Large Facial Basal Cell Carcinoma Treated With Multimodal Combination Therapy

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Large basal cell carcinomas (BCCs) with mixed intratumoral histology can present treatment challenges. Although a single treatment modality may be appropriate for some portions of the tumor, it may prove to be inadequate or overly aggressive for others. We describe a patient with a large facial BCC who was referred to our clinic for Mohs micrographic surgery. Biopsies revealed both noduloinfiltrative and superficial patterns. To excise the tumor completely would have been disfiguring, and topical therapy alone would have been inadequate. A multimodal approach using Mohs micrographic surgery to excise the central nodular portion and topical imiquimod to treat the surrounding superficial portion resulted in an excellent clinical outcome. This approach, which minimizes morbidity by capitalizing on the benefits of various techniques, can be applied to any BCC demonstrating distinct nodular and superficial portions.

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Large facial basal cell carcinomas (BCCs) with variable histologic patterns can represent treatment dilemmas. Many BCCs demonstrate the simultaneous presence of a nodular infiltrative pattern in the center and superficial pattern at the periphery of the tumor.[1] Facial BCCs are best treated by surgical excision with margin control, which may not be feasible for very large lesions. Because one of the primary objectives of Mohs micrographic surgery is tissue sparing, this objective is not served if superficial BCCs confined to the epidermis can be effectively treated by another modality. The advent of topical immunomodulators for superficial BCCs offers an attractive adjunct to surgical or destructive techniques. We report a patient with a large facial BCC with mixed histologic features that was managed using combination therapy with Mohs micrographic surgery and topical imiquimod. Although the tumor in its entirety was essentially surgically unresectable without substantial morbidity and disfigurement, this combined approach offered the patient effective alternative therapy.

Case Report

An 89-year-old man with a history of multiple nonmelanoma skin cancers presented to a Veterans Administration hospital with a 3.5×3.2-cm ill-defined firm plaque on the left cheek with a surrounding area of peripheral erythema extending to the periorbital region, temple, and forehead (Figure 1). Initial biopsy of the central plaque revealed BCC and the patient was referred for Mohs micrographic surgery. At the time of surgery, frozen section surveillance biopsies of different areas of the tumor revealed nodular and infiltrating histology in the center and superficial BCC at the periphery. The noduloinfiltrative component was cleared in 2 stages of Mohs micrographic surgery with a defect size of 5.0×6.0 cm. The defect was closed using a full-thickness skin graft from the anterior neck (Figure 2). Because of the extensive nature of the superficial component, a decision was made to use nonsurgical therapy.

When the patient returned for follow-up 1 month after surgery, the graft site was well-healed with persistent erythema at the periphery consistent with residual superficial BCC. Imiquimod cream 5% was initiated (every other day for 10 weeks).

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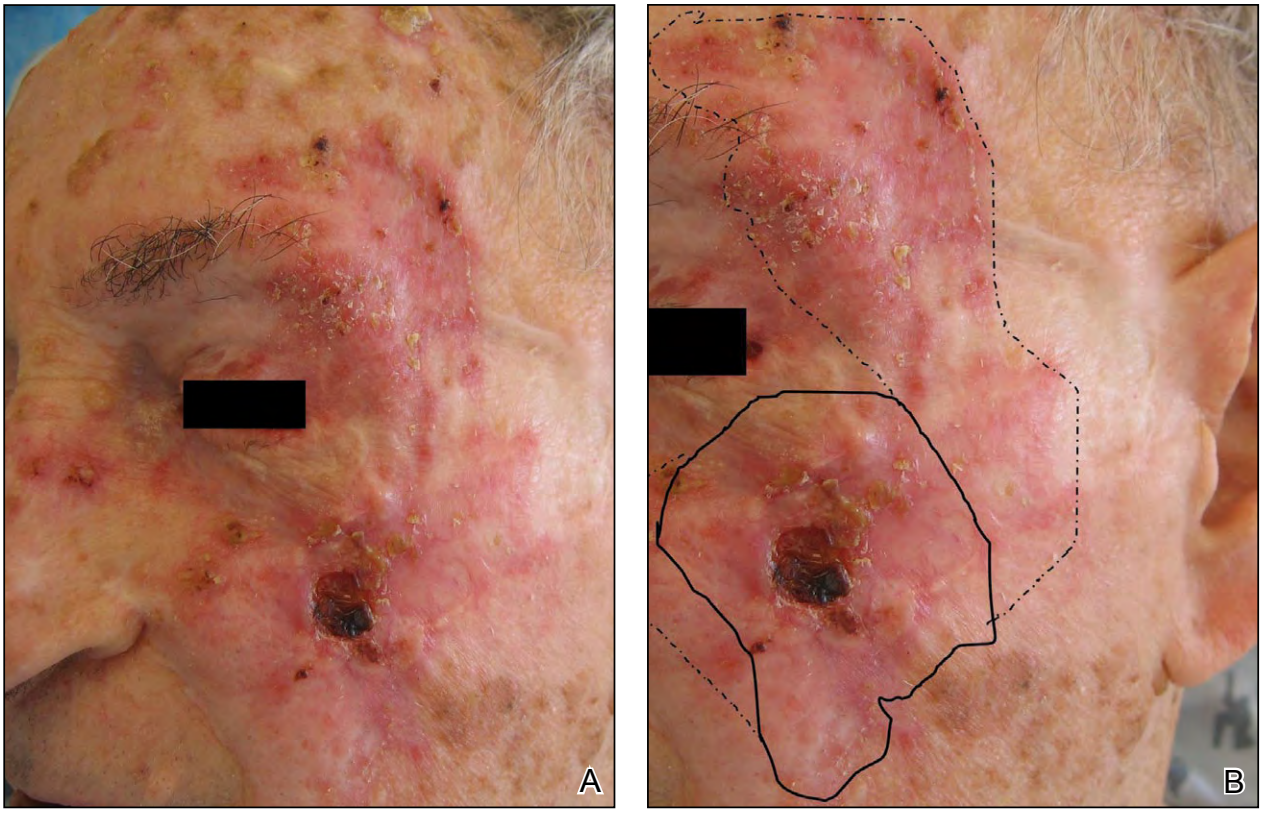

Figure 1. A large facial basal cell carcinoma with a central ulcerated firm plaque and peripheral erythema (A). Solid lines surround the noduloinfiltrative area treated by Mohs micrographic surgery; dotted lines correspond to the clinical margins of the superficial component (B).

Two months after completion of treatment, the patient showed clinical resolution of the superficial BCC and the presence of postinflammatory erythema. The patient refused surveillance biopsy. He remained clinically tumor free with the exception of a BCC that subsequently occurred on the left lower eyelid (Figure 3). Imiquimod had not been applied near the eyelids because of the risk for ocular irritation. The lower lid BCC was treated with Mohs micrographic surgery. No additional BCCs developed within the treatment site before the patient died of unrelated causes 2 years later.

Comment

It is common for BCCs to have multiple histologic subtypes within the same tumor,[1] yet histology is one of the most important factors to influence treatment selection. Our patient's original biopsy at an outside institution demonstrated nodular BCC. Examination of frozen sections during his Mohs resection revealed both nodular and infiltrative patterns in the central portion of the tumor with extensive superficial BCC at the periphery. Continuing to take layers in an attempt to clear the superficial BCC would have created an unnecessarily large wound with associated morbidity.

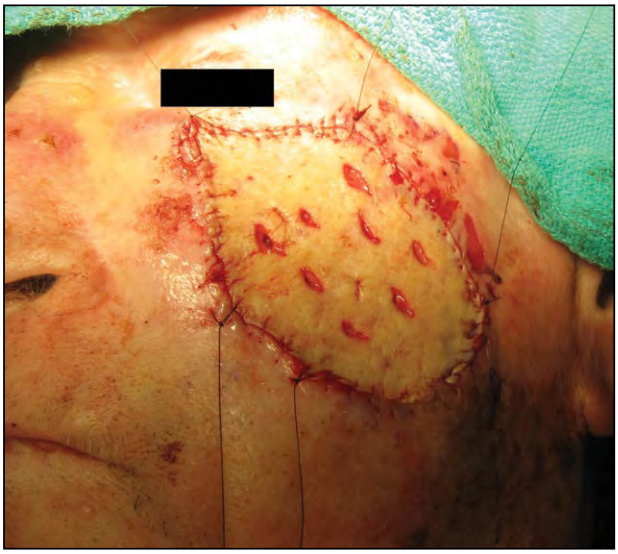

Figure 2. The defect from Mohs micrographic surgery was closed with a full-thickness skin graft from the anterior neck.

Topical therapy for superficial BCC with an agent such as imiquimod or 5-fluorouracil is an attractive alternative. Imiquimod was approved by the

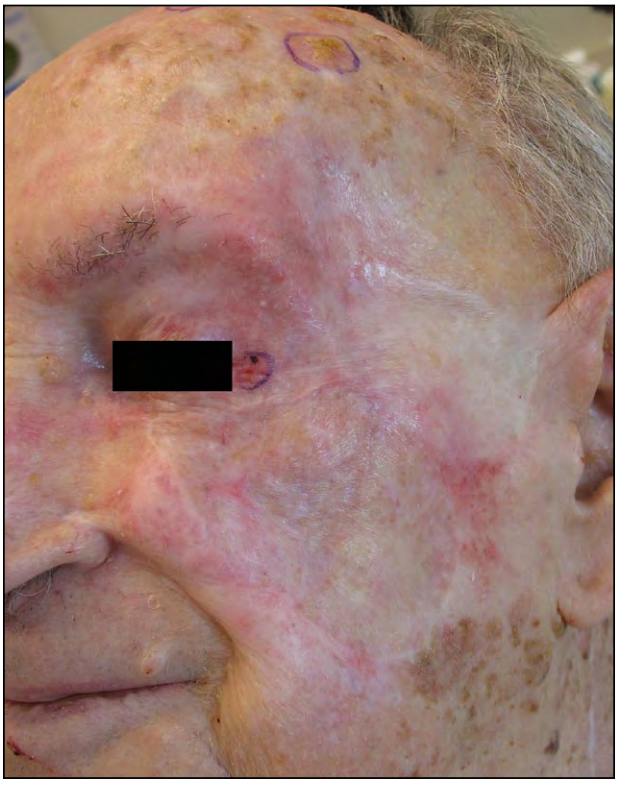

Figure 3. Two months after completion of topical imiquimod therapy, a nodular basal cell carcinoma was present on the left lower eyelid, which was not treated with imiquimod.

US Food and Drug Administration for the treatment of genital warts in 1997, actinic keratoses (AKs) in March 2004, and superficial BCC in July 2004.[2] It is an immune response modifier mediated by the toll-like receptors 7 and 8. Imiquimod recruits innate immunity, upregulates IFN-α, and increases antigen presentation, which produces a local inflammatory response with erythema, crusting, and itching. For BCC, it is thought that the resulting inflammation promotes apoptosis and eradication of the neoplastic cells.[3] Failure to initiate a local inflammatory response often heralds lower clearance rates and may be due to polymorphisms in toll-like receptors that impair imiquimod binding.[4,5] In phase 3 imiquimod trials, a 75% clinical and 82% histological cure rate for superficial BCC was reported with application 5 days weekly for 6 weeks. In this trial, it was noted that imiquimod's efficacy appeared to be proportional to the intensity of clinical inflammation.[6] In our experience, adequate inflammatory response fails to occur in approximately one-third of patients but may be improved by epidermal barrier disruption (unpublished observation).

An alternative topical therapy for superficial BCC is 5-fluorouracil, which has been long used for the treatment of AK. It was approved by the US Food and Drug Administration for the treatment of AK and was subsequently approved for superficial BCC in 2004.[7] 5-Fluorouracil interferes with DNA synthesis by impeding methylation of deoxyuridylic acid and effectively inhibiting thymidylic acid. Used twice daily for up to 12 weeks, it was shown to have a histologic cure rate of 90% for superficial BCC, which is comparable to imiquimod.[8] Local inflammation may be severe enough to preclude completion of treatment. Our patient was reluctant to use it based on prior intense inflammation when treating his AKs.

Conclusion

Our patient did well with clinical resolution of his large facial BCC using a multimodal therapeutic approach directed towards the different histologic subtypes of BCC: Mohs micrographic surgery for the noduloinfiltrative component and imiquimod for the extensive superficial component. Because of the possibility of a persistent tumor, close clinical follow-up and routine surveillance biopsies are warranted.

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