

Letter to the Editor

Apparent Response of Cutaneous Merkel Cell Tumor to Topical Imiquimod

Dear *Cutis*®:

I just read the review article by Boyse et al entitled "Merkel Cell Carcinoma: A Case Report With Treatment Summary and Updates" (*Cutis*. 2004;74:350-356). The author posed the question, "Could combined chemoimmunotherapy be a useful complement to the modest success of radiation treatment?" I describe a case report of just such a method.

After having read articles on the successful treatment of melanoma and metastatic melanoma to the skin with topical imiquimod,¹⁻⁵ I was impressed, to say the least.

In April 2003, a long-time patient, aged 79 years, presented to my office with a 1-month history of an irregular dermal nodule measuring 2.6 cm in diameter on the right forehead. My wariness of this lesion was confirmed when the results of 2 skin biopsies showed Merkel cell tumor (a neuroendocrine malignancy that usually is fatal). Results of special stains confirmed the diagnosis.

The surgical oncologist was not eager to perform wide excision because of the extent of the tumor. Radiation therapy was recommended. At my suggestion, based on what I had read, the patient consented to trying topical imiquimod. I informed the oncologists that the patient was going to apply imiquimod cream every day to the entire forehead area, as I noted some new papules arising in the skin of the left forehead that I feared were additional Merkel cell tumors. After one week, the patient developed a brisk inflammatory response.

Results of positron-emission tomography and computed tomography scans performed at this time showed no tumor of the forehead or elsewhere, except a right intraparotid nodule. After 2 weeks of topical imiquimod therapy, I performed 2 more skin biopsies of the right forehead area because radiation treatments were scheduled. Histologic evaluation results revealed no residual Merkel cell tumor, and results of special stains were negative. The topical imiquimod cleared the forehead completely but did not affect the nodule in the right parotid; excision of the parotid gland

revealed the nodule was a Merkel cell tumor. During the patient's hospitalization, postoperative radiation was delivered to the right parotid surgical site. An elective knee replacement was done during this time; unfortunately, the patient developed sepsis and died.

Briefly, topical imiquimod is a novel topical immunomodulating drug first used for the treatment of genital warts. The drug works by inducing cytokines such as interferon, interleukin, and tumor necrosis factors, and by enlisting the aid of the Langerhans cell (the antigen-presenting cell of the skin) in this antitumor process.

If a patient presented with a severe malignancy such as a melanoma or Merkel cell tumor, and nodal metastases had not occurred, I would apply imiquimod daily to the site (after having received biopsy results). After an appreciable inflammatory response had been induced (eg, after 3 weeks), the area would be excised. In our aggressive surgical approach to serious malignancies, we may be missing the critical step in getting the body's immune system to recognize the problem.

Sincerely,
Don R. Scott, MD

The author reports no conflict of interest.

REFERENCES

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Author Response

In our opinion, against highly lethal tumors with early distal micrometastasis such as Merkel cell carcinoma, topical imiquimod is unlikely to have a favorable effect on outcome, even when used at the time of the initial diagnosis. The case report from Dr. Scott illustrates this point with the development of an intraparotid nodule. Unfortunately, due to the patient's death from complications of his knee replacement, we are not able to learn more about his

tumor response with regard to how the treatment would have worked.

The potential uses for imiquimod are just beginning to be realized. In the future, imiquimod may have a place as an adjuvant treatment modality for Merkel cell carcinoma. Dr. Scott's suggestion of using imiquimod as a first-line therapy for 3 weeks and then proceeding to surgical excision may be too long to wait for removal of the tumor because of the aggressive nature of Merkel cell carcinoma. For now, surgical excision remains the standard of care for this aggressive tumor.

Sincerely,
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