Current Management of Malignant Melanoma

The incidence of cutaneous melanoma is increasing worldwide; this annual rate of increase, 4%, is higher than for any other malignancy, except lung cancer in women. It has been estimated that by the year 2000, 1 in every 90 persons will develop melanoma. The cause of this rising incidence is unknown but may be related to increasing ultraviolet exposure due to loss of the earth's protective ozone layers. Because the cure rate for thin melanomas, those that measure 0.75 mm in thickness or less, is more than 95%, we need national programs to focus public awareness on changing pigmented lesions. Public campaigns in Australia and Scotland have demonstrated the effectiveness of such programs in establishing early diagnosis, when surgical treatment is most effective.

There are two important questions regarding the current surgical management of primary cutaneous melanoma.

1. How widely should the primary lesions be excised?
2. How should regional lymph nodes be managed?

Two papers in this issue of *Annals of Surgery* have implications for both questions. In an important paper on late melanoma recurrences, Crowley and Siegler review 168 patients with late (10 or more years) recurrences; this information was collected from the large melanoma database at Duke University. Of a total of 651 patients who had been followed for 10 or more years, 168 (approximately 25%) developed late recurrences. This is the highest incidence of late recurrences yet reported and emphasizes the importance of long-term follow-up. They observed recurrences of ocular melanoma 45 and 47 years after treatment of the primary lesion. Recurrences of cutaneous melanoma have been delayed as long as 40 years, particularly in women whose primary lesion was on the extremity. Of particular importance for primary surgical treatment is the observation that 70% of the delayed recurrences after 10 years occurred in the local skin surrounding the primary site or in the regional lymph nodes. This indicates that cutaneous melanoma may remain clinically dormant for long periods of time. It also underscores the importance of long-term follow-up in evaluating newer, more conservative surgical approaches.

The extent of surgical resection of skin and subcutaneous tissues surrounding the primary melanoma remains controversial. No one has shown how close the surgeon can come to a primary melanoma without increasing the incidence of local recurrence. Since W. Sampson Handley, in 1907, recommended a 5-cm radial margin around the primary lesion, such a margin has been the treatment of choice until very recently. A number of investigators have reported that thin lesions (measuring less than 0.76 mm) rarely recur with margins of 1 to 2 cm. A recently reported World Health Organization (WHO) melanoma group trial randomized lesions up to 2 mm in thickness to narrow excisions of 1 cm *versus* a 4-cm radial margin. There was no statistically significant difference in the local recurrence rate in this randomized trial, but all the observed local recurrences were in the narrow-margin group. Follow-up on this series was short, and such a trial must have a longer follow-up to be accepted as valid.

Until the optimum width of excision of a primary melanoma can be determined by longer follow-up of current trials, we have adopted the following guidelines based on the observation that the risk of local recurrence is directly proportional to the depth of the primary melanoma:

1. Clark's level II melanoma, or thin Level III lesions that measure less than 0.75 mm in thickness: Excision with 2 to 3 cm radial margins.
2. Clark's level III melanoma, lesions that are thicker than 0.75 mm, and all Clark's Level IV melanomas: Excision with 3 to 4 cm radial margins.
3. Clark's level V melanoma and all melanomas thicker than 4 mm: Wide excision with 5-cm radial margins around the primary site, which includes the underlying fascia, because these lesions are more likely to have microsatellites surrounding the primary lesion and involvement of the subdermal lymphatics close to the primary lesion.

Except on the face, from a practical standpoint, there is little difference between narrow and wide excisions in regard to the cosmetic result, as long as the defect can be closed primarily by rotation and advancement flap techniques.

Surgical Management of the Regional Lymph Nodes

There is general agreement that regional lymphadenectomy is indicated for the patient who has suspicious or pathologically proved metastases to the regional lymph nodes. Contrary to the pessimism in the early literature, as shown in this issue's paper by Bevilacqua, Coit, and associates from Memorial Sloan-Kettering Cancer Center, 32% of these patients with axillary metastases will survive 10 years. Furthermore patients with only one clinically positive lymph node had a 50% chance of long-term survival.

At initial examination, 90% of melanoma patients have no clinical evidence of metastases to the regional lymph nodes or distant sites. Such clinical stage I (CSI) patients present a common therapeutic dilemma regarding the management of the regional nodes. Some surgeons advise immediate elective lymph node dissection (ELND) for these patients; others adopt a program of 'watch and wait,' with careful follow-up examinations and delayed therapeutic lymphadenectomy if metastases develop in the regional nodes. The benefit of elective or prophylactic lymph node dissection for patients who are CSI is controversial. Several long-term, retrospective, biostatistical studies from single institutions have demonstrated a small but significant therapeutic benefit from ELND for patients with CSI melanomas of an intermediate Clark's level or Breslow thickness. Furthermore the survival rates after lymph node dissection are 15% to 25% higher for patients with clinically occult metastases than for patients who have clinically detectable disease. As noted by the Memorial Sloan-Kettering group, there was a statistically significant improved survival rate at 5 years in patients with occult metastatic disease. This improved survival rate presumably was due to resection of metastatic disease at an early point in its natural history while it is still confined to the lymphatic basin.

Despite this apparent benefit of ELND, randomized clinical trials have not demonstrated a statistically significant overall survival advantage from ELND when the entire group of patients with CSI cutaneous melanoma undergo ELND. However data from the randomized WHO trial indicate that patients with intermediate level melanoma of the extremities who underwent ELND had survival rates that were approximately 11% higher than did patients who underwent delayed therapeutic lymphadenectomy. This difference was not statistically significant because there were small numbers of patients in this subset of the trial.

Two large randomized trials are in progress for melanomas of intermediate depth, 1.5 to 3.99 mm in thickness, by the American Cooperative Groups and the WHO Melanoma Group. However the results of these trials will not be available for many years and will require long-term follow-up, as emphasized by Crowley and Siegler in their paper in this issue. Until these data are available, each surgeon must make an individual decision for each patient when recommending ELND. However the difficulty, in our mobile society, of maintaining close follow-up of these patients at 3-month intervals for periods of 10 years or more must be recognized. It has been our policy to recommend regional lymphadenectomy for all those patients who are of young or middle age and who have lesions measuring more than 1.5 mm in thickness. In our center the incidence of clinically occult nodal metastases in this group of patients is 36%. Because the incidence of occult metastases will be low (about 10%) for lesions thinner than 1.5 mm, the use of ELND in this group is highly individualized, and no general guidelines can be proposed.

We are investigating an alternative approach to this problem of accurately staging patients with CSI melanoma. New operative techniques have been developed for identifying the lymphatic drainage path from the site of the primary melanoma to the individual sentinel lymph node(s) within the regional lymphatic basin. This permits selective lymphadenectomy of these draining lymph nodes and intraoperative examination by frozen section, resulting in accurate pathologic staging. Thus, with a relatively minor procedure, surgeons can select those patients who have metastatic disease who will benefit from a therapeutic lymph node dissection, and thereby avoid the morbidity of radical lymphadenectomy in the patients who do not have nodal metastases.

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