Combination of Topical Imiquimod and Oral Acitretin in the Treatment of Multiple Large Basal- and Squamous-Cell Carcinomas of the Face

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Abstract

Historically, both basal- and squamous-cell carcinoma skin cancers have been treated surgically with high cure rates and good cosmetic results. However, patients with multiple large facial tumors may experience significant cosmetic scarring with surgery, and therefore represent a patient population that may benefit from a trial of medical therapy. The following case involves a 65-year-old white male who presented with multiple basal- and squamous-cell carcinomas of the face who refused surgical or radiation treatment. We treated the patient using combination therapy of topical imiquimod and oral acitretin, resulting in remarkable clearance of all cancerous facial lesions.

Figure 1

Introduction

The treatment of basal- and squamous-cell carcinomas generally involves surgical removal and occasionally radiotherapy.[1,2] Additionally, medical therapies such as topical imiquimod, topical 5-fluorouracil, oral acitretin, and most recently vismodegib have become a part of the armamentarium in cutaneous tumor therapy.[3,4] Despite these medical innovations, the standard of care remains surgical.[5] The majority of basal- and squamous-cell carcinomas may be excised, especially with the increasing availability of Mohs surgery.[2] In the event that a patient cannot undergo surgery or if the tumor is too large, radiation therapy may also be considered.[5] Generally, surgical and/or radiation therapies result in cure of non-melanoma skin cancers without a major adverse effect on cosmesis or quality of life.

The case presented herein represents one of the rare patients with multiple facial basal- and squamous-cell carcinomas who would experience significant surgical scarring with excision. Ultimately, the patient refused surgery and also opted against radiation therapy. We report that the combination therapy of topical imiquimod and oral acitretin resulted in complete resolution of the basal- and squamous-cell tumors after 16 months of follow-up.

Case Report

A 65-year-old man presented with multiple basal- and squamous-cell carcinomas of the face. Physical exam revealed large, erythematous, crusted plaques over the left side of the face (Figure 1) and smaller plaques on the right side of the face. Over a three-month time period, he was diagnosed with the following pathologies and sizes: a large, well-differentiated squamous-cell carcinoma of the left temple (5.5 cm x 6 cm) (Figure 2), a large squamous-cell carcinoma in

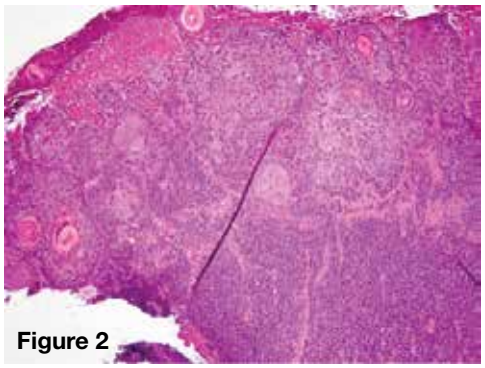
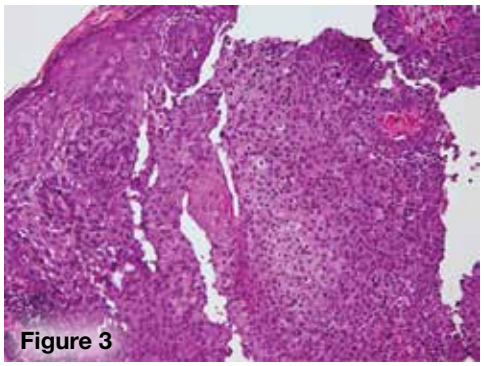


Figure 2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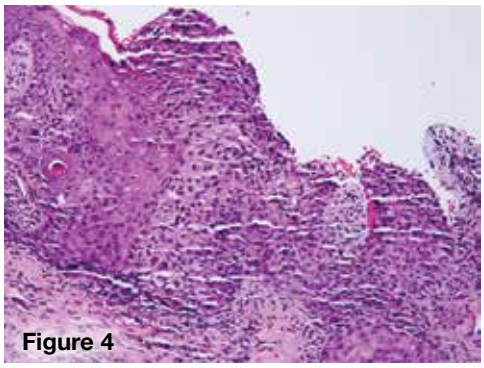
Figure 4

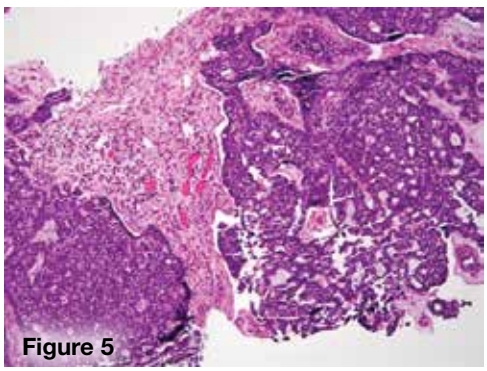
Figure 5

situ involving the base of the biopsy of the left cheek (8.5 cm x 4.5 cm) (Figure 3), squamous-cell carcinoma in situ of the left ear (0.5 cm x 0.5 cm) (Figure 4), and basal-cell carcinomas of the right upper chest (2.1 cm x 1.8 cm), right ear (0.5 cm x 0.5 cm) (Figure 5), right nasal sidewall (0.5 cm x 0.5 cm), and right forearm (2.2 cm x 2 cm) .

The basal-cell carcinomas of the right nasal sidewall and right forearm were treated with Mohs surgery without complications. As can be seen in Figure 1, the coalescence of the large, well-differentiated squamous cell carcinoma of the left temple and the large squamous-cell carcinoma in situ of the left cheek covered a significant portion of the patient's face, and surgical removal would likely have resulted in poor cosmesis. Initially, the patient was offered Mohs surgery and superficial radiation therapy, both of which he refused. He had a consultation with a radiation oncologist, who performed a PET-CT scan showing no evidence of metastatic disease. After informing the patient of the possible risk of death without surgery or radiation, we proceeded with treatment with the combination of topical imiquimod and oral acitretin. He was prescribed imiquimod 5% cream nightly with acitretin 10 mg daily for 12 weeks. After 12 weeks, he continued the acitretin 10 mg daily and decreased imiquimod 5% cream application to weekly.

After 16 months of therapy without any evidence of recurrence or adverse effects, the patient continues on this regimen as maintenance. As of publication, there is complete clinical resolution of his skin cancers (Figure 6), and the patient is very pleased with the cosmetic result.


Figure 6

Discussion

To our knowledge, our case is the first to report effective treatment with prolonged success of 16 months of multiple large basal- and squamous-cell carcinomas of the face with the combination of topical imiquimod and oral acitretin without surgical removal. We suggest this combination therapy may be a novel treatment approach for patients who are not surgical or radiation candidates. The combination of topical imiquimod and oral acitretin has been previously reported in preventing the recurrence of a highly aggressive squamous-cell carcinoma after the tumor was initially surgically excised in a patient status post renal transplant.[6] Another case found this combination effective for the treatment of multiple keratoacanthomas.[7] Acitretin as monotherapy for prevention of squamous-cell carcinoma in renal transplant patients has been established.[8,9] In additional, acitretin therapy alone was effective in case reports for the treatment of multiple squamous-cell carcinomas and keratoacanthomas.[10-12]

The combination of topical imiquimod and oral acitretin for the treatment of basal-cell carcinomas is limited to a few case reports.[13-16] A young boy with xeroderma pigmentosum with multiple facial and oral basal-cell carcinomas was treated with topical imiquimod and oral acitretin for four to six weeks.[13] At six-month follow-up, all tumors were clinically clear. In another report, two patients with giant basal-cell carcinomas were treated with topical imiquimod and oral acitretin to promote tumor regression prior to surgical or radiation therapy.[14] Additionally, topical imiquimod and oral acitretin have been successfully combined to treat extensive bowenoid papulosis in a patient with HIV.[15] While the literature contains examples of cases using this combination therapy in basal- and squamous-cell carcinomas, our case is unique given the large sizes of tumors, mixed pathology, and the extraordinary results with extensive follow-up at 16 months.

The rationale behind the combination of imiquimod cream and acitretin for anti-tumor therapy exists if one considers their individual mechanisms. In particular, imiquimod is an immune-response modifier.[17] Imiquimod stimulates cytokine production (interferon-alpha, interferon-gamma, and interleukin-12), thereby activating cell-mediated immunity, specifically anti-tumor activity.[17,18] The efficacy of imiquimod in treating superficial basal-cell carcinomas has been well-established with 43% to 100% efficacy, while the efficacy in squamous-cell carcinomas ranges from 73% to 88% for squamous-cell carcinoma in situ and 71% for invasive squamous-cell carcinoma.[3] Acitretin is a retinoid and thus mediates its effects via binding to nuclear-receptor genes and controlling cellular differentiation and proliferation and reducing keratinization.[19] The role of acitretin in skin-cancer therapy has emerged in the renal transplant population as a means of non-melanoma skin cancer prophylaxis.[8,9] Taken together, imiquimod works to activate the immune system to attack the tumor cells, while acitretin works to prevent further production of tumor cells.

Conclusion

Overall, this patient's case suggests an innovative medical therapy of basal- and squamous-cell carcinomas with topical imiquimod and oral acitretin. For patients who would suffer from significant surgical scarring or radiation side effects, we believe that dermatologists should be aware of the potential prolonged response with this therapy that may result in a more resectable tumor or in a complete tumor response.

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