

The standard of care for Merkel cell carcinoma should include adjuvant radiation and lymph node surgery

To the Editor: With a mortality rate of roughly 25%, Merkel cell carcinoma (MCC) is more commonly fatal than any other skin malignancy, including melanoma.¹ Fortunately, MCC is 100 times more rare than melanoma (about 400 US cases per year), but this poses a problem in terms of defining optimal therapy for this tumor because large randomized trials cannot easily be performed.

We read with interest the November 2000 article by Akhtar et al,² in which the clinical course and treatment of 10 patients with MCC as well as a review of literature on MCC were presented. Although we agree that the optimal treatment regimen for MCC has not been conclusively defined by randomized trials, we have concerns about the authors' statement that "It is not known whether prophylactic lymph node dissection and/or radiation and adjuvant radiation increases survival." It seemed to us that this statement sends the message that patients with MCC should not routinely be treated with these adjuvant modalities. In contrast to Akhtar et al, we believe that the literature, summarized below, strongly supports a role for both radiation therapy and lymph node surgery in the initial treatment of MCC.

There are numerous studies that support the value of adjuvant radiation therapy in improving both locoregional control of the tumor as well as survival time.³⁻¹⁰ For example, in a cohort from the Royal Brisbane Hospital, Australia, the local recurrence rate of MCC dropped from 100% (of 38 patients) who did not receive radiation therapy to 30% (of 34 patients) who received sufficient radiation therapy.³ Moreover, the median recurrence time increased from 5.5 months for patients with surgery alone to 16.5 months for patients with surgery and radiation therapy in this Australian cohort.³ Similar results were noted in a study from M. D. Anderson Cancer Center, Houston, Texas, where the local recurrence rate of MCC was 44% (of 34 patients) in the group who did not receive radiation compared with 12% (of 26 patients) in the cohort treated with adjuvant radiation therapy.⁴ Two further studies from Heidelberg, Germany, and Massachusetts General Hospital, Boston, showed complete locoregional control of MCC when immediate postoperative radiotherapy of the primary tumor site was given. If these studies are combined, 35% (of 34 patients) who did not receive adjuvant radiation of the primary tumor site showed an in-field recurrence of the tumor. In contrast, 0% (of 14 patients) who were treated with adequate radiation had a locoregional recurrence.^{5,6}

The efficacy of radiotherapy in MCC is further supported by reports of 4 cases of localized disease that were not treated with complete surgical excision but primarily with radiotherapy. Regional recurrence was not found in any of the cases.⁷⁻⁹ Moreover, the addition of radiation led to an improvement in survival: in one review of 35 patients, the 2-year survival for radiation-treated patients was 77% as compared with 40% for those who did not receive radiation, although this was not statistically significant.¹⁰

Surgical treatment of the draining lymph nodes has also been shown to improve survival of MCC.

From a study involving a total of 144 patients, the most common site of first recurrence of MCC is the draining lymph node region^{10,11} and control of lymph node involvement improves survival.¹⁰ In a study at Memorial Sloan-Kettering, elective lymph node dissection was the only independently predictive marker of relapse-free survival of MCC.¹¹ Although elective lymph node dissection is associated with significant morbidity, recent studies suggest the sentinel lymph node technique is highly sensitive in the detection of nodal involvement of MCC. Two studies showed that, of 30 patients with MCC treated with the sentinel lymph node technique, there was no recurrence of the tumor in those 26 patients with histologically negative sentinel lymph nodes. The other 4 patients with positive sentinel nodes received a complete dissection, which revealed further tumor involvement in every case.^{11,12} Because these studies demonstrate the sentinel lymph node technique has good sensitivity in MCC, it appears likely this technique would allow the survival benefit of lymph node dissection to be preserved while its morbidity is decreased.¹²⁻¹⁴

On the basis of the above data, we believe a multimodal approach with wide primary excision, adjuvant radiation to both the primary site and draining lymph node bed, and lymph node surgery is the best initial treatment for MCC. Although we agree with Akhtar et al that the quoted studies are not optimally controlled, randomized trials of large numbers of patients, we think the data strongly suggest that adjuvant radiation and lymph node surgery are effective in the treatment of MCC. Because limited data exist on this rare, highly malignant tumor, it is in the interest of our patients to act on reasonable presumptions from the existing studies. If MCC metastasizes, it is fatal, so great effort must be put into avoiding this by the most effective therapy. We believe that radiation and lymph node surgery are safe procedures that should be included as part of the routine initial treatment for this most deadly of all skin cancers.

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