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Parotid Region Lymphatic Mapping and Sentinel Lymphadenectomy for Cutaneous Melanoma

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Background: Routine elective superficial parotidectomy for patients with primary cutaneous melanomas of the scalp, auricle, or face has been questioned. We evaluated an alternative, i.e., lymphatic mapping and sentinel lymphadenectomy, for patients with primary cutaneous melanomas draining to the region of the parotid gland.

Patients: Retrospective review of our large (>8000 patients) melanoma database identified 39 patients with primary melanomas (American Joint Committee on Cancer stage I or II) of the scalp (n = 19), auricle (n = 11), or face (n = 9) who underwent intraoperative lymphatic mapping to identify a sentinel node (SN) in the region of the parotid gland, between June 1985 and July 1997.

Results: A SN was identified in the parotid region of 37 patients (94.9%), four of whom had SN metastases. The mean number of SN obtained was 2.3/patient (range, 1-4/patient). The two patients (5.1%) for whom a parotid-region SN could not be identified underwent superficial parotidectomy during the same operation. Among the 33 patients with tumor-free SN, with a median follow-up period of 33.2 months (range, 1-121 months), there was one (3.1%) intraparotid recurrence; thus, the false-negative rate was 3.1%. The procedure-related surgical morbidity rate was only 2.6% (one case of temporary facial nerve paresis).

Conclusions: For patients with primary melanomas of the scalp, auricle, or face, sentinel lymphadenectomy can be performed accurately in the parotid region and offers a low-morbidity alternative to routine elective superficial parotidectomy.

Key Words: Melanoma—Sentinel node—Parotid gland.

Although retrospective reviews[1] suggest a survival benefit when patients with melanoma are treated with immediate elective lymph node dissection (ELND) of the regional lymphatic basin, no prospective randomized trial has supported routine ELND of the regional lymph nodes.[2–4] Because of the variable lymphatic drainage patterns in the head and neck region, these prospective trials have not specifically examined the role of ELND and elective parotidectomy in the management of cutaneous melanoma of the head and neck region.

Morton et al.[5] described lymphatic mapping and sentinel lymphadenectomy (SLND) as a less morbid procedure to identify patients with melanoma harboring clinically occult metastatic melanoma in the regional lymph nodes. Using a vital blue dye, those authors initially reported an accuracy rate of 82% for intraoperative mapping of lymphatic drainage from primary melanomas of the head and neck[6]; the sentinel node (SN) was identified in the cervical lymphatic basin in 90% of cases. Subsequent studies of lymphatic mapping based on observation of the blue dye plus detection of a radiopharmaceutical agent have increased the SN identification rate to 95-96% in patients with head and neck melanomas.[7–10]

SLND is technically more challenging in the area of the parotid gland than in other lymphatic drainage sites. We therefore examined its accuracy, sensitivity, and

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morbidity in patients with cutaneous melanoma draining to the region of the parotid gland.

PATIENTS AND METHODS

Patients

The melanoma database of our institution was reviewed to identify all patients treated between June 1985 and July 1997 for American Joint Committee on Cancer stage I or II melanoma of the scalp, auricle, or face. Our study population consisted of the 39 patients (35 male and 4 female patients) for whom intraoperative lymphatic mapping was undertaken to identify a SN in the parotid region. This group excluded patients with clinically palpable parotid region lymphadenopathy (including intraparotid metastases) and patients who had already undergone wide local excision of the primary tumor, requiring a skin graft or rotational skin flap, or any other surgical intervention that would disrupt the lymphatic drainage pattern from the primary tumor. Lymphoscintigram reports, surgical notes, histopathological findings, and the postoperative course were recorded for analysis.

Preoperative Cutaneous Lymphoscintigraphy

Because the lymphatic drainage patterns from melanomas of the head and neck are often ambiguous,[6] preoperative cutaneous lymphoscintigraphy has been routine for all of our patients with cutaneous melanomas of the scalp, auricle, or face since 1992 (except for a brief period immediately after the 1994 earthquake in Northridge, CA). The technique is described elsewhere.[8,11] Briefly, before surgery, 500-800 μCi of a radiopharmaceutical agent was injected intradermally in four quadrants around the primary melanoma site. One of two technetium-labeled agents, i.e., ^{99m}Tc-albumin colloid (DuPont de Nemours, Billerica, MA) or ^{99m}Tc-sulfur colloid (CisUS, Bedford, MA), was used. Dynamic and static images of the drainage patterns and the site of the regional SN were obtained using a stationary gamma-particle scintillation camera. The precise locations of lymphatic channels and SN were confirmed using a hand-held gamma probe (Neoprobe 1000, Neoprobe Corp., Dublin, OH, or C-TRAK, Carewise Medical, Palo Alto, CA) and were marked on the skin with indelible ink. If the primary melanoma was on the cheek, the amount of radiopharmaceutical agent injected was decreased to 200-300 μCi.

Intraoperative Lymphatic Mapping and SLND

The operating surgeon reviewed the preoperative lymphoscintigram and, if the mapping pattern was ambiguous, consulted directly with the nuclear medicine physician who performed the study. If the lymphoscintigram identified a second drainage basin outside the parotid region, this basin was considered separately with respect to intraoperative lymphatic mapping and SLND.

After induction of general anesthesia, 0.5-1.0 ml of isosulfan blue dye (Lymphazurin; Hirsch Industries, Richmond, VA) was injected intradermally, through a 25-gauge needle, around the border of the primary melanoma or around the biopsy site (if the primary melanoma had previously been excised). If the interval between preoperative lymphoscintigraphy and intraoperative lymphatic mapping was $<$24 hours, no radiopharmaceutical agent was injected with the dye. If the interval was $>$24 hours, ^{99m}Tc-human serum albumin (Amersham-Mediphysics, Arlington Heights, IL) was concurrently injected by the operating surgeon.

The site of injection was gently massaged to promote uptake in the afferent lymphatic channel. The hand-held gamma probe was used to verify that the skin mark made by the nuclear medicine physician corresponded to the area of greatest radioactivity.

After 3-5 minutes, a preauricular incision was made and a skin flap was raised. Using the tips of fine-tipped hemostats to perform blunt dissection, the blue-stained lymphatic channel was identified and traced to the first blue-stained node (SN) in the basin. If the blue-stained lymphatic channel passed through the parotid gland, its course was followed through the glandular tissue. When a blue SN was identified, the hand-held gamma probe was positioned over it to determine whether this node also had the highest radioactive count in the basin. The SN was excised, and the gamma probe was used to measure the residual count in the lymphatic basin. If the residual count was less than the preincision measurement, then the SN procedure was considered successful and no further dissection was performed. If the residual count in the lymphatic basin was greater than the preincision measurement, then further dissection for blue and/or radioactive SN was undertaken. This process was repeated until the residual count in the lymphatic basin was less than the preincision measurement. Dye injections were repeated every 20 minutes as necessary for observation of the lymphatic channel and SN.

While the SN was being examined for evidence of metastasis, the primary melanoma was excised using margins of 1-3 cm (depending on the depth of invasion and the site of the lesion). If pathological examination revealed SN metastasis, complete parotidectomy with preservation of the facial nerve was performed.

Histopathological Evaluation of SN

The techniques of pathological examination have been previously described.[5] Briefly, each SN was bisected from the hilum to the periphery; one half was immediately processed for frozen-section examination by routine hematoxylin and eosin (H&E) staining, and the other half was processed for immunohistochemical (IHC) staining using antibody to S-100 protein and the melanoma-reactive monoclonal antibody HMB45 (Dako, Carpenteria, CA), with an automated immunoperoxidase system (Ventana ES; Ventana Medical Systems, Tucson, AZ). All nodal tissue was subsequently fixed in 10% formaldehyde solution, embedded in paraffin, and sectioned for re-examination after surgery. When parotidectomy was performed, the same assays were used for postoperative analysis of nonsentinel nodes.

RESULTS

Patient demographic data and primary tumor characteristics are shown in Table 1. Most (90%) patients were male. Primary melanomas were on the scalp (19 patients), auricle (11 patients), or face (9 patients). The median Breslow thickness was 1.6 mm (range, 0.6-5.0 mm).

A SN was identified in the parotid basin of 37 (94.9%) patients. Intraoperative mapping of the parotid region was unsuccessful in two (5.1%) patients, neither of whom had undergone preoperative lymphoscintigraphy. Both underwent superficial parotidectomy, and the surgical specimens revealed no evidence of metastatic melanoma.

The mean number of SN obtained was 2.3/patient (range, 1-4/patient) (Table 2). Metastatic tumor was identified in SN from four (10.5%) patients, whose primary melanomas showed a mean Breslow thickness of 2.78 mm (range, 0.73-5.00 mm). Tumor-positive SN were anterior to the parotid gland (two patients), in an intraparotid location (one patient), or at the inferior edge of the gland (one patient) (Table 3, Fig. 1). For two of the patients, SN metastases were easily identified using routine H&E staining; for the other two patients, SN metastases were suggested by H&E staining and confirmed by IHC staining. Each patient with a tumor-involved SN underwent parotidectomy and modified radical neck dissection. There was no residual metastatic melanoma in the parotid specimens, but two of the four patients exhibited metastatic melanoma in the modified neck dissection specimen.

Preoperative lymphoscintigraphy was performed for 25 (64%) patients and demonstrated drainage to a second lymphatic region for six (24.0%) patients (posterior auricular region for three and cervical region for three). For five of the six patients, a SN was identified in both drainage basins; for the remaining patient, a SN was not identified in the posterior auricular region. One patient demonstrated a tumor-involved posterior auricular SN and a tumor-free parotid SN. No patient with dual-basin drainage developed clinical lymphadenopathy in the nonparotid basin during the follow-up period.

The 33 patients whose parotid-region SN were tumor-free were monitored for a median of 33.2 months (range, 1-121 months), during which period only one (3.1%) patient developed a regional recurrence. This recurrence was an intraparotid metastasis that was treated surgically with a total parotidectomy and modified radical neck dissection. The original H&E- and IHC-stained slides of the parotid-region SN were reviewed, and no evidence of metastatic melanoma was identified. Six additional levels of the SN were examined with S-100 protein and HMB45 IHC analyses; no melanoma cells were seen. Therefore, the false-negative rate for parotid-region SLND was 3.1%.

There were no procedure-related deaths, and the procedure-related morbidity was minimal. One (2.6%) pa-

TABLE 1. *Patient demographic data and primary melanoma characteristics*

Age (y)	
Mean ± SE	56 ± 2.5
Range	18–87
Gender	
Male	35
Female	4
Primary melanoma site	
Scalp	19
Auricle	11
Face	9
Breslow thickness	
<0.75 mm	3
0.76–1.50 mm	13
1.51–4.0 mm	18
>4 mm	4
Unknown	1
Median (range) (mm)	1.6 (0.6–5)
Clark level	
II	2
III	12
IV	22
V	2
Unknown	1

TABLE 2. *Results of SLND in the parotid region*

No. of excised SN	No. of patients
1	28 (57%)
2	13 (27%)
3	4 (8%)
4	4 (8%)

TABLE 3. *Anatomic distribution of SN excised from the parotid region*

Location	No. of excised SN
Intraparotid	27 (55%)
Anterior to the parotid gland	11 (22%)
Infraparotid	3 (6%)
Supraparotid	1 (2%)

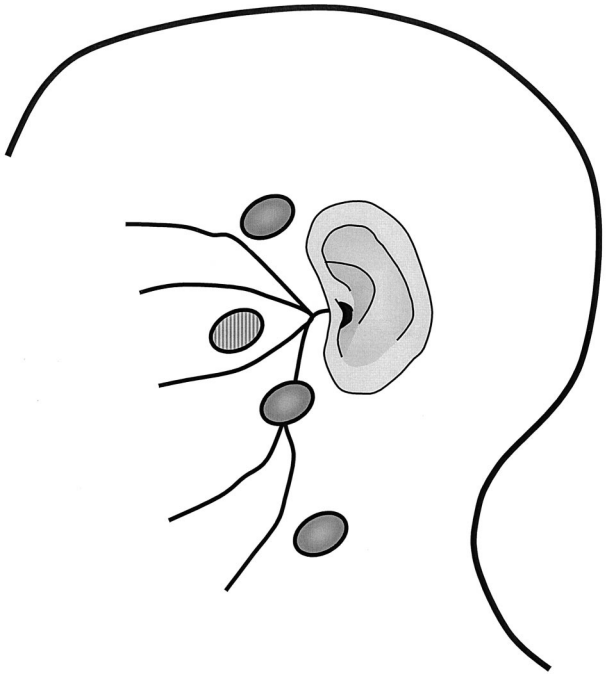

FIG. 1. Relative positions of SN located in supraparotid, intraparotid, anterior to the parotid gland, and infraparotid locations (*top* to *bottom*). *Shaded area*, parotid gland.

tient experienced temporary facial nerve paresis that completely resolved. There were no cases of permanent facial nerve paralysis, Frey's syndrome (gustatory sweating), or injury to Stensen's duct.

DISCUSSION

For melanoma patients with clinically palpable lymphadenopathy in the region of the parotid gland, most investigators advocate a therapeutic parotidectomy and ipsilateral modified radical neck dissection.[12–14] However, postoperative locoregional recurrence in both the parotid bed and the cervical region has been troublesome. Ang et al.[15] reported improved locoregional control in patients with head and neck melanomas who received postoperative adjuvant radiation therapy. A prospective multicenter trial addressing this issue is currently accruing patients (Radiation Oncology Group Trial).

Investigators who question the wisdom of elective parotidectomy cite the low incidence (2.4%, 2 of 82 patients) of metastatic melanoma among patients whose parotid gland is clinically free of tumor.[12] Because no prospective trial of ELND has demonstrated a survival benefit,[2–4] the morbidity associated with routine elective parotidectomy does not seem justified. SLND is a less morbid and highly accurate method of staging the regional lymphatic basin in patients with cutaneous melanoma.[5] In this study, we demonstrated that, at our institution, SLND in the region of the parotid gland accurately staged 97% of melanomas (34 of 35 patients). The one false-negative result occurred in a patient who presented with a palpable intraparotid mass 4.5 years after SLND. This patient underwent a complete parotidectomy and modified radical neck dissection and remains disease-free 2 years later.

Some investigators question the safety of performing SLND in the parotid region.[12,16] In our study, the only procedure-related complication was one case of temporary facial nerve paresis, which resolved completely. Our low morbidity rate can be attributed to meticulous dissection when the blue-stained lymphatic channel courses through the parenchyma of the parotid gland, close to the facial nerve. We advocate judicious use of the electrocautery device in this area, to avoid nerve paresis.

A major factor in our 95% rate (37 of 39 patients) of successful SLND in the parotid region is accurate delineation of the regional lymphatic drainage pattern for each patient.[16,17] Lymphatic drainage from the scalp, auricle, or face cannot be predicted by anatomic site; lesions anterior to the auricle do not always drain through the parotid gland or directly to the anterior cervical nodes, and lesions posterior to the ear may not drain to the posterior auricular nodes or posterior cervical nodes (Fig. 2). In fact, O'Brien et al.[16] demonstrated with preoperative lymphoscintigraphy that 34% of their patients with head and neck melanomas did not exhibit lymphatic drainage patterns that could be predicted by anatomic location alone. Therefore, preoperative lymphoscintigrams are required to identify basins that should be explored during surgery. In our study, the two patients for whom intraoperative mapping failed to identify a SN were among those who had not undergone preoperative lymphoscintigraphic mapping. Since institution of a policy of routine preoperative lymphoscintigraphy in 1992, all parotid-region SN have been identified. ^{99m}Tc-filtered sulfur colloid is our currently preferred radiopharmaceutical agent because of its predictable uptake and migration in afferent lymphatic channels.

SLND in the region of the parotid gland presents several unique technical challenges. First, for cheek mel-

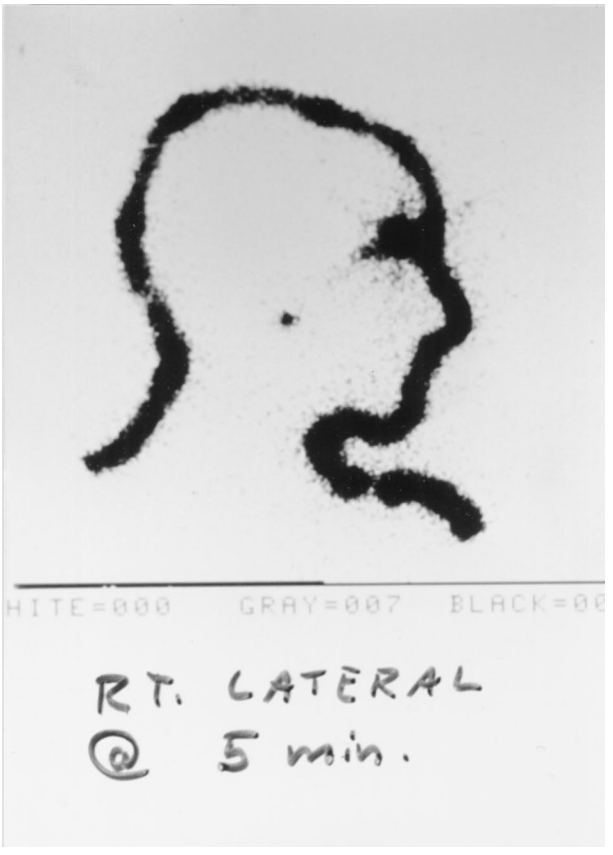

FIG. 2. Lymphoscintigram showing lymphatic drainage patterns in the parotid region.

anomas the nuclear medicine physician must decrease the amount of radiopharmaceutical agent injected and must be extremely careful to avoid skin extravasation. This minimizes the chance of radioactivity at the injection site obscuring a parotid-region SN. Second, the surgeon must raise a thin preauricular skin flap to ensure that a SN anterior to the parotid gland is not included within the skin flap. Third, SN in the parotid region tend to be small; the surgeon must be diligent and patient to dissect these 5-6-mm nodes. Finally, given the proximity of the facial nerve, the surgeon must be extremely cautious when dissecting through the parenchyma of the parotid gland.

In conclusion, SLND of the parotid region is an accurate method to stage cutaneous melanoma of the scalp, auricle, or face and offers a low-morbidity alternative to routine elective superficial parotidectomy. Each patient should undergo preoperative lymphoscintigraphy to document the regional lymphatic drainage pattern from the primary tumor.

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