial parotidectomy with concomitant deep lobe parotidectomy and neck dissection for cSCC or MM metastatic to the parotid superficial lobe LNs at a tertiary referral center. An en bloc deep lobe parotidectomy is defined as removal of all remaining parotid gland after superficial parotidectomy and includes the tissue deep to the FN. The FN was preserved in most cases (total parotidectomy with FN preservation). However, any FN branches directly invaded by tumor were resected with negative margins using frozen section pathological techniques. Branches not directly invaded by tumor were preserved (total parotidectomy with partial FN sacrifice). Last, if the main trunk of the FN was invaded by tumor or if no FN branches could be spared because of tumor involvement, the main trunk was sacrificed (total parotidectomy with complete FN sacrifice). The FN function was assessed in patients who underwent FN preservation procedures, and the weakest scores documented within the first month following surgery and at 1 year after surgery were recorded using the grading system by House and Brackmann. Pathology reports were reviewed, and patients were included in the study if the final pathological examination demonstrated parotidectomy specimens positive for metastatic cSCC or MM. The total numbers of LNs involved by metastatic disease in each lobe of the parotid gland, superficial and deep, and in the neck dissection were recorded. Patients were excluded if the cutaneous tumors had directly invaded the parotid gland and did not represent metastatic disease or if a massive metastatic tumor focus involved both the parotid superficial and deep lobes such that the origin within the parotid gland could not be determined. Also, any patient in whom a total parotidectomy or neck dissection was not performed was excluded.

Standard statistical analysis was used to summarize the data. Comparisons of cSCC and MM mean numbers of LNs in parotidectomy specimens were made using unpaired t test. Risk factors for metastatic spread of cSCC to parotid deep lobe LNs were identified by univariate analysis. Associations were summarized using odds ratios and corresponding 95% CIs calculated with the parameters estimated in the models. The following outcomes were estimated using the Kaplan-Meier method: disease-free survival (survival free of any recurrence), disease-specific survival (survival from disease), overall survival (survival from all causes), local control (survival free of any parotid-area recurrence), locoregional control (survival free of any parotid-area and neck recurrence), and distant control (survival free of any distant metastasis). Risk factors for poor outcomes were identified using hazard ratios (HRs) and corresponding 95% CIs calculated with the parameters estimated in the models. P ≤ .05 was considered statistically significant.

Analyses were performed using a software program (JMP, version 9.0; SAS Institute Inc).

Results

Patients With cSCC and MM, Tumor Characteristics, and Treatments

Sixty-five adults were included who underwent deep lobe parotidectomy and ipsilateral neck dissection following superficial parotidectomy with frozen section pathological confirmation of metastatic cSCC (n = 42) or MM (n = 23) to the parotid superficial lobe LNs. Patient demographics and treatments are listed in Table 1. Sixty patients were male, including 38 of 42 patients with cSCC (90%) and 22 of 23 patients with MM (96%). The mean ages at the time of parotidectomy were 74.7 and 67.5 years for patients with cSCC and MM, respectively. The median follow-up times were 36.4 and 30.6 months for patients with cSCC and MM, respectively. Most patients underwent total parotidectomy with FN preservation, including 32 patients with cSCC (76%) and 21 patients with MM (91%). In patients undergoing total parotidectomy with FN preservation, the median early postoperative House-Brackmann score was 3 (range, 1-6). At 1 year after
surgery, the median House-Brackmann score was 1 (range, 1-3). The remaining patients had direct FN invasion with metastatic tumor requiring partial or total FN sacrifice. Most patients also underwent adjuvant therapy in the form of irradiation or chemoradiotherapy, including 36 patients with cSCC (86%) and 14 patients with MM (61%).

Tumor, staging, and pathological characteristics are listed in Table 2. Most cutaneous primaries originated from the face, scalp, or ear. All patients had metastatic spread to the parotid superficial lobe LNs. Eleven of 42 patients with cSCC (26%) and 3 of 23 patients with MM (13%) had separate metastasis to both the superficial and deep parotid lobe LNs. No cases were observed of isolated parotid deep lobe metastasis in which the superficial lobe was absent of tumor. Thirteen patients with cSCC (31%) and 6 patients with MM (26%) had positive cervical LN metastasis following neck dissection. Pathological staging was performed, including the parotid staging system (P stage) by O’Brien et al.12 and the seventh edition of the American Joint Committee on Cancer Cancer Staging Manual.16

The means and ranges of positive and total LNs from each parotid lobe specimen are listed in Table 3. When comparing metastatic cSCC and MM, similar means of positive and total LNs were observed in the parotid superficial and deep lobes. The cSCC and MM superficial lobe specimens contained 1.7 and 1.8 mean positive LNs ($P = .76$) out of 5.9 and 6.3 mean total LNs ($P = .75$), respectively. The cSCC and MM deep lobe specimens contained 0.4 and 0.4 mean positive LNs ($P = .76$) out of 1.8 and 2.6 mean total LNs ($P = .14$), respectively. The total numbers and ranges of LNs in the parotid superficial and deep lobes are similar to those reported previously.7-5

**Risk Factors for cSCC and Patient Outcomes**

Features associated with metastatic spread of cSCC to the parotid deep lobe were identified and are listed in Table 4. By univariate analysis, risk factors that reached statistical significance included positive neck metastasis and N2 neck disease. Sex, age, FN invasion, extracapsular spread, location of cutaneous primary, and size of parotid superficial lobe metastasis did not correlate with an increased risk of parotid deep lobe metastasis.
Three of 42 patients with cSCC (7%) developed local recurrence within or adjacent to the parotid bed following total parotidectomy, neck dissection, and postoperative irradiation. Two patients developed recurrence adjacent to the parotid bed, one within the masseter muscle and the other along the skull base adjacent to the parapharyngeal space. One patient developed intradural recurrence in the skin overlying the parotid bed. The cSCC 5-year local control rates in patients without parotid deep lobe metastasis and with parotid deep lobe metastasis were 92% (24 of 26) and 89% (8 of 9), respectively (P = .69) (Figure 1A). Two patients with cSCC developed local recurrence in the neck following total parotidectomy, neck dissection, and adjuvant irradiation. The cSCC 5-year locoregional control rates in patients without parotid deep lobe metastasis and with parotid deep lobe metastasis were 88% (23 of 26) and 78% (7 of 9), respectively (P = .35) (Figure 1B). Nine of 42 patients with cSCC (21%) developed distant metastasis. Freedom from distant metastasis at 5 years was significantly improved in patients who did not have parotid deep lobe metastasis (76%) compared with those who had parotid deep lobe metastasis (36%) (P < .01) (Figure 1C). Patients who had parotid deep lobe metastasis also had statistically significant decreases in disease-free survival (P < .01), disease-specific survival (P < .02), and overall survival (P < .01) compared with patients who did not have deep lobe metastasis (Figure 2).

In the final model, cSCC parotid deep lobe metastasis was a significant risk factor for several variables. It was a significant predictor of distant metastatic disease (HR, 5.35; 95% CI, 1.30-20.65; P = .02), disease recurrence (HR, 3.49; 95% CI, 1.15-9.85; P = .03), death from disease (HR, 3.73; 95% CI, 1.07-12.07; P = .04), and death from all causes (HR, 2.89; 95% CI, 1.19-6.69; P = .02).

**Risk Factors for MM and Patient Outcomes**

For metastatic MM, 0 of 23 patients (0%) developed parotid-area local recurrence. However, 6 of 23 patients (26%) developed regional recurrence in the neck. In addition, 11 of 23 patients (48%) developed distant metastatic disease. The 3 patients with deep lobe metastasis all had regional recurrence in the neck within 10 months following surgery, and deep lobe metastasis was a significant risk factor for locoregional failure (P < .001). One patient with parotid deep lobe metastasis developed distant metastasis to the liver and adrenal gland. Two of 3 patients with parotid deep lobe metastasis died of their disease, while the third was alive with disease at the last follow-up date. Analysis of possible risk factors for metastasis to the parotid deep lobe was not performed because there were only 3 such cases.

**Discussion**

Metastatic cutaneous malignancies of the head and neck, including cSCC and MM, are aggressive cancers frequently involving the parotid-area LNs. In such cases, controversy exists about the extent of surgical resection. Many centers routinely perform superficial parotidectomy and neck dissection with postoperative irradiation in patients with metastatic cSCC or MM to the parotid superficial lobe. Some surgeons may not remove the parotid deep lobe because few LNs lie in the deep lobe and irradiation can be used to treat any deep lobe metastasis. This argument to leave the parotid deep lobe LNs at the time of surgery is in contrast to the general practice to perform neck dissection for cervical LN removal when there is metastasis to the superficial lobe of the parotid gland. At our institution, total parotidectomy with FN preservation and neck dissection is routinely performed at the same operation for patients with metastasis to the parotid superficial lobe confirmed by frozen section pathological techniques.

Approximately 20% to 25% of the parotid gland, including LNs, is contained within the parotid deep lobe. Without a true barrier to metastatic spread from the parotid superficial lobe to the deep lobe, one may expect a 20% to 50% risk of metastasis.
25% rate of metastasis to the deep lobe LNs when the superficial lobe LNs are involved with tumor. In this series, the finding of parotid deep lobe metastasis was consistent with the approximate proportion of deep lobe LNs, namely, 26% (11 of 42) for patients with cSCC and 13% (3 of 23) for patients with MM (22% [14 of 65] for all patients). To our knowledge, this information has not previously been reported. Most patients with tumor involving the parotid deep lobe were found to have separate foci of tumor metastasis within both the superficial and deep lobes. Our findings show that some...
patients with cutaneous malignancies metastatic to the parotid superficial lobe LNs will have occult metastasis in the deep lobe. No patients were found to have isolated parotid deep lobe metastasis without also having superficial lobe metastasis. Therefore, the idea of skip metastasis directly to the deep lobe and not involving the superficial lobe is unlikely or rare with cutaneous malignancies.

Patients with metastatic cSCC and MM to the parotid superficial lobe LNs had similar rates of metastatic spread to cervical LNs, namely, 31% (13 of 42) and 26% (6 of 23), respectively (29% [19 of 65] for all patients). This finding is consistent with prior studies. Our results showed a similar finding of metastasis to the parotid deep lobe LNs, with an overall rate of 22% (14 of 65). In addition, parotid deep lobe metastasis and cervical metastasis often occurred in the same patients. Six of 11 patients with cSCC metastasis and 2 of 3 patients with MM metastasis to the parotid deep lobe had cervical LN metastasis. The data from this series suggest that the pattern of spread for many metastatic cutaneous malignancies of the head and neck is from the first LN echelon within the parotid superficial lobe to second LN echelons within the parotid deep lobe and neck. Metastatic spread to the parotid deep lobe and neck occurred at similar frequencies and often occurred together, with both representing a more advanced and aggressive cancer. As such, we recommend considering total parotidectomy with ipsilateral neck dissection in patients with parotid superficial lobe LN metastasis.

The treatment approach described has allowed for excellent parotid-area local control, 93% (39 of 42) for patients with cSCC and 100% for patients with MM. Ideally, a comparison group of patients with metastatic cSCC or MM to the parotid superficial lobe who did not receive a parotid deep lobe removal would be used to analyze the benefit of deep lobe parotidectomy. Unfortunately, a comparison group was not available at our institution. However, our low parotid-area recurrence rate is better than the rates among other studies in the literature (range, 11%-44%). The low local recurrence rate in this series is likely attributable to the routine resection of the entire parotid gland, both superficial and deep lobes, in patients with parotid superficial lobe LN metastasis. The parotid deep lobe can be safely removed en bloc with FN preservation as has been described in earlier studies. In addition, the long-term FN outcomes are not significantly different compared with superficial parotidectomy, with a median House-Brackmann score of 1 at 1 year following surgery. Most patients with recurrent metastatic cSCC and MM had distant failure (21% [9 of 42] and 48% [11 of 23], respectively). In patients with cSCC, parotid deep lobe metastasis was a significant risk factor for distant metastasis and poorer survival outcomes. This information is valuable in counseling patients and physicians on the prognosis of parotid deep lobe metastasis. Despite poor distant control and overall outcomes, locoregional control is of importance in slowing disease progression and improving symptoms. Therefore, these patients should be treated with multimodality therapy, including appropriate extent of surgical resection.

Conclusions

In summary, surgical removal of the parotid deep lobe should be considered when superficial parotidectomy specimens contain metastatic cSCC or MM. The frequency of parotid deep lobe metastasis almost approaches the frequency of cervical metastasis. Removing the parotid deep lobe and treating with adjuvant therapy leads to a lower rate of parotid-area local recurrence compared with other series in which the parotid deep lobe is not routinely removed but rather the parotid superficial lobe is routinely removed and then treated with adjuvant therapy. The presence of parotid deep lobe metastasis remains a harbinger of increased risk of distant disease and poor outcomes, and this new information is useful in treatment planning and in counseling patients and physicians.


