

Sentinel lymph-node biopsy after previous wide local excision for melanoma

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Objective: To document experience with sentinel lymph-node biopsy in patients who have already undergone a wide local excision for melanoma because in many centres previous wide excision has been a contraindication for sentinel lymph-node biopsy. **Design:** A prospective cohort study. **Setting:** A tertiary care academic cancer centre. **Patients:** One hundred patients who presented with cutaneous melanoma (depth >1 mm or Clark level IV) after having undergone wide local excision of the primary lesion that was not situated in the head or neck. The follow-up was 3 years. **Interventions:** Sentinel lymph-node biopsy. Patients with truncal melanoma had preoperative lymphoscintigraphy to document the nodal basins at risk. Technetium-99m sulfur colloid (0.5–1 mCi in 0.5 mL) was injected intradermally around the scar, and the sentinel lymph node was excised with the aid of a hand-held gamma detector. **Outcome measures:** Accuracy of the biopsy and false-negative rates in this setting. **Results:** Of the 100 patients, 44 had truncal and 56 had extremity lesions. The average tumour depth was 3.47 mm and 3.07 mm respectively. Thirty-one patients had a sentinel lymph node positive for melanoma metastasis. Biopsies were positive for melanoma in 18 (41%) truncal lesions and 13 (23%) extremity lesions. There were 3 (9%) false-negative sentinel lymph-node biopsies as diagnosed by clinically evident nodal disease subsequently appearing in the nodal basin subjected to biopsy. Two occurred in patients after large rotation flap closures of truncal lesions. The third patient had a subungual melanoma of the great toe. No disease was found in the 2 nodes dissected. Two of the 3 false-negative biopsy results were obtained before serial sections and immunohistochemical staining were used to examine the sentinel lymph nodes. **Conclusions:** Sentinel lymph-node biopsies can successfully identify clinically occult nodal metastases in patients who have had previous wide local excision of a melanoma, but the false-negative rate in patients with rotation flap closures should be taken into consideration.

Objectif : Documenter l'expérience relative à la biopsie du ganglion lymphatique sentinelle chez les patients ayant déjà subi une exérèse locale étendue d'un mélanome parce qu'une exérèse étendue antérieure constituait, dans beaucoup de centres, une contre-indication à la biopsie du ganglion lymphatique sentinelle. **Conception :** Étude de cohortes prospective. **Contexte :** Centre de cancérologie universitaire de soins tertiaires. **Patients :** Cent patients qui se sont présentés avec un mélanome de la peau (profondeur >1 mm ou niveau de Clark IV) après avoir subi une exérèse locale étendue de la lésion primaire qui n'était pas située sur le crâne ou dans le cou. Le suivi a duré trois ans. **Interventions :** Biopsie du ganglion lymphatique sentinelle. Les patients qui avaient un mélanome au tronc ont subi une lymphoscintigraphie préopératoire qui visait à repérer les bassins ganglionnaires à risque. On a injecté sous la peau, autour de la cicatrice, un colloïde de soufre et de technétium-99m (0,5–1 mCi dans 0,5 mL) et procédé à l'exérèse du ganglion lymphatique sentinelle à l'aide d'un gammamètre manuel. **Mesures de résultats :** Précision de la biopsie et taux de résultats faussement négatifs dans ce contexte. **Résultats :** Sur les 100 patients, 44 avaient une lésion au tronc et 56 en avaient une aux membres. La profondeur moyenne de la tumeur atteignait 3,47 mm et 3,07 mm respectivement. Trente-et-un patients présentaient un ganglion lymphatique sentinelle positif indiquant que le mélanome avait produit des métastases. Les biopsies ont donné un résultat positif pour le mélanome dans le cas de 18 (41 %) lésions au tronc et de 13 (23 %) lésions aux membres. Trois (9 %) des biopsies du ganglion lymphatique sentinelle ont donné des résultats faussement négatifs diagnostiqués par une maladie ganglionnaire évidente sur le plan clinique qui a fait son apparition par la suite dans le bassin ganglionnaire visé par la biopsie. Deux ont fait leur apparition chez des patients

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après la fermeture des lésions au tronc au moyen d'un grand lambeau de rotation. Le troisième patient avait un mélanome sous-unguéal du gros orteil. On n'a pas trouvé de maladie dans les deux ganglions disséqués. La biopsie a produit deux des trois résultats faussement négatifs avant des coupes sérielles et l'utilisation d'une coloration immunohistochimique pour examiner les ganglions lymphatiques sentinelles. **Conclusions** : Les biopsies du ganglion lymphatique sentinelle peuvent réussir à repérer des métastases ganglionnaires occultes sur le plan clinique chez des patients ayant déjà subi l'exérèse locale étendue d'un mélanome, mais il faudrait tenir compte du taux de résultats faussement négatifs chez les patients dont l'aire excisée a été refermée au moyen d'un lambeau de rotation.

Sentinel lymph-node biopsy is an important advance in the staging and management of melanoma.¹⁻⁴ Generally, sentinel lymph-node biopsy has been performed at the same time as the wide local excision.⁵ The purpose of this study was to document our experience with sentinel lymph-node biopsy in patients who have already had wide local excision as this has not been an absolute exclusion criterion in our institution.

Patients and methods

Since July 1996, sentinel lymph-node biopsies have been performed in 100 patients who had already undergone a wide local excision for primary cutaneous melanoma at least 1 mm deep or with Clark's level IV invasion. Patients with primary lesions on the head and neck were not included. Those who had their primaries on the trunk underwent preoperative lymphoscintigraphy to determine the nodal basins at risk. If flow was seen to 3 or more nodal basins, the patient was not considered eligible for a sentinel lymph-node biopsy. At the time of surgery, unfiltered technetium-99m sulfur colloid (0.5–1 mCi in 0.5 mL) was injected intradermally in 4 to 6 aliquots around the scar 1 to 2 hours preoperatively. Between 0.5 and 1 hour after injection, scanning was performed and the skin over the hot spots marked. At operation, the hot spots were identified with the aid of a hand-held gamma probe and the sentinel node(s) excised through a small skin incision. All hot nodes were removed until background radioactivity was less than 10% of the hottest node. Blue dye was not generally used in these patients.

Fifty-six patients had primary le-

sions on their extremities. Forty-four patients had truncal primary lesions, 10 had lesions that drained to 2 separate basins (8 back, 1 abdomen, 1 buttock). Mean tumour thickness was 3.25 mm (median 2.45 mm, range from 0.88–15 mm). Ten patients had subungual melanomas.

The referral pattern was such that we believe we saw patients with deeper melanomas or poorer prognostic features (site, sex, ulceration, etc.) than in the general melanoma patient population in our area. Patients were referred to our cancer centre by community oncologists and plastic surgeons after wide local excision.

Pathologic assessment of the sentinel nodes was routine for the first 23 patients. Intensive examination began in October 1997 whereby nodes were bivalved or cut into 3-mm blocks, and 5 serial sections were taken from each block. Sections 1, 3 and 5 were stained with hematoxylin-eosin and sections 2 and 4 had immunohistochemical staining with S-100 and HMB-45 according to the description of Cochran.⁶ Extra sections were taken as necessary for accurate evaluation. Care was taken to differentiate benign intracapsular nevus cells from melanoma micrometastases. The polymerase chain reaction was not used.

Patients who had a sentinel node biopsy positive for micrometastases underwent completion lymphadenectomy at a later date and were considered for adjuvant interferon treatment.

The 100 patients in this series were compared with a composite of the first 150 patients who had sentinel node biopsies at our institution with or without simultaneous wide excision.

Results

At least 1 sentinel lymph node was identified in all 100 patients and 110 nodal basins. Sixty-two nodal basins had 2 or more sentinel nodes, and the average number of sentinel nodes recovered was 1.92 per basin.

Thirty-one patients had sentinel lymph nodes positive for melanoma metastases, and the rate of sentinel lymph-node positivity in relation to tumour thickness (stage) is shown in Table 1. Thicker lesions had greater rates of sentinel lymph-node positivity. At the time of a subsequent completion lymphadenectomy, 29% had other positive nodes in the dissected basin.

When broken down by site, 18 (41%) of 44 patients with truncal melanomas had sentinel nodes positive for metastatic disease. The mean tumour thickness in this group was 3.47 mm (median 2.69 mm). Of the 56 patients with extremity melanomas, 13 (23%) had sentinel lymph nodes positive for metastatic disease. The mean tumour thickness was 3.07 mm (median 2.13 mm). Thus, the patients with truncal melanomas had a higher sentinel node positivity rate and also had thicker lesions.

When the patients in this series were compared with the first 150 patients who had sentinel node biopsies at our institution with or without si-

Table 1
Sentinel Lymph-Node Positivity for Metastatic Melanoma After Previous Wide Local Excision, According to Tumour Vertical Height

Vertical height, mm	Positive, %
≥1-<2	17
≥2-<4	35
≥4	38

multaneous wide excision within each tumour stage category, large differences were not seen (Fig. 1), although no clinically detected false-negative sentinel node biopsy results have yet been seen in those who undergo concurrent wide excision and sentinel node biopsy at our institution.

In 3 patients who had pathologically negative sentinel lymph nodes on biopsy, clinically evident regional disease developed during the follow-up period (median follow-up 23 mo). Two of these lesions were on the anterior chest of male patients and the respective thicknesses were 2.39 mm and 5.30 mm. Both lesions were resected and closed with rotation flaps at an outside institution. There were no problems during the sentinel lymph-node biopsy procedure. A definite hot node was resected, but regional lymphadenopathy appeared within 9 months and biopsies confirmed the presence of metastatic nodal disease. Therapeutic lymphadenectomy was performed after appropriate restaging, and distant metastases have occurred in 1 of the 2 patients, while the other remains disease free 3 years after the initial sentinel node biopsy. These were the only 2 patients with previous rotation flap closure of a truncal melanoma. The third patient had a subungual melanoma of his great toe. The sen-

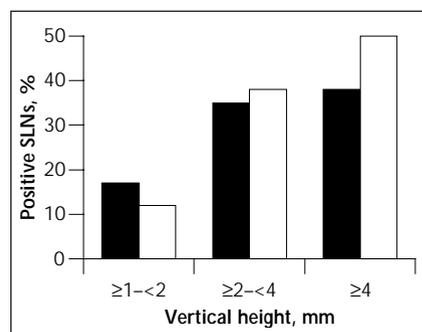


FIG. 1. The percentage of sentinel lymph nodes (SLNs) positive for metastatic melanoma in patients who had a previous wide local excision ($n = 100$, black bars) compared with those who had simultaneous wide local excision and sentinel node biopsy ($n = 150$, white bars), grouped according to tumour height.

tinell lymph-node biopsy was performed without incident, and 2 nodes were recovered. No tumour was detected, but only 2 sections were taken of each node. This biopsy was performed at a different institution, and the slides have not been available for serial sectioning and review. Three years after his "negative" sentinel lymph-node biopsy, regional adenopathy became evident and therapeutic node dissection was performed. Six months later, in-transit metastases were found within the leg and he has undergone hyperthermic lymph perfusion. No systemic metastases have yet materialized.

Discussion

This study illustrates the fact that sentinel node biopsies can be performed with good results in patients who have already had a wide excision of their primary melanoma.

The rates of sentinel lymph-node biopsy are comparable to those in other reports^{2,7} and to those performed in our institution with simultaneous wide local excision. If anything, this study has shown increased rates of sentinel lymph-node positivity after previous wide local excision. This is probably because of our referral practice, which tends to attract poor-risk patients. The community surgeons and oncologists were generally not performing sentinel lymph-node biopsies during this time. Two of our 3 false-negative results occurred in the only 2 patients who had rotation flap closures. Karakousis and Grigoriopoulos⁸ have also reported a false-negative result of a biopsy in a patient with previous rotation flap closure. It appears that this type of closure is a contraindication to this procedure.

Sentinel lymph-node biopsy is important in the management of melanoma² and patients who have had previous wide local excision and primary closure or skin grafting should not categorically be denied this valuable technique. Patients are informed that there may be a slightly

higher rate of false negativity, but the amount is not known. The technical success rate has been excellent (100%). If the primary site has ambiguous drainage but the preoperative lymphoscintigram shows defined drainage to 1 or 2 nodal basins, it appears that previous excision does not disrupt the lymphatic pathways excessively. Thus, this procedure appears to be accurate and reasonable to perform in this population.

Sentinel lymph-node biopsy can identify clinically occult nodal metastases after a previous wide local excision, but the false-negative rate in patients with rotation flap closures should be taken into consideration.

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