Surgical Treatment of Melanoma

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"Malignant melanoma writes its message in the skin with its own ink ... some see, but do not comprehend."[1] Effective treatment of melanoma begins with early recognition. Paranoid suspicion of any irregular, pigmented, nodular or ulcerated dermal lesion, when coupled with excisional biopsy, merits approbation even though many such lesions prove benign.

Biopsy

In addressing controversial aspects of biopsy, infiltration of tissue with local anesthetic around a melanoma jeopardizes neither local control nor survival[2]. Similarly, a delay of treatment for as much as 4 weeks following even incisional biopsy fails to alter local control or prognosis. Shave biopsies of melanomas should be avoided, as this technique interferes with accurate depth assessment and makes appropriate treatment selection nearly impossible.

Primary excision

Historical recommendations concerning margins of excisions in the treatment of primary melanoma seem largely a function of surgical tradition rather than science. In collected, retrospective series, local recurrence following primary surgical treatment approximates 3%[7]. Presence of risk factors such as ulceration of the primary tumor thickness > 4 mm, or location in the hand, foot or scalp has been reported as increasing local recurrence rates to 10% or more. A prospective study of 612 patients with non-ulcerated extremity melanoma < 2mm in depth, randomized to 1 cm versus 3 cm excision margins, failed to detect any significant difference in local control or survival. All 4 patients with local recurrence in this study underwent excision with 1 cm margins, however, and all had melanomas thicker than 1 mm; 2 of the 4 died of disease[4]. Thus, while 1 cm margins seem fine for < 1 mm thick melanomas, thicker lesions may warrant wider excision. An ongoing, prospective, randomized intergroup trial, in patients with non-ulcerated melanomas 1 mm to 4 mm thick, comparing primary excision with 2 cm margins versus 4 cm margins, should clarify this issue.

Tradition dictates primary excision of melanomas en bloc with the underlying superficial muscular fascia. Olsen's view that resection of fascia might allow dissemination from subdermal lymphatics[8] prompted some to abandon this tradition. In a retrospective, non-randomized comparison, both local recurrence and survival in 107 patients with melanoma excised en bloc including underlying fascia, closely matched that in 95 patients whose underlying fascia was left undisturbed. Fascial excision can probably be done safely only in those with thicker melanomas.

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Therapeutic treatment of involved lymph nodes

In a group of 1,134 patients undergoing therapeutic lymphadenectomy for pathologically involved regional lymph nodes, Morton and colleagues report 5-, 10-, and 15-year survival rates of 46%, 41%, and 38% respectively. Multivariate analysis of this large group demonstrates that an increasing number of involved nodes, greater Breslow thickness of the primary, and torso, head or neck location all independently decrease survival. Male gender and degree of involved nodal enlargement impact the result adversely with borderline statistical significance[10]. Patients with only 1 positive node enjoy 5-year survival of 79%[10]. Contrary to prevailing opinions that patients with involved nodes inevitably harbor occult distant metastases, results indicate a surprising proportion can be cured by means of a radical regional procedure. Radical lymphadenectomy remains the mainstay of treatment in such patients.

Some patients present with regional lymph node involvement without a detectable primary lesion. Overall survival of these patients following regional lymphadenectomy approximates that in patients in whom one can identify a primary[11].

Elective lymphadenectomy

After 2 prospective, randomized trials of elective lymphadenectomy versus observation (with therapeutic lymphadenectomy if indicated) failed to reveal any significant difference in 10-year survival, most surgeons abandoned unselective, routine, elective lymphadenectomy in melanoma patients[12-14]. Balch, analyzing biologic risk of both nodal and distant metastases according to thickness of the primary lesion, emphasizes that, while benefit seems unlikely in both those with relatively thin melanomas, ie low risk of lymph node involvement, and in those with advanced, thick melanomas >4mm deep, ie high risk of systemic spread—the so-called "intermediate subgroup"—at high risk for occult nodal disease but at lower risk for occult systemic metastases, might indeed benefit from elective lymphadenectomy[15]. Analyzing data from both large retrospective, and prospective, randomized lymphadenectomy series, Balch identified apparent survival advantage in this variably defined "intermediate subgroup"[13].

To further evaluate elective lymphadenectomy in this subgroup, patients were added to an ongoing intergroup trial of 1-mm to 4 mm-thick melanomas, underwent secondary randomization: Elective lymphadenectomy versus observation. Results of this trial should finally lay to rest any residual controversy concerning elective lymphadenectomy.

An alternate approach to elective nodal surgery in melanoma patients with nonpalpable nodes, pioneered by Morton and colleagues, involved selecting patients for lymphadenectomy based on results of dye-directed biopsy of sentinel nodes; if such sentinel nodes harbor microscopic disease, lymphadenectomy is performed[16]. Given the reality of "skip"

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OZONE DEPLETION: CAUSES, POTENTIAL EFFECTS, AND REMEDIES *(continued from page 122)*

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metastases in melanoma, and the threshold of resolution inherent in even the best pathologist's microscopic analysis, having a "negative" sentinel node may not guarantee freedom from eventual nodal involvement. This intriguing approach certainly merits further study, however.

Locally advanced melanoma and in-transit metastases

Major amputation in patients with recurrent, locally advanced, or in-transit melanoma—usually performed in the setting of extensive, necrotic, bleeding or fungating lesions with or without in-transit metastases—generates long-term, disease-free survival in 20% to 49% of patients, again indicating that even extensive local-regional disease does not inevitably presage systemic involvement[17].

Hyperthermic, isolated extremity perfusion combined with chemotherapy and lymph node dissection (and often surgical excision of gross disease) generates long-term survival similar to amputation[17-20]. Today most surgeons preferentially treat patients presenting with locally advanced disease and in-transit metastases in this manner.

Adjuvant hyperthermic limb perfusion and elective lymphadenectomy

Encouraged by the apparent ability of hyperthermic, isolated-limb perfusion to control locally advanced and in-transit disease, Ghussen and colleagues at the University of Cologne conducted a prospective, randomized trial of this versus elective node dissection alone. At almost 6 years median follow-up, they report 90% 5-year actuarial survival in the perfused group versus 62% in the group not perfused ($p < 0.01$)[21]. In contrast to others[18-20], they report no limb-loss complications from the treatment. Results of this treatment remain unsurpassed by other adjuvant treatment schemes, but have not yet been independently confirmed or reproduced by others.

Surgical resection of isolated metastatic disease

Overett and Shiu, reporting results of a retrospective study of 176 patients undergoing surgical resection of distant metastatic deposits of melanoma, found that 33% of such patients undergoing complete resection of single-site disease survived 5 years. In contrast, those undergoing incomplete resection suffered prolonged hospitalization, considerable morbidity and negligible benefit, this emphasizes the importance of mature surgical judgment and judicious selection of patients when considering such an approach[22].

Summary

Surgical resection of disease constitutes the mainstay in primary treatment of localized and regional melanoma, offering long-term survival far in excess of any competing treatment to date. Some highly selected patients can even benefit from surgical treatment of isolated distant disease if complete resection can be achieved. Adjuvant treatments performed in conjunction with surgical procedures such as isolated hyperthermic limb perfusion continue to hold promise for improving survival.

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