

Sentinel lymph-node biopsy for melanoma of the trunk and extremities: the McGill experience

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Objective: To determine the effectiveness of sentinel lymph-node (SLN) biopsy for melanoma of the trunk and extremities. **Design:** Case series review. **Setting:** Royal Victoria Hospital, a Canadian university hospital. **Patients:** Thirty-six patients (18 women and 18 men) seen between October 1996 and December 1998 with melanoma 1 mm or more in thickness with clinically negative lymph-node basins. Follow-up was 396 days. **Interventions:** SLN biopsy. Technetium-99m filtered sulfur colloid (0.5 mCi) was injected intradermally around the melanoma or the excision scar 10 to 15 minutes before the surgical skin preparation. The identification of the SLN(s) was done with a hand-held gamma probe. Local anesthesia was used mostly for inguinal SLN biopsy whereas general anesthesia was usually required for axillary SLN biopsy. Preoperative lymphoscintigraphy was used only for trunk melanomas. **Outcome measures:** Morbidity, successful identification of the sentinel node and locoregional recurrence. **Results:** The mean age of patients at diagnosis was 53.4 years (range from 22–76 yr). The melanomas were distributed between the lower extremities (20 patients), upper extremities (8 patients) and trunk (8 patients). The mean Breslow thickness was 2.35 mm (range from 1–8 mm). Lymphoscintigraphy accurately localized the lymph-node drainage basin for trunk melanomas. In 1 patient the SLN could not be identified because the radiocolloid failed to migrate (failure rate 2.8%). The average number of SLNs removed was 1.97. Eight patients (22%) had sentinel nodes positive for malignant disease. The postoperative complication rate was 8.5%. Seven of 8 patients with positive SLNs underwent a complete node dissection (1 patient refused). Of the completion dissections only 2 patients had positive non-SLNs. All patients with positive nodes received interferon alpha-2b as adjuvant treatment. At follow-up, 34 patients are alive with no evidence of disease, 1 patient with a positive SLN is alive with distant metastatic disease and 1 patient with a negative SLN is dead of disseminated disease. **Conclusion:** SLN biopsy is a feasible technique with an acceptable failure rate and is thus a useful tool in the surgical management of melanoma.

Objectif : Déterminer l'efficacité de la biopsie du ganglion lymphatique sentinelle (GLS) dans le cas du mélanome du tronc et des membres. **Conception :** Étude d'une série de cas. **Contexte :** Un hôpital universitaire canadien, l'Hôpital Royal Victoria. **Patients :** Trente-six patients (18 femmes et 18 hommes) traités entre octobre 1996 et décembre 1998 qui avaient un mélanome d'une épaisseur de 1 mm ou plus et des bassins de ganglions lymphatiques négatifs sur le plan clinique. Le suivi a été de 396 jours. **Interventions :** Biopsie du GLS. On a injecté au niveau sous-cutané un colloïde de soufre filtré au technétium-99m (0,5 mCi) autour du mélanome ou de la cicatrice d'exérèse, de 10 à 15 minutes avant la préparation chirurgicale de la peau. On a repéré le ou les GLS au moyen d'un gammamètre manuel. On a utilisé l'anesthésie locale surtout pour une biopsie des GLS inguinaux, tandis qu'il a fallu habituellement administrer une anesthésie générale pour une biopsie des GLS axillaires. On a utilisé une lymphoscintigraphie préopératoire seulement dans le cas des mélanomes au tronc. **Mesures de résultats :** Morbidité, repérage réussi du ganglion sentinelle et récurrence loco-régionale. **Résultats :** Au moment du diagnostic, les patients avaient en moyenne 53,4 ans (intervalle de 22 à 76 ans). Les mélanomes étaient répartis entre les membres inférieurs (20 patients), les membres supérieurs (huit pa-

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tients) et le tronc (huit patients). L'épaisseur moyenne de Breslow s'établissait à 2,35 mm (intervalle de 1 à 8 mm). La lymphoscintigraphie a permis de localiser avec précision le bassin de drainage des ganglions lymphatiques dans le cas des mélanomes au tronc. Chez un patient, on n'a pu repérer le GLS parce que le radiocolloïde n'a pas migré (taux d'échec de 2,8 %). Le nombre moyen de GLS excisés s'est établi à 1,97. Chez huit patients (22 %), les ganglions sentinelles étaient positifs pour la malignité. Le taux de complications postopératoires a atteint 8,5 %. Sept des huit patients qui avaient des GLS positifs ont subi une exérèse complète des ganglions (un patient a refusé). Après les exérèses, deux patients seulement avaient des ganglions lymphatiques non sentinelles positifs. Tous les patients qui avaient des ganglions positifs ont reçu un traitement adjuvant à l'interféron alpha-2b. Au moment du suivi, 34 patients sont vivants et ne présentent aucun signe de maladie, un patient qui avait un GLS positif est vivant mais avec des métastases éloignées et un patient qui avait un GLS négatif est mort d'une maladie disséminée. **Conclusion** : La biopsie du GLS est une technique faisable qui présente un taux d'échec acceptable et constitue donc un outil utile pour la prise en charge chirurgicale du mélanome.

The sentinel lymph node (SLN) is the first node draining a tumour. This node is a good indicator of the status of the rest of the nodal basin. In truncal melanomas there may be more than 1 drainage basin with therefore more than 1 sentinel node. The reported false-negative rate in SLN mapping for melanoma varies between 0 and 2%.¹⁻⁴ The SLN biopsy technique for melanoma was first described by Morton, using blue dye.¹ Then it was done with radiocolloid alone⁵ and more recently with a combination of blue dye and radiocolloid.⁵⁻¹⁰ The success rate of identification of the SLN is higher using radiocolloid with or without blue dye, and reaches 96% to 100%⁵⁻¹⁰ depending on the series. Krag and associates^{5,6} have shown that the SLN biopsy technique using radiocolloid is easy, fast to learn and reliable.⁷⁻¹¹

The goal of the current study was to evaluate our experience at the Royal Victoria Hospital in Montreal with the technique of SLN biopsy using radiocolloid alone, specifically looking at the accuracy of SLN identification, complications and local recurrence in dissected basins.

Methods

Between October 1996 and December 1998, 36 patients (18 women, 18 men) were selected for SLN biopsy. Eligibility criteria were melanoma of the trunk or extremities, Breslow thickness of 1 mm or more and no evidence of disease on clinical examination of the lymph nodes. The exclusion criteria were a

previous wide local excision closed with a graft or rotation flap, and pregnant women.

Mapping technique

Lymphoscintigraphy was done using filtered technetium-99m sulfur colloid the week before surgery and only for trunk melanomas. On the day of surgery the patient was injected in the operating room 10 to 15 minutes before the incision was made. ^{99m}Tc unfiltered sulfur colloid was used for the first 3 cases and then changed to filtered ^{99m}Tc sulfur colloid due to the more reliable migration of the radiocolloid. A total of 0.5 mCi in 0.5 mL was injected intradermally at 4 to 6 different sites around the melanoma or the scar. The identification of the SLN was done with a hand-held gamma probe (C-Trak, Carewise Medical, Palo Alto, Calif.). Before skin preparation, the migration of the radiocolloid to the nodal basin was checked with the probe; then the patient was prepared for surgery as usual. A 2- to 4-cm skin incision was made over the hot spot of radioactivity and was oriented not to compromise a possible future complete nodal dissection. A node was judged to be the SLN if its radioactivity was at least 10 times that of non-SLNs (or the wound after SLN excision). The wound was closed and wide local excision of the primary melanoma site was done if needed. All the counts with the gamma probe were taken over 10 seconds with a 30% window set to capture technetium at a threshold of 130 keV.

Pathological analysis

The SLN was sent to pathology for final analysis, no frozen sections were obtained. The node was measured and bisected then put in formalin for fixation. After 24 hours the node was divided into multiple sections for embedding, all tissues were submitted for study. A single section from each resulting tissue block was stained with hematoxylin-eosin, and the discretion of the pathologist was used in interpreting the sections.

A complete node dissection was done in all patients whose SLN was positive for malignant disease but was not done in patients with no disease in the SLN. All patients with positive nodes were offered adjuvant treatment with interferon alpha-2b for 1 year, at the dose recommended by the Eastern Cooperative Oncology Group trial EST 1684.¹²

Outcome analysis

Charts of patients who underwent SLN biopsy were reviewed for complications such as wound infections, seroma and pain. The percentage of positive SLNs was obtained from the pathology reports. Follow-up was 396 days (median 13.5 mo). Local failure in the dissected basin(s) at follow-up was obtained from the melanoma charts chest.

Findings

The mean age of the patients at the time of diagnosis was 53.4 years (median 55 yr). The mean Breslow thick-

ness of the melanomas was 2.35 mm (range from 1–8 mm, median 2.4 mm). The relation of Breslow thickness to SLN positivity is shown in Table I. Eight patients had Clark's level III melanomas and 26 level IV. In 2 patients Clark's level was unknown. The sites of primary melanoma were: lower extremity 20, upper extremity 8 and trunk 8. The type of anesthesia used for the biopsy varied with the site of the SLN dissection: inguinal SLNs were removed under local or regional anesthesia in most patients; all axillary SLNs were removed under general anesthesia. Sixty-nine nodes were removed in 35 patients for a mean of 1.97 nodes per patient.

In 1 patient an SLN could not be identified for a 2.8% failure rate. This patient was the third in the series and we were then using ^{99m}Tc unfiltered sulfur colloid, which we thought did not migrate because of its larger particle size. The patient was injected with the radiocolloid 15 minutes before the procedure and there was no migration to the nodal basin after 45 minutes of waiting. A second injection was given. After an additional waiting time of 30 minutes without migration of the radiocolloid, the procedure was terminated. Since then we have used filtered ^{99m}Tc sulfur colloid with good migration. In 8 of the 35 patients SLN showed evidence of malignant disease for a 23% positivity rate. All the positive SLN nodes were in patients whose melanoma was between 1.5 and 4 mm thick.

Of the 8 patients with a positive SLN, 7 underwent a complete dissection of the nodal basin. In these 7 patients 2 were found to have metastases in non-SLNs.

Table 1

Breslow Thickness in Relation to Positivity of Sentinel Lymph Nodes

Breslow thickness, mm	Patients, no.	Positive nodes, no.
1.0–1.49	9	0
1.5–4.00	23	8
>4.00	2	0
Unknown	2	0

Three patients (8.6%) had minor complications after the biopsy. The first, obese, patient had an infected shave biopsy of the thigh. The wound had to be opened and packed, and healing was uncomplicated thereafter. The second patient had cellulitis with an inguinal seroma, which was treated with aspiration and antibiotics. The third patient, an obese woman, had leg swelling 2 weeks after the SLN biopsy. There was no infection and Doppler examination was negative for deep venous thrombosis. The swelling had resolved completely 4 months later.

At the 396-day follow-up, 34 patients were alive without evidence of disease recurrence in the dissected basin. One patient was alive with distant metastatic disease. This patient had a foot melanoma with a positive SLN biopsy and refused the completion nodal dissection. She received interferon alpha-2b for 1 year, and 2 months after the end of the treatment, brain and liver metastases were diagnosed. One patient died 1 year after an SLN biopsy that was negative; 3 months after the biopsy, multiple skin melanomas were diagnosed and diffuse distant metastatic disease was diagnosed 6 months later. The patient with failure of migration of radiocolloid presented 1 year after with a clinically enlarged inguinal lymph node. A superficial inguinal lymph-node dissection was done and the clinically enlarged node was positive for tumour metastasis.

Discussion

This study summarizes the results of our initial experience with SLN biopsy in patients with melanoma. Our choice of technique was influenced by the publications of Krag and associates from the University of Vermont, using radiocolloid with a hand-held gamma probe for identification of the SLN. In their hands there was a high rate (98%–100%)^{5,6} of identification of the SLN, and the

technique was rapidly learned. In our small series, the SLN was found in all patients except 1 because of failure of migration of the radiocolloid, for a success rate of 97%. This failure occurred at the beginning of our experience using unfiltered ^{99m}Tc sulfur colloid. Since switching to filtered sulfur colloid, which is injected 15 minutes before the surgical procedure, identification of the SLN has not been a problem and to date there have been no local failures, indicating that we have been identifying the true sentinel node. The use of filtered sulfur colloid requires minimal delay between injection and biopsy due to the rapid migration times. Although we have had better success with the filtered than the unfiltered sulfur colloid this simply underlines the inherent difficulties in making up the colloid reproducibly, emphasizing the importance of close collaboration with one's department of nuclear medicine. Preoperative lymphoscintigraphy was used only for trunk melanomas. No interval nodes were found in the 8 trunk melanoma patients on lymphoscintigraphy or at surgery. Lymphoscintigraphy was not done for extremity melanomas because the lymphatic drainage is usually predictable. The popliteal region for distal lower extremity melanomas, the epitrochlear, supraclavicular and the cervical regions for upper extremity melanomas were routinely scanned with the hand-held gamma probe at surgery, to seek and assess any abnormal drainage. None was found. Thompson and colleagues¹³ have described 17% drainage in an interval node for trunk melanomas, 2.5% to 16% for distal lower extremity melanomas and 5.5% to 21% for distal upper extremity melanomas. The clinicopathologic correlation of these interval nodes was not discussed by the authors so the significance of these lymphoscintigraphic pictures remains uncertain.

Using hematoxylin–eosin staining we obtained a positivity rate of 22%

which is comparable to the rates published in the literature.^{3,5,7,8,10,11} The completion dissection of the nodal basin was done only in patients with positive SLNs. The decision not to do a completion nodal dissection in patients with negative SLNs is based on the fact that except for clinical trials no prophylactic nodal dissection is done at our institution. The overall complication rate was low, and all complications were minor. All were in patients with inguinal SLN biopsy.

With a median follow-up of 13.5 months there were no regional recurrences and only 1 distant recurrence in a patient with a negative SLN. Gershenwald and associates¹⁴ reviewed 243 patients with a negative SLN to determine the pattern and causes of recurrence. They found that 27 patients (11% of their cohort) had local, in-transit and regional nodal or distant metastases after a median follow-up of 35 months. Of these, only 10 (4.1%) had a nodal recurrence, and detailed analysis of the sentinel nodes demonstrated occult metastases in 80% by either serial sectioning or immunohistochemical staining. Similarly Gadd and associates¹⁵ after a median follow-up of 23 months found a 12% recurrence in patients with a negative SLN. Of these recurrences, 8% (7 patients) were nodal, with a median time to recurrence of 12 months. Serial sectioning and immunoperoxidase staining were successful in identifying tumour only in 3 of these 7 patients. Thus, with a median follow-up of 13.5 months we should have detected more regional nodal recurrences in our study. Despite the apparent accuracy of SLN identification we have opted to increase the number of sections studied since this is relatively inexpensive compared with immunohistochemical investigation and should further improve our detection of metastatic disease. This

emphasizes the accuracy of nodal identification and the importance of SLN status as a prognostic marker.

A longer follow-up and a larger number of patients will be necessary to confirm our findings. However, our results are comparable to those of large series published in the literature.

Conclusions

SLN biopsy is a feasible technique, with an acceptable failure rate and a low complication rate. It is a useful tool in the surgical management of melanoma and should be considered the standard of care.

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