Resolution of Tinea Pedis With Imiquimod Cream 5% in a Patient With Nodular Basal Cell Carcinoma

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A 73-year-old white man with nodular basal cell carcinoma (nBCC) of the toe and interdigital tinea pedis was treated with imiquimod cream 5% once daily for 4 weeks and twice daily for 10 weeks. Results of a posttreatment potassium hydroxide (KOH) preparation and biopsy confirmed clearance of both tinea pedis and nBCC, respectively.

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Imiquimod 5% cream is a topical immune modulator that has been used to treat a variety of dermatologic conditions, including viral infections and nonmelanoma skin cancer.[1-3] Imiquimod is a toll-like receptor agonist. Although the exact mechanism of action has not been fully elucidated, imiquimod stimulates both the cellular innate and adaptive immune response. Toll-like receptors play a role in mammalian host defense.[4] Shortly after application, imiquimod induces local production of cytokines, including tumor necrosis factor α, interferon α, interferon γ, and interleukins 6 and 12.[5] A cytokine shift toward the type 1 helper T-cell (T_H1) pathway may be at least partially responsible for imiquimod's efficacy against a broad range of infectious and neoplastic conditions. I present the case of a patient who was successfully treated with imiquimod cream 5% for nodular basal cell carcinoma (nBCC) of the toe, which also resulted in resolution of concurrent tinea pedis in the adjacent toe web.

Case Report

A 73-year-old white man with poorly controlled type 1 diabetes mellitus was referred by his family practitioner for treatment of a growing 8-mm lesion on the middle phalanx of the left fourth toe. Results of a punch biopsy performed by his family practitioner 5 weeks before dermatologic evaluation revealed an nBCC that extended to the deep and lateral margins of the examined sections (Figure 1).

Physical examination revealed a thin elderly man with a noninflamed 6-mm biopsy site on the middle left fourth toe. Thin scaly plaques with subtle inflammation also were noted in all of the webs on the foot (Figure 2). Results of a potassium hydroxide (KOH) preparation of a skin scraping from the web proximal to the biopsy site revealed numerous branching hyphae, indicating tinea pedis. Results of a fungal culture of the scrapings were positive for *Trichophyton rubrum*.

Superficial destruction, excision, Mohs micrographic surgery with full-thickness skin graft, and radiation therapy were considered for the treatment of the nBCC. The patient's advanced age and underlying diabetes, as well as the location of the nBCC, made him a poor surgical candidate. Because of the significant risk of poor or delayed healing, dehiscence, and infection, imiquimod therapy was selected on the basis of the noninvasive nature of the treatment and previous reports of the drug's effectiveness in treating nBCC.[6,7] No specific treatment for the tinea pedis was instituted at that time.

Imiquimod cream 5% was applied once daily (7 d/wk) as a thin layer to the biopsy site and surrounding 5 mm of skin, which appeared healthy. At 4 weeks, there appeared to be insufficient inflammation induced by imiquimod, perhaps because of decreased penetration at the acral location. A study of imiquimod's effectiveness in BCC demonstrated that more prominent inflammatory responses are associated with higher cure rates.[8] Therefore, therapy was increased to twice daily (7 d/wk). Three to 4 days after increasing the dosage, the patient noted

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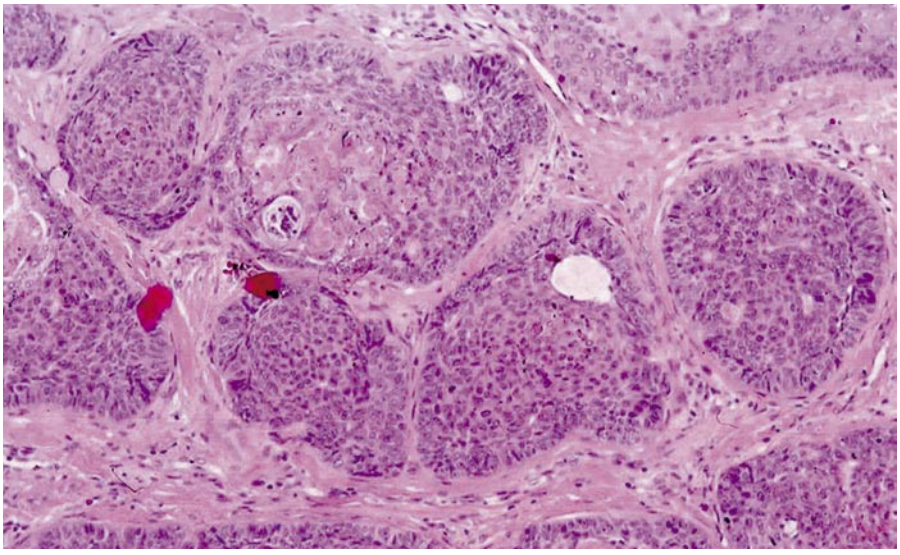

Figure 1. Punch biopsy results demonstrate islands of atypical basaloid cells in the dermis (H&E, original magnification ×200).

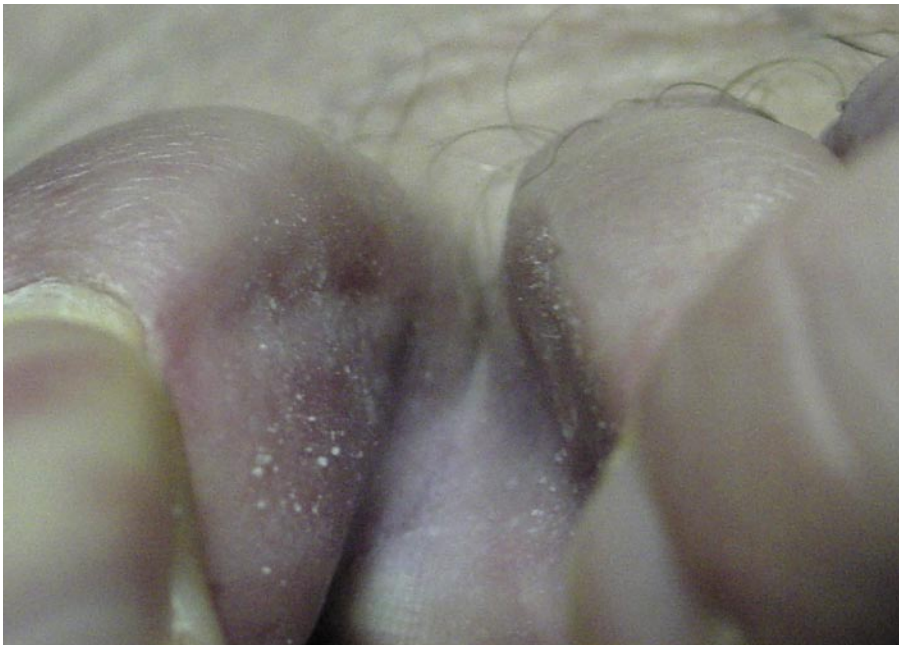

Figure 2. Baseline presentation of tinea pedis. Fine scale and mild erythema of toe web space were noted at the biopsy site.

the development of brisk erythema at and around the biopsy site.

Six weeks later, bright red erythema was noted at the biopsy site and throughout the entire interdigital web (Figure 3A). Results of a repeat KOH preparation of a skin scraping from the web proximal to the biopsy site were negative for fungal elements. Small erosions were noted at the site of the previous fungal infection. Results of a repeat fungal culture of the scrapings were negative. The patient had not experienced any substantial pain during treatment but reported an occasional burning sensation at the application site. He was instructed to apply imiquimod cream 5% twice daily (7 d/wk) to every web for an additional 4 weeks.

The patient was evaluated one week posttreatment (week 15). After completing a course of treatment with imiquimod cream 5% once daily for 4 weeks and twice daily for 10 weeks, there were no clinically visible signs of residual nBCC on the toe or tinea pedis in the webs (Figure 3B). Results of a repeat KOH preparation of scrapings from 2 additional webs were negative, confirming the clinical outcome. Furthermore, a scoop/shave biopsy taken at the original site of the BCC revealed no residual nBCC or evidence of fungal

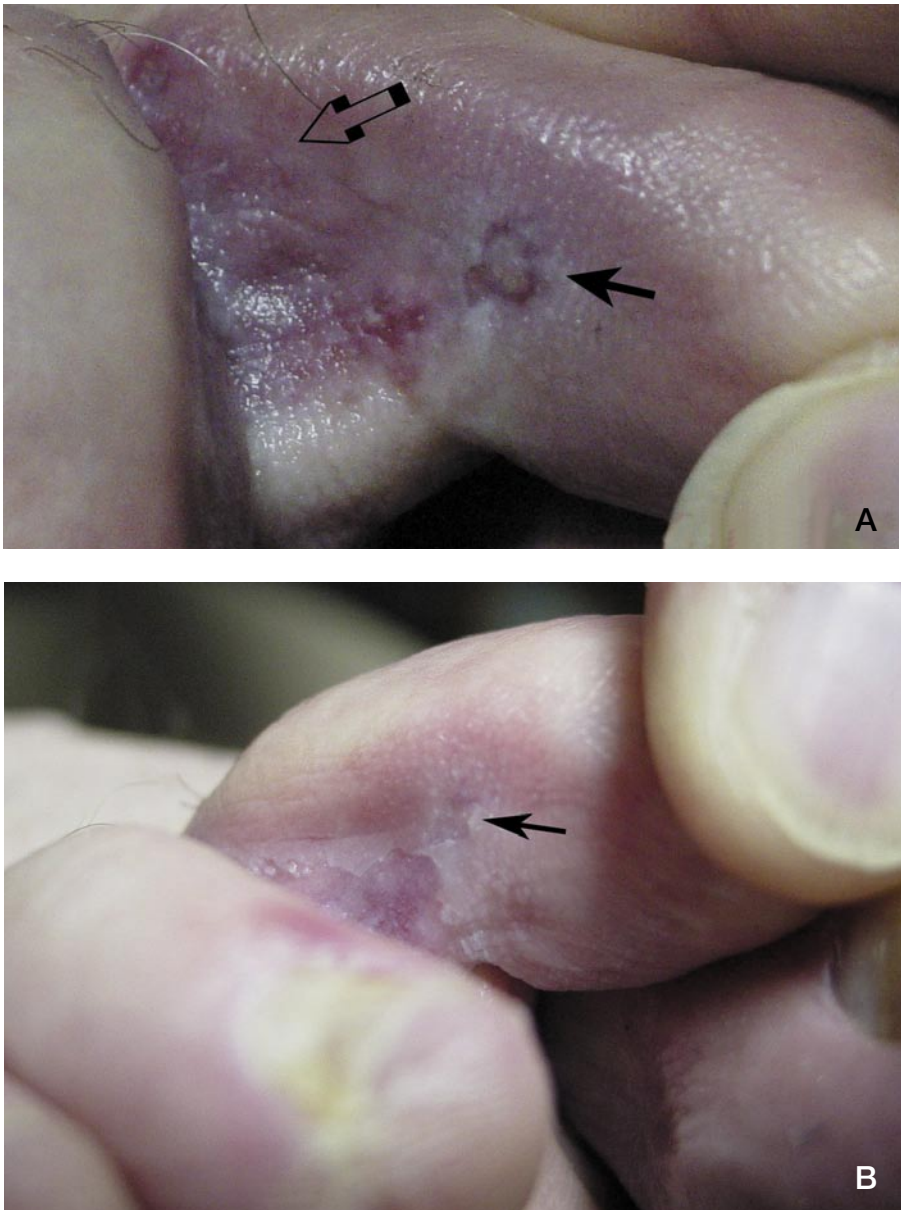

Figure 3. Interdigital web after treatment with imiquimod cream 5% applied once daily (7 d/wk) for 4 weeks and twice daily (7 d/wk) for 2 weeks (A). Solid arrow identifies the original biopsy site. Substantial red interdigital erythema was observed and is marked by the open arrow. Small erosions also were observed in the web space. Complete clearance of webs at one week posttreatment (week 15)(B). Residual web maceration at the site of the previous tinea infection was noted. Arrow indicates biospy site.

infection. The patient was followed clinically every 3 to 4 months, and at 14 months, no recurrence of the nBCC was observed.

Comment

The mechanism of action of imiquimod cream 5% and its role as a toll-like receptor agonist provides dermatologists with an innovative tool for their treatment armamentarium. Imiquimod's potent local stimulation of proinflammatory cytokines in monocytes, macrophages, and dendritic cells activates innate and cell-mediated immunity, thereby allowing the body's own immune system to effectively target tumor cells and infectious agents. This case illustrates the potential utility of imiquimod and provides further proof of concept for the proposed mechanism of action of imiquimod.

Tinea pedis can be a chronic condition, particularly in patients with impaired immune systems (eg, the elderly).[9] In fact, an inverse relationship between the degree of local inflammation resulting from fungal infection and chronicity of that infection has been suggested.[10] An imbalance favoring a type 2 helper T-cell response may be a cause of the chronicity of dermatophyte infections.[10-12]

Presumably, during the application of imiquimod cream 5% to the patient's nBCC, local proinflammatory cytokine production and up-regulation

of the T_H1 response, as well as possible local migration of the drug through physical activity, resulted in an up-regulation of the cell-mediated immune mechanism, with subsequent clearing of the tinea pedis. This suggests that imiquimod cream 5% may have been useful in boosting the local inflammatory response to effectively target the infection.[13]

Further evidence supporting the hypothesis that imiquimod was responsible for clearing the dermatophyte infection in this patient comes from negative results of KOH staining of other toe webs after imiquimod treatment. I do not advocate the use of imiquimod cream 5% as a primary therapy for garden variety tinea pedis; however, clinical situations may arise in which imiquimod cream 5% or other immune response modifiers might be useful. For example, imiquimod cream 5% may be used as adjunctive therapy to help clear persistent infections or to reduce recurrence rates of these infections by stimulating or bolstering a previously ineffective immune response. It would be interesting to examine whether other dermatophyte infections, such as chronic onychomycosis, would respond to imiquimod therapy.

Conclusion

In this patient, imiquimod cream 5% proved to be a useful therapy for nBCC and concurrent tinea pedis. Further investigation is warranted to examine the role of imiquimod in treating dermatophytoses.

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