Sentinel node biopsy confers no added protection to patients with melanoma

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Clinically apparent metastases involving the regional lymph nodes are a common occurrence in cutaneous melanoma and heralds, in the majority of patients, dissemination of the tumour. Progression usually takes place within two years from this clinical manifestation and depends on the number of lymph nodes involved and on whether the tumour has breached the lymph node capsule. The risk of such regional lymph node metastases increases as the grade of the primary lesion worsens. Thicker, ulcerated, bleeding primary lesions with a high mitotic count are likely to be early offenders.^{1,2}

In order to improve outcomes it became fashionable to perform immediate (elective or prophylactic) lymphadenectomies at the time of initial diagnosis of the primary tumour, in the hope that resection of regional lymph nodes harbouring microscopic metastases would add protection. However, this approach, studied in randomized trials, showed no improvement in overall survival versus delayed lymphadenectomy performed when regional lymph node metastases became clinically apparent.³ Instead, it exposed patients to complications resulting from the procedure; notably—in a substantial percentage of patients—intractable lymphoedema, and potentially an increased risk of in-transit metastases.

The technique of lymphatic mapping and sentinel node biopsy was developed as a minimally invasive surgical alternative to elective lymph node dissection in order to identify patients with occult nodal metastases who might benefit from total lymphadenectomy.³ Sentinel node biopsy has been hailed as a 'surgical revolution' in melanoma and is becoming entrenched into the routine management of the disease.⁴ This approach is conceptually no different to the objectives of prophylactic lymphadenectomy; namely the resection of microscopically involved lymph nodes before regional lymph node metastases become clinically apparent. Behind this approach is the assumption that the metastatic cells detected microscopically at the time of prophylactic lymphadenectomies are the same cells which, if left behind,

proliferate and give rise to clinically palpable, regionally metastatic lymph nodes, and subsequently to dissemination.

Biopsy of the sentinel node, when positive for microscopic metastases, is followed by a complete (total) lymphadenectomy of the involved regional lymph node basin, thus becoming an elective lymphadenectomy with the ensuing complications. The role of regional lymph node surgery has recently been hotly debated in the literature, with conflicting observations and views regarding its contribution to the risk of in-transit metastases. Proponents of the sentinel node biopsy argue that any risk of in-transit lesions is devoid of the surgical procedure and is related entirely to the adverse prognostic factors of the primary lesion.^{5,6} Others have reservations about this view.⁷

Whatever the truth about the risk of in-transit metastases in relation to sentinel node biopsy, one would have anticipated intuitively that this approach could not be expected to make a difference in survival for the simple reason that such occult metastases harboured in regional lymph nodes—whether detectable by routine microscopy or by immunocytochemistry—would have occurred and would have been resected in the earlier randomized studies of elective lymph node dissections, which showed no difference in survival. Predictably, the randomized study which sought to resolve this issue, recently published in the *New England Journal of Medicine*, showed no difference in overall survival for patients who underwent a sentinel node biopsy versus those who were randomized to observation and who underwent a lymphadenectomy when they developed clinically palpable metastatic lymph nodes.^{3,8,9}

It has been argued that even if sentinel node biopsy does not directly lead to a survival benefit, it is valuable because it provides superior prognostic information than that derived from the primary lesion.¹⁰ Unfortunately this thesis is untenable because the prognostic value of the sentinel node status can only be regarded as superior when all prognostic resources provided by the primary lesion have been exhaustively investigated in the studies that purport such superiority.¹¹

What has now become a fashionable practice, established before the publication of the results of the randomized trial, is likely to continue in the foreseeable future despite the (broadly acknowledged) fact that sentinel

node biopsy does not confer added protection to the patient with cutaneous melanoma.^{12–14}

Consider the possibility of treating those patients whose sentinel node biopsy is positive for microscopic metastases with high-dose interferon, as proposed by Balch and Cascinelli¹⁵ in their companion Editorial to the paper by Morton *et al.*³ Thousands of patients have endured this potent molecule, at considerable inconvenience and financial cost, for a potential—and clinically inconsequential—extension of freedom from relapse.¹⁶ There is no convincing evidence that interferon improves overall survival of patients with microscopic metastases from melanoma in the regional lymph nodes.^{17,18} There is also no evidence that the survival of patients treated with interferon for clinically apparent regional nodal metastases is superior to the best reported results in the literature.¹⁷

What does all this mean for the patient with melanoma? A staging surgical procedure which will not improve the chances of survival but which, like the staging splenectomies for Hodgkin's lymphoma in the old days, may well be performed to the patient's detriment. Add now the possibility of treating these patients with adjuvant interferon for microscopically detectable metastases and the patient ends up in a state of 'double jeopardy'; two unwarranted interventions of no demonstrable survival benefit.

Advances in the treatment of melanoma are urgently needed, as they are for every other cancer. This does not, however, mean that in the process patients should endure procedures or treatments emanating from 'evidence-based medicine' that show no evidence of benefit.

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