

# Topical Imiquimod Clears Invasive Melanoma

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## PRACTICE POINTS

- Topical imiquimod may clear invasive melanoma as well as melanoma in situ.
- Further study is required to confirm the role of topical imiquimod in melanoma treatment.

*Malignant melanoma has continually shown a pattern of increased incidence and mortality in the last 50 years. Currently, wide local excision is the mainstay of treatment of primary cutaneous melanomas. Imiquimod has been shown to clear cases of melanoma in situ, but its role in the treatment of invasive cutaneous melanomas is unknown. We present the case of a patient who achieved complete histologic clearance of invasive melanoma following treatment with topical imiquimod.*

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**M**alignant melanoma has continually shown a pattern of increased incidence and mortality over the last 50 years, especially in fair-skinned individuals. In fact, malignant melanoma has the highest mortality rate of all skin cancers in white individuals. Currently, wide local surgical excision is the mainstay of treatment of primary cutaneous melanomas.<sup>1</sup> The margins vary in size according to the Breslow thickness (or depth) of the involved tumor. As such, advancements in melanoma treatment continue to be studied. We present the case of

a patient with invasive melanoma that was cleared with topical imiquimod.

## Case Report

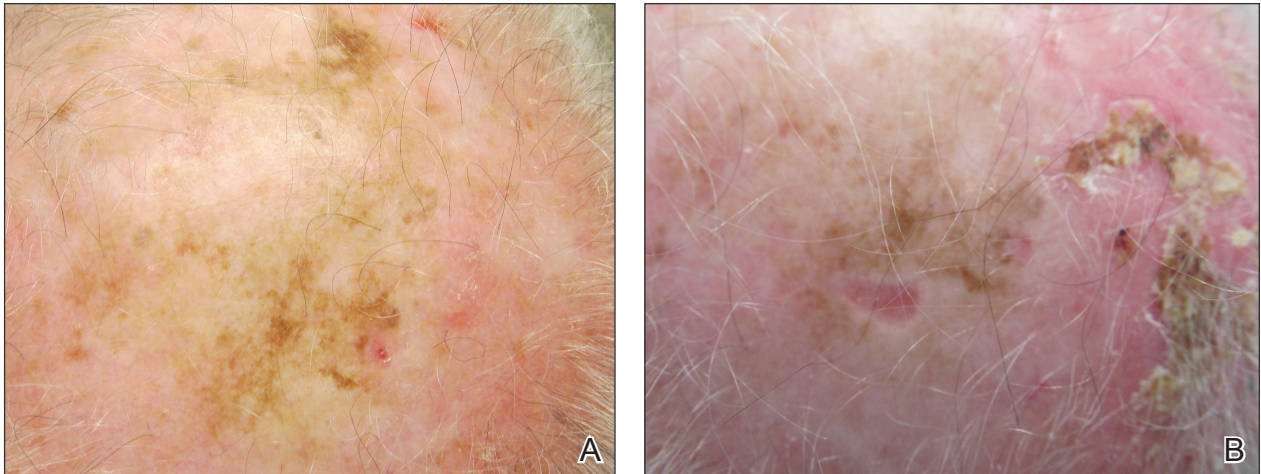
A 71-year-old man presented with biopsy-proven malignant melanoma on the right posterior scalp that was diagnosed a few weeks prior. The melanoma was invasive with a depth of 0.73 mm. The patient also had an approximately 8-cm, irregular, patchy area of hyperpigmentation involving almost the entire crown of the head (Figure 1A). The biopsy site used for melanoma diagnosis was on the right posterior aspect of the hyperpigmented area where a symptomatic pigmented papule was located. To determine if the rest of this macule represented an extension of the proven malignancy, surveillance biopsies were taken at the 12 o'clock (anterior aspect), 3 o'clock, 6 o'clock, and 9 o'clock positions on the head. All of the biopsies came back as lentigo simplex, which presented a clinical problem in that the boundaries of the invasive melanoma merged with the lentigo simplex and were not clinically apparent. Because an exact boundary could not be visualized, the entire area was treated with imiquimod cream 5% once nightly at bedtime for 4 weeks prior to excision of the original biopsy site. There was a notable decrease in hyperpigmentation in the treated area after 4 weeks of therapy (Figure 1B). The original biopsy site was then excised with a 0.6-cm margin and a complex linear repair was performed. Histologic examination of the excised specimen showed no residual melanoma.

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The authors report no conflict of interest.

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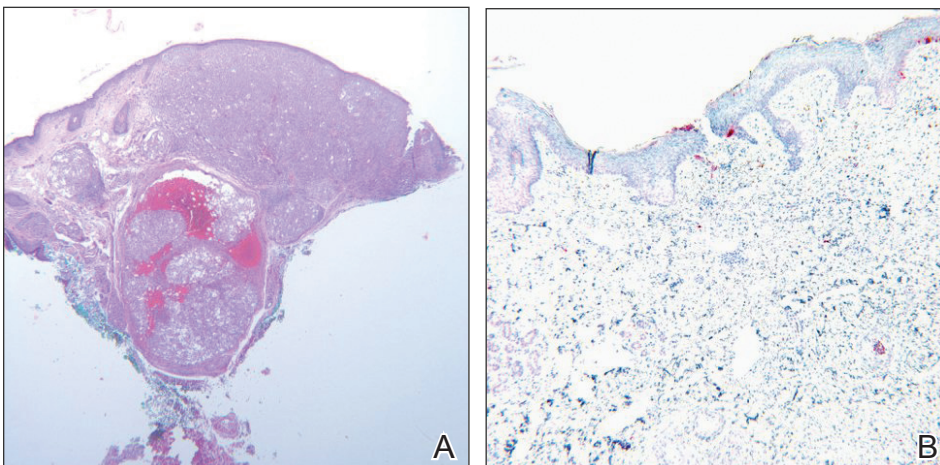
**Figure 1.** A patchy area of hyperpigmentation on the crown of the head near a melanoma biopsy site before (A) and after 4 weeks of topical imiquimod therapy (B).

**Comment**

Although surgical excision is the recommended treatment of cutaneous melanoma,<sup>1</sup> in some cases the defect following an excision can be quite large or even disfiguring. To minimize the size of the excision site, other treatment modalities should be studied. Imiquimod is an immunomodulating agent that exerts antitumor and antiviral effects. The US Food and Drug Administration has approved imiquimod for treatment of genital warts, actinic keratoses, and superficial basal cell carcinoma.<sup>2</sup> The most common side effects of topical imiquimod involve application-site reactions such as erythema, swelling, and crusting of the treated area. Ulceration of the skin also is possible. A small percentage of individuals have experienced systemic flulike symptoms after using topical imiquimod. Topical imiquimod has been used off label to treat non-invasive forms of melanoma. The topical therapy

has been reported to clear melanoma in situ and lentigo maligna.<sup>2,3</sup> In addition, imiquimod has been used as a palliative therapy for cutaneous metastatic melanoma.<sup>4,5</sup> In another case of a primary melanoma that responded to topical imiquimod, clinical and histological clearance of a recurrent oral mucosa melanoma was obtained.<sup>6</sup>

Moon and Spencer<sup>7</sup> reported a case of an invasive melanoma that was cleared with topical imiquimod. A 93-year-old woman presented with a central 2.75-mm thick invasive melanoma surrounded by a large area of melanoma in situ involving the left cheek and eyelid. The excised tissue was stained for CD31 and D2-40 to rule out intravascular and intralymphatic spread (Figure 2A). The standard-of-care treatment for this case would involve surgical excision with 2-cm margins and a sentinel lymph node biopsy, but given the morbidity involved with the surgery, an alternative treatment



**Figure 2.** Histology showed the invasive melanoma component before (A)(H&E, original magnification  $\times 40$ ) and after 5 weeks of topical imiquimod therapy with no residual melanoma (B)(Melan-A, original magnification  $\times 100$ ).

plan was made with the patient. The patient completed 5 weeks of topical imiquimod therapy and then underwent wide local excision with a 1-cm margin. Extensive histological examination of the excised specimen showed no residual melanoma; in fact, there was a near absence of junctional melanocytes that would normally have been seen. The specimen underwent immunoperoxidase staining for Melan-A (Figure 2B). The patient was followed for 14 months with no evidence of recurrence.<sup>7</sup>

### Conclusion

We describe a patient who achieved complete histologic clearance of invasive melanoma following treatment with topical imiquimod. Four weeks of topical therapy completely cleared an invasive melanoma that was 0.73-mm thick. Follow-up was recommended for the patient because long-term outcomes of this therapy are unknown. More studies demonstrating reliability and reproducibility are needed to evaluate the role of topical imiquimod in melanoma treatment; however, our case shows the potential of this topical modality.

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