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Management of Regional Lymph Node Basins in Melanoma

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ABSTRACT

Of all malignancies, melanoma has the most rapid increase in incidence; in 2009 it was estimated to have had the fifth highest number of new cases overall. Surgical therapy remains the primary and most effective intervention for this disease. Over the past 20 years there has been a significant paradigm shift in the management of the regional nodal basin, driven predominantly by the introduction of sentinel lymph node biopsy (SLNB). This new technique has drastically altered the method of detecting nodal disease and has become a routine component of melanoma treatment. In addition to SLNB, a better understanding of ultrasound, fine-needle biopsy, and the considerable efforts to minimize the morbidity of surgical intervention has led to innovations in the management of patients with regional metastases. An overview of the current therapeutic options for managing patients with nodal disease follows.

INTRODUCTION

Melanoma will be diagnosed in approximately 70,000 patients in the United States in 2010, and of all malignancies it is the cancer with the most rapid increase in incidence.[1] Despite many advances in the understanding of melanoma pathobiology in recent years, the prognosis for patients with widely metastatic melanoma remains dismal. Melanoma preferentially spreads via the lymphatics, making management of the regional nodal basin a paramount concern in the treatment of the disease. Management of the regional lymphatics has undergone a substantial paradigm shift in the past 20 years. The introduction of sentinel lymph node biopsy (SLNB) has drastically altered the method of detection of nodal disease. Prior to the widespread use of this technique, metastases were diagnosed either via elective lymph node dissection (which is now obsolete) or via clinically evident (radiographic or physical examination) disease. In the era of SLNB, the majority of the metastases will be diagnosed using this innovative approach, with only a small percentage being identified via clinical or radiographic examination.[2] Of patients with primary lesions that justify an evaluation of the draining lymphatics (lesions >1 mm in Breslow depth and certain high-risk melanomas <1 mm in depth), only 17% of patients will harbor nodal metastases.[3] It is important to note that despite this overall risk, the true risk of nodal metastases is directly proportional to the Breslow depth, the single greatest predictor of outcome in melanoma. This is discussed in greater detail subsequently.

Systemic therapy for melanoma remains largely ineffective. As a result, surgical intervention remains the best potential for cure. In the subset of patients who harbor nodal disease, early surgical intervention has been shown to provide a measurable survival benefit over delayed therapeutic lymphadenectomy.[4] Given this difference, complete lymphadenectomy, particularly in the setting of microscopic disease, remains the standard of care for any patient who suffers from regionally metastatic melanoma. In spite of these data, a distressing statistic was recently reported: Only 50% of patients appear to receive the recommended therapy, with many being referred for other treatment or no intervention at all.[5] Complicating the matter of treatment of patients with nodal metastases is the fact that there are differences in the extent of surgery performed, depending on the method by which the disease is identified (SLNB or clinical disease). For example, in patients with disease in the groin detected by SLNB, most patients in the United States are offered only inguinofemoral lymphadenectomy rather than inguinopelvic lymphadenectomy, which is advocated for clinically detected metastases. Similarly, there is an ongoing debate regarding dissection of the level 3 nodes in the axilla. Although debates are still ongoing regarding extent of surgery, what may be most important is that there is a

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significant prognostic disparity between clinically detected disease and sentinel node-detected disease. This disparity is so significant that it continues to form a delineating aspect of the current American Joint Committee on Cancer staging system, and as a result the subsequent discussion has been divided by the method of detection of nodal disease (microscopic vs macroscopic).

CLINICALLY NEGATIVE NODAL BASIN

When melanoma is first diagnosed in a patient, the likelihood of coexisting lymph node metastases is related to a multifactorial series of predictive histopathologic characteristics, with Breslow depth being one of the strongest. The future is likely to demonstrate that genetic markers of prognosis and biologic behavior will be better able to predict the presence of nodal metastases than any current histologic information. Elective lymphadenectomy was once the standard of care, but it subjected patients to unnecessary surgery nearly 85% of the time.[6-9] Morton and colleagues[3,10] introduced the concept of SLNB for melanoma in 1992 and established the validity of the procedure through the Multicenter Selective Lymphadenectomy Trial-1 (MSLT-1), published in 2006. This prospective trial, along with a considerable amount of other evidence,[11-14] forms the foundation for early intervention in setting of nodal metastases for melanoma. Sentinel lymph node biopsy is based on the well-supported premise that lymphatic metastases from melanoma follow an orderly progression through afferent lymphatic channels to sentinel lymph nodes before spreading to nonsentinel lymph nodes and subsequent distant sites.[15] As mentioned previously, evidence is clear that Breslow depth is a direct predictor of the risk of nodal metastases. The likelihood of detecting positive nodes on SLNB is approximately 1.7% if the lesion is $<$0.76 mm without any high-risk features, 3.9% if the lesion is between 0.76 and 1.0 mm without mitotic figures and nearly 8% with mitotic figures or other high-risk features, 17% for lesions between 1.0 and 4.0 mm thick, and more than 20% for lesions $>$4.0 mm in thickness.[16-19]

Importantly, SLNB has been shown to be a highly accurate procedure with a very low incidence of nodal recurrences after a negative biopsy. In large reported series of patients undergoing the procedure, the incidence of nodal recurrences in a mapped basin ranges from 1.7% to 9%.[3,20-24] Although many factors play a role in why patients have a nodal recurrence after negative sentinel node biopsy, a number of specific reasons have been postulated, including obstruction of the draining lymphatics,[25] anatomic location making detection and examination complicated (specifically head and neck primary),[24] limitations of pathologic analysis (ie, not able to sample the entire node, minute foci of missed disease), and surgical technique.[26] Sondak and Zager,[26] in an editorial accompanying an article analyzing the incidence of false-negative SLNB in the Sunbelt Melanoma Trial, cover this concept comprehensively. Although the incidence of in-field recurrences after negative SLNB is low, this number is not to be confused with the true calculation of a false-negative biopsy, which is specifically addressed in the article by Scoggins et al[22] and is actually higher than the percentage reported for nodal recurrences. Despite this, given the overall accuracy of this procedure and its low morbidity compared with elective lymphadenectomy, it has garnered widespread acceptance.

SLNB is now considered to be the standard of care in those patients with primary melanomas $>$1.0 mm in thickness with clinically negative nodal basins. Most agree that SLNB should also be considered in those patients with lesions $<$1.0 mm in Breslow depth when there are high-risk characteristics present (ulceration, mitotic rate $>1/mm^2$, lymphovascular invasion, and those with ambiguous depth secondary to a positive margins), although the incidence of nodal involvement is much lower in these lesions, as mentioned previously.[27] Furthermore, because Clark's level has been shown to be a poor predictor of SLN involvement, many melanoma experts currently use a threshold of 0.76 mm in depth as an indication for SLNB in patients who are considered safe for general anesthesia. In addition to these histologic risk factors, age has been shown to be a factor in the risk of sentinel node involvement, with younger patients having a higher incidence of nodal metastases and older patients having a lower incidence than would otherwise be expected.[28] The National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines reaffirm that the evidence for SLNB in the cohort of patients with thin lesions $<$1.0 mm remains unclear and larger series with longer-term follow-up will be required to better assess the prognostic significance.[29]

The MSLT was the first prospective randomized trial to compare immediate SLNB at the time of wide excision with wide excision followed by observation. In the observation group, lymphadenectomy was performed only in those who developed clinically positive nodes after local excision. In this study of 1,269 patients with intermediate-thickness (1.2-3.5 mm) melanomas, the mean estimated 5-year disease-free survival rate was significantly higher in the biopsy group versus the observation group (78.3% $\pm$ 1.6% vs 73.1% $\pm$ 2.1%). More importantly, among patients who harbored occult nodal metastases, the 5-year overall survival was significantly higher in the group

who underwent immediate completion lymph node dissection (CLND) at the time of SLNB versus those in whom lymphadenectomy was delayed until clinical diagnosis (72.3% vs 52.4%).[3] This prospective trial, along with a considerable amount of other evidence, forms the foundation for early intervention in the setting of nodal metastases for melanoma. The impact of early detection of nodal metastases is strongly supported by the results of these data.

The addition of lymphoscintigraphy and the intraoperative use of a gamma detecting probe has greatly facilitated the successful implementation of sentinel node biopsy and has truly enhanced nodal staging by thoroughly examining lymphatic drainage patterns from a given anatomic location.[30] With widespread application of these technological advances, greater attention has turned toward lymph node basins that are situated outside the axillary, inguinal, and cervical regions, variably designated as ''interval,'' ''unusual,'' and ''aberrant.''[31-37] More than one study has demonstrated that nearly 90% of these unusual nodes identified during SLN procedures for distal extremity lesions are located in either the epitrochlear or popliteal nodal basin[31-33,35]; management of these sites is discussed specifically later in this article. Nodes outside these basins, however, must be considered separately, especially because they are generally not associated with a ''dissectible'' bed. Because these nodes may be sentinel, identification of nodal involvement microscopically is now a more common occurrence than it was prior to the SLN era, when essentially all of the ''in-transit'' or interval nodal disease was clinically apparent. In the event that one encounters a positive node in a location outside a true nodal basin, removal of the node at the time of SLNB is considered adequate treatment. Management of the nodal basin associated with the lesion should be defined by the sentinel node status of that basin, not by the status of the interval node. Removal of all sentinel nodes remains critical to the management of patients with melanoma and therefore these interval nodes should not be ignored but, rather, biopsied as a routine part of sentinel node biopsy.

It is not uncommon for patients, at the initial diagnosis of melanoma, to undergo routine laboratory and radiographic evaluation. This is often driven by referring physicians prior to presentation to a melanoma specialist. It is therefore important that we at least comment on this practice. In asymptomatic patients with SLNB-detected disease, there is no role for routine staging for synchronous distant metastases, and it is our practice to proceed with surgical intervention without additional imaging in this patient population.[38,39] In the current treatment paradigm, NCCN guidelines continue to support this concept. The recommendations from the NCCN regarding staging remain seated in the concept of ''clinician's choice'' or in response to signs or symptoms, unless patients have confirmed stage IV disease.[29]

Although there is no role for routine radiographic *staging* for asymptomatic patients with clinically node-negative melanoma, in some centers nodal ultrasound has been advocated as an initial approach to decrease the number of patients undergoing SLNB. Some authors advocate this imaging prior to patients undergoing SLNB, occasionally in conjunction with lymphoscintigraphy, to identify clinically occult disease without needing to use SLNB at all.[40] Several recent studies have investigated this approach.

Ultrasound is certainly a very helpful, noninvasive adjunct in the evaluation of lymph node basins in melanoma. Physical examination scrutinizing the regional lymph node basins is a critical component in the initial or follow-up evaluation of patients with melanoma; however, micrometastases are not detectable by palpation. As a result, there has been considerable interest in the role of ultrasound in the follow-up and management of patients. Several recent studies have demonstrated the utility of detecting metastatic deposits in the range of 2 to 5 mm.[41-45] However, it is also important to recognize that high-frequency ultrasound, even in expert hands, does not appear to be an adequate surrogate for SLNB. In a recent study SLNB was performed within 24 hours of lymphoscintigraphy and high-resolution ultrasound examination, thereby comparing ultrasound findings with pathologic data. The sensitivity, specificity, negative predictive value, and positive predictive value of ultrasound were demonstrated to be 24.3%, 96.8%, 60.3%, and 86.2%, respectively. With such a low sensitivity, and thereby high false-negative rate, ultrasound technology is not yet a reliable alternative to SLNB.[45] In a separate analysis, Voit and colleagues[41] demonstrated the ability to detect 65% of nodal metastases prior to SLNB, advocating that ultrasound should be a routine part of the pre-SLNB evaluation of patients with melanoma. Even though there is strong evidence of the benefit of ultrasound in the evaluation and follow-up of these patients, its routine use to screen patients prior to SLNB must be considered in the setting of a cost-benefit analysis and has yet to be proven as standard of care.

CLINICALLY POSITIVE NODAL BASIN

In those patients who do not undergo SLNB and develop clinical nodal metastases, or in whom concurrent, clinically detectable nodal disease is identified at the time of presentation, prognosis and treatment are considerably different than in those with

micrometastatic disease. Individuals with macroscopic, or palpable, nodal metastases have been shown to have a significantly worse survival than those who present with microscopic disease, even after accounting for lead-time bias.[2,46] In this group of patients, it is our practice to obtain a staging evaluation prior to surgical intervention. In patients in whom distant metastases are identified, systemic therapy can be initiated without delay, treating all sites of disease, in contrast to intervening surgically as the primary therapy, thus delaying treatment of unresectable lesions. Additionally, the extent of surgery recommended for the patient with clinical nodal disease differs in some sites, particularly the groin. In the case of palpable inguinal lymphadenopathy, there is a high incidence of associated external iliac and obturator nodal involvement, which necessitates surgical removal for definitive therapy. It is therefore common to perform an ilioinguinal lymph node dissection rather than an isolated inguinofemoral nodal dissection when patients present with palpable adenopathy in the groin.[47]

In patients who present with palpable adenopathy and either a history of melanoma or a new diagnosis of a primary lesion, we strongly advocate fine-needle aspiration (FNA) biopsy over excisional biopsy for histologic confirmation of disease.[48] Numerous studies in which FNA biopsies were performed in patients with melanoma and verified by either histopathologic diagnosis or clinical follow-up have demonstrated a sensitivity ranging from 92% to 96% and a specificity of approximately 99%.[49,50] The accuracy and utility of FNA biopsy has been demonstrated in a multitude of cancers but is particularly useful in the follow-up of the patient with melanoma. Recently, with the increased use of ultrasound, FNA biopsy has become even more useful, often being applied in conjunction with high-frequency ultrasound to diagnose patients with recurrence as early as possible.[41] In our melanoma clinic, we have a cytopathology suite so that FNA biopsy can be performed in real time, with nearly immediate results provided to both patients and clinicians.

THERAPEUTIC AND COMPLETION LYMPHADENECTOMY

Once metastases have been identified, the next intervention remains completion lymphadenectomy, in the case of SLNB, or therapeutic lymphadenectomy, in the case of clinically detected disease. There is evidence that indicates the use of this approach is less than one would hope, with as many as 50% of patients not getting the appropriate surgical intervention.[5] Furthermore, some authors have recently questioned the need for CLND in patients with minimal disease burden.[51] However, it is imperative that clinicians treating patients with melanoma recognize that until the results of current prospective trials demonstrate that a selective approach is reasonable, completion lymphadenectomy remains the standard of care and should be offered to all patients with nodal metastases who are not in a clinical trial.

Lymphadenectomy is generally well tolerated; however, careful evaluation of each patient, regional dissection, and clinical scenario is essential. Those patients who cannot tolerate general anesthesia are typically excluded, as are patients with widely metastatic disease who would not benefit from regional control. In addition, there are specific considerations in each of the lymph node basins typically approached in lymphadenectomy: axillary, cervical, inguinofemoral, ilioinguinal, and, less often, epitrochlear and popliteal. As a general rule, SLNB incisions should be oriented such that CLND can be performed while incorporating the biopsy scar en bloc with the lymphadenectomy specimen. An in-depth description of the exact techniques and anatomic dissection boundaries employed in each lymph node basin is beyond the scope of this article, but a review of the fundamental principles and complications of each region are discussed later.[52]

In axillary lymphadenectomy, the dissection includes levels I, II, and III, the fibrofatty tissue superficial and superior to the axillary vein, and occasionally it requires the division of pectoralis minor in order to gain access to the medial tissue of level III. The most common complications after axillary dissection are infection and seroma. In addition, slightly $<10\%$ of patients will develop some measure of lymphedema, although with a lower incidence of swelling than seen with breast cancer. During this extensive dissection there is also a risk of injury (albeit uncommon, particularly in experienced hands) to the axillary vein, the brachial plexus, the long thoracic nerve, and the thoracodorsal nerve.

The cervical lymph node basin is one that has been shown to harbor not only metastatic deposits from the head and neck but also the upper trunk. Management of head and neck melanoma can independently justify its own monograph. We recommend that lymphoscintigraphy and SLNB be routinely used in the cervical region, but there are some generally predictable patterns that melanomas of the head and neck tend to follow. Despite these expected patterns of drainage, the head and neck region is one of the greatest sources of failure of SLNB, largely because of the complexity of drainage and the close proximity of the primary lesion to the draining nodal basin, which frequently compromises the ability to discern nodes from background activity.[24,53,54] The current recommendation for the surgical treatment of most nodal metastases to the

cervical nodal basin is that patients undergo a modified, or functional, neck dissection inclusive of at least levels II, III, IV, and V (posterolateral neck dissection). In the era of SLNB, some authors consider a selective neck dissection inclusive of fewer nodal levels rather than more. This should be considered only in those patients who are found to have occult metastases on SLNB. We believe that of all anatomic regions, head and neck melanoma should routinely be referred to a specialty center with significant experience in melanoma and head and neck surgery.

Although epitrochlear lymph node dissections are only rarely performed, they have recently become a more common procedure with the advent of lymphatic mapping and SLNB. The yield of nodes from the epitrochlear area is typically low, and most often an epitrochlear dissection is performed in conjunction with an axillary dissection. The procedure is relatively straightforward, and infrequent complications consist of simple seroma formation and wound infection.

Like epitrochlear lymphadenectomy, popliteal lymphadenectomy is also a relatively rare procedure that has recently achieved greater significance in the SLN era. The task of removing the lymph node containing fibrofatty contents of the popliteal fossa is complicated only by the tedious task of peeling it from the major neurovascular structures of the lower leg.

Groin dissections are the regional nodal basin with the greatest disparity between SLNB disease and clinically detected disease. Groin dissections for primary lesions of the lower extremities and trunk may encompass the superficial inguinofemoral nodes, the iliac/obturator or ''pelvic'' nodes, or both. The extent of the dissection is determined by 2 factors: the method of identification of metastases (SLNB or clinical detection) or the presence of metastases on imaging in the pelvis. Most authors continue to advocate an inguinofemoral (''superficial groin'') dissection for disease identified by SLNB unless imaging identifies iliac or obturator adenopathy, while for disease identified via clinical examination or radiographic techniques, the recommendation is to perform an ilioinguinal (''superficial groin and deep pelvic'') dissection.[55,56] Many authors continue to advocate routine biopsy and intraoperative evaluation of Cloquet's node (alternatively described as the highest node in the femoral canal or the first node in the pelvis).[4] We have abandoned the routine use of this procedure, largely because of an analysis of our data in conjunction with that from the H. Lee Moffitt Cancer Center, which was presented at the World Melanoma Congress in 2009 (unpublished data, K. Delman). We still consider biopsy of Cloquet's node, however, in patients who demonstrated drainage to this node on lymphoscintigraphy at their original SLNB. Finally, in patients who have more than 3 pathologically involved nodes in the groin, we recommend subsequent pelvic lymphadenectomy.

Unfortunately, as mentioned previously, for many patients with positive sentinel nodes in the groin undergoing completion lymphadenectomy is not recommended.[5] Groin dissections are well known to have high wound-associated morbidity, and some studies report complications rates as high as 50%.[57-59] These complications include seroma or hematoma formation, cellulitis, flap or wound necrosis, wound dehiscence with exposed femoral vessels and possible hemorrhage, and an incidence of lower extremity lymphedema of more than 20%. Wound complications are so common that many authors advocate routine sartorius muscle transposition to protect the vessels should there be complete wound disruption. In the past year, practices aimed at reducing the morbidity from inguinal dissection have been the focus of seminars at the Annual Cancer Symposium of the Society of Surgical Oncology, several sessions at the World Melanoma Congress, and several monographs.[60]

It is important to acknowledge that regardless of the extent of disease present in a nodal basin, in patients with disease limited to the lymph nodes, surgical resection remains the approach with the only potential for cure and with the best outcomes. In fact, there is considerable evidence demonstrating that surgical resection alone may afford long-term survival.[61] Whenever possible, surgical extirpation should be offered to these patients as the first line of treatment, unless they are enrolled in a clinical trial. Furthermore, nodal metastases, even when bulky, tend to be resectable without significant injury to adjacent organs or structures, making the argument to pursue a surgical approach even more sound.

LYMPHADENECTOMY: ADVANCEMENT

At our institution we have focused on improving the substantial morbidity associated with groin dissections. In 2003, Bishoff et al[62] first described the successful use of an endoscopic approach to groin dissection in cadaveric specimens with penile squamous cell carcinoma. Unfortunately, they were unsuccessful at translating this to clinical utility. Further reports in the urology literature published by Tobias-Machado et al[63-65] and Sotelo et al[66,67] have described and further developed the concept of endoscopic groin dissection technique, with preliminary results demonstrating a reduced surgical morbidity.

At Emory we have modified the urologic description of videoscopic inguinal dissection and adapted it to the anatomically appropriate inguinal lymphadenectomy performed in patients with melanoma.[68,69] The procedure all but eliminates the inguinal incision and is therefore likely to reduce complications in a procedure

in which the predominance of the difficulties is the result of that incision. Among a fairly small cohort of patients (N = 25) who have undergone the procedure, our complication rate of 12% (3 of 25 dissections) is significantly lower than that of 50% published even in recent series of open groin dissection.

The overall adequacy of lymphadenectomy is another facet of surgical management that remains to be well quantified and standardized. Standardization of surgical procedures continues to be a goal that is nearly impossible to achieve; however, we continue to strive to at least set benchmarks to ensure that patients get an oncologically acceptable operation. The Sydney Melanoma Unit recently published their average number of lymph nodes removed during regional lymph node dissection, as this measure has been shown to be a reliable predictor of surgical quality in other tumors.[70] The cervical dissections were divided into those of 3 levels or less and those of 4 levels or more. They advocated that standards should ensure that axillary dissections should have at least 10 nodes, groin dissections 7 or more, limited cervical dissection 6 or more, and formal modified radical neck dissection more than 20 nodes.[70] Although lymph node counts continue to be a multifactorial number (extent of surgery, ability of pathologist to identify and count the nodes, size and morphology of nodes, ie, whether they are matted), this number at least gives us a rough benchmark to target.

MSLT-2 TRIAL FOR PATIENTS WITH POSITIVE SENTINEL LYMPH NODE

Retrospective studies have shown that approximately 70% to 80% of those with micrometastases on SLNB will have no other nonsentinel lymph node involvement on CLND. Furthermore, as mentioned previously, some authors also argue that patients with nodal metastases <1 mm in diameter have an outcome identical to those who are node-negative.[51] In an effort to spare this subset of patients the morbidity of CLND, numerous studies have sought to identify those patients in whom a positive SLNB could be followed by observation alone and in which subset of patients nonsentinel nodes are most likely to be involved with tumor.[71] In a recent study at our institution, Page et al[72] examined a number of risk factors and predictive models in a retrospective review of 70 patients who had undergone SLNB, and none of these were able to predict nonsentinel lymph node involvement prior to CLND.

In an effort to answer the question of what patients (if any) necessitate a completion lymphadenectomy after SLNB, Morton and colleagues have orchestrated the second phase of the Multicenter Selective Lymphadenectomy Trial, MSLT-2. The primary goal of MSLT-2 is to determine whether there is a disease-specific survival benefit observed in those patients who receive a CLND after positive nodal involvement on SLNB over those patients in whom a positive SLNB is followed postoperatively with serial nodal ultrasound. With the recent series of publications documenting the utility of ultrasound in the surveillance of patients with melanoma, the validity of these 2 comparison arms has been confirmed. There are a host of secondary goals for this study, and enrollment is ongoing. As with MSLT-1, it is likely that MSLT-2 will have a significant impact on the management of patients with melanoma.

ADJUVANT THERAPY: MEDICAL AND RADIATION

There is no doubt that surgical removal of regional disease is the most effective method of control and should be attempted whenever possible. Unfortunately, unlike with regional metastases, widely metastatic melanoma is nearly always associated with a poor prognosis. There is an array of biochemical and immunologic chemotherapeutic agents employed in current clinical practice; however, there is no clear consensus regarding standard therapy. Survival outcome data from these therapeutic regimens do not reveal a clear frontrunner, which is most likely the result of the low level of activity of all agents currently used in treating melanoma.[73,74] Even though there have been some modest advances in systemic therapy leading to improved disease-free survival, no agent has been shown to significantly improve locoregional control or overall survival.

Despite these disappointing results regarding systemic therapy, adjuvant interferon-α continues to be the standard of care for patients with regional disease. We strongly advocate enrollment in a trial for any patient who is a candidate, recognizing that the regimen of interferon has a considerable toxicity profile and a very limited benefit. Although these limitations are certainly concerning, studies have demonstrated a benefit to a small subset of patients, enough to maintain it as the standard of care. Furthermore, a recent prospective, randomized trial comparing biochemotherapy and interferon in the adjuvant setting was stopped early because on interim analysis biochemotherapy was not demonstrating any benefit over interferon.[75] Our current practice continues to be to offer patients interferon if an appropriate trial is not available for them.

Adjuvant radiation therapy (RT), despite the historic belief that melanoma is resistant to radiation, has shown some promise in the reduction of locoregional recurrence. In the axillary basin, control rates have been demonstrated as high as 88% at 5 years when treated with hypofractionated RT, which is significantly

higher than the 30% to 50% seen in comparable, high-risk patients treated with surgery alone.[76] Furthermore, a retrospective analysis of patients with cervical metastases who received RT after excision of nodal disease revealed comparable results. The 5-year local control rate was 93% and the distant metastasis-free survival rate was 59%.[77] Similarly, in the head and neck lymph node basin, regional control after RT has been reliably effective and safe, and may be considered in patients who are unable to tolerate general anesthesia, and therefore for whom neck dissection and systemic therapy are not options.[78] Despite impressive results in the cervical and axillary nodal basins, the groin remains a difficult area in which to advocate radiation. Radiation therapy in this region has met with significant morbidity and equivocal results concerning regional control.[79] Even though controversy still remains surrounding the routine use of RT in patients with nodal metastases, we advocate its application on a case-by-case basis, favoring it more readily in the cervical nodal basins and making considerable efforts to avoid it in the inguinal region. As a guideline, unresectable disease, extranodal extension, and/or involvement of 4 or more nodes are indications we use for consideration of RT.

SUMMARY

Surgical intervention should be the first consideration for regional metastases from melanoma. The extent of dissection is largely defined by the method in which metastases are identified, with clinically detected disease indicating a need for a more extensive dissection than that which is performed for a positive SLNB. Routine staging is not warranted for patients with SLN-detected disease unless they are symptomatic, but may be warranted in patients who present with clinical disease. Adjuvant therapy with radiation should be considered on a case-by-case basis, and interferon or trial-based systemic therapy should at least be offered to all patients.

It is significant to note that of all therapeutic modalities available for patients with melanoma, surgical extirpation remains the most effective option. In patients who are good candidates for surgery, this should be considered the first option. In general, patients with a new diagnosis of melanoma can be referred first to the surgical oncologist and subsequently to the medical oncologist, if indicated. In our center, it is not uncommon for patients to be routinely followed by the surgical oncologist only, particularly because many patients decline adjuvant interferon-α.

The most concerning report about the current state of the management of patients with melanoma was the recent study of Bilimoria et al[5] that as little as 50% of patients with regional disease actually receive the recommended standard of care. Bilimoria et al[80] set out to further elucidate this variation and disparity in quality of cancer care delivered in the United States. An expert panel was assembled who agreed on 26 valid quality measures encompassing various aspects of melanoma care, 10 of which were able to be assessed by using the National Cancer Data Base. The data revealed an extraordinarily wide range of adherence. In the patient-level assessment, a range of 11.8% to 96.5% of patients received the recommended level of care. At the hospital-level assessment, adherence ranged from 3.7% to 83% on each of the 10 quality measures.[80] This wide range in the quality of care delivered to patients with melanoma points directly to the need for improvement and standardization. On a regular basis, hospitals and cancer centers must be able to use quality indicators such as these to assess the current level of care being delivered and to identify areas for improvement.

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