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INTRODUCTION

During the coronavirus disease of 2019 (COVID-19) pandemic, the National Comprehensive Cancer Network, many medical organizations, and physicians have proposed delaying localized treatments for skin cancers, including melanomas. Physicians, who were conditioned to treating cutaneous cancers expeditiously, had to weigh the benefits of early cancer treatment for their patients versus potentially exposing them to SARS-CoV-2. The pandemic also ushered in the wide-spread adoption and acceptance of using telemedicine modalities for medical care by physicians and patients. Although this shift in healthcare delivery has allowed patients to practice social distancing and avoid in-person visits, there are many limitations in terms of medical care, especially with skin cancer treatments.

Although MIS is typically treated via surgical excision, reports have shown that topical imiquimod, 5-fluorouracil, and certain retinoids used as a mono or dual therapy have been effective treatments for MIS.

We present a patient who had two effective treatments of MISs in a pandemic setting with a combination of topical imiquimod 5% cream, 5-fluorouracil 2% solution, and tretinoin 0.1% cream. During the treatment phase, the patient had no person-to-person medical visits and was monitored with a telemedicine application.

CASE REPORT

A 66-year-old male physician had two biopsy-proven MISs on the left forearm (1.2 cm irregular pigmented patch) (Figure 1A) and left upper arm (6 mm asymmetric brown colored macule) diagnosed before the COVID-19 pandemic. He reported being a non-smoker but had a history of asthma with occasional bouts of acute bronchitis. His medications included theophylline and an albuterol inhaler. The patient (Fitzpatrick skin type I) also had an extensive sun-exposure history as a child and presented with multiple keratinocyte carcinomas (KCs) and actinic keratoses in adulthood. In the past, he had successful treatments of his KCs with the triple combination approach of topical imiquimod 5% cream, 5-fluorouracil 2% solution, and tretinoin 0.1% cream.

After his diagnosis of two MISs, the patient was instructed to see a surgical oncologist for the removal of both lesions. Due to the onset of the pandemic, which created a lack of available surgical appointments, he could not address both his MISs and had to resort to teledermatology. With the reality of these restrictions, unwillingness to have visits that could risk SARS-CoV-2 exposure, and concerns about having melanomas, the patient requested an alternative treatment that required no in-person interaction. After extensive consideration of the higher risks of undergoing non-surgical therapies and being fully informed of all options, the patient opted for a topical therapy protocol. The treatment involved a combination of 1/5 packet of imiquimod 5% cream, one drop of 5-fluorouracil 2% solution, and 1/5 of a pea-sized quantity of tretinoin 0.1% cream applied to each of his MISs with a bandage overnight. Although the patient was instructed to use 30 applications within a 42-day period, the patient completed his treatment protocols over 30 days. During these treatments, the patient employed a store-and-forward app (DermTRAC; Winchester, CA), which allowed him to report his progress and side-effects of treatment (Figure 1B) and receive customized medical instructions. Although the patient had a moderate amount of oozing, erythema, crusting, scaling, and burning in both treatment areas (Figure 1B), the patient could tolerate the cutaneous side-effects and compliantly use the topical medications. Three months after the conclusion of his treatment, the patient followed up with his dermatologist and had two tangential whole-lesional site biopsies, both demonstrating dermal cicatrix and absence of MIS (Figure 2C).

CLINICAL IMAGES

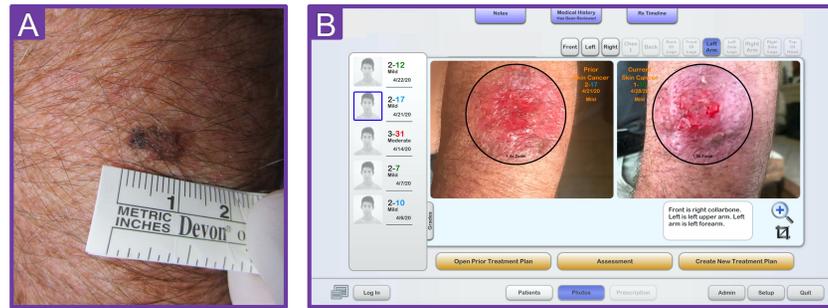


Figure 1. A) Clinical image of melanoma in situ on the left forearm. B) Dashboard of the store-and-forward app (DermTRAC) demonstrating transformed images of treated melanoma in situ on the left forearm. In the sequential images during treatment, there is a demonstration of erythema, oozing, and ulceration.

DISCUSSION

Although the standard treatment of MIS is a surgical modality, the pandemic period warranted a non-surgical approach. Many medical organizations also recommended the delay of skin cancer treatments during the pandemic, but some reports expressed dissenting opinions about delaying the evaluation and treatment of pigmented lesions. Studies have demonstrated the efficacy of topical treatments of melanoma or MIS solely with imiquimod, imiquimod and 5-fluorouracil, and imiquimod and tazarotene. Although tazarotene has been shown to have efficacy against MIS while tretinoin does not, the use of the triple combination with tretinoin was chosen over the combination with tazarotene as a treatment. In the authors' experience, patients with skin Type I and a history of extensive sun damage background displayed unacceptable amounts of inflammation with a tazarotene combination therapy. Other patients with MIS who have darker skin types and less sun exposure history may do well with the latter combination.

Imiquimod is thought to act through the innate immune system as a Toll-like receptor 7 agonist that can inhibit the proliferation of human melanocytes. Additionally, through their distinct mechanisms of action, 5-fluorouracil (anti-metabolite) and imiquimod (immune system enhancement) are thought to provide synergistic antitumor effects. Imiquimod stimulates the production of numerous inflammatory cytokines that upregulate the enzyme thymidine phosphorylase, which is accountable for converting 5-fluorouracil to its functional end product. This synergism, combined with the proposed penetration enhancement with retinoids and chemoprevention offered by tretinoin, could result in the use of less medication, fewer side-effects, improved clearance, and shorter duration of treatment. Since the presence of inflammation is an essential measure of the treatment's efficacy and a potential cause for discontinuation of therapy, the use of the store-and-forward app is an indispensable tool for monitoring and guiding the patient's treatment progress.

Our patient, who was relatively healthy with a couple of risk factors (age and asthma) for severe symptoms with COVID-19, was an ideal candidate for this treatment protocol. This treatment regimen may be even more warranted for those patients with multiple risk factors for developing dangerous symptoms with COVID-19, such as significantly advanced age, lung problems, weakened immune system, cancers, chronic kidney or liver disease, certain blood disorders, heart disease, diabetes, and obesity.

CONCLUSIONS

This description is the first reported case of MIS being treated with telehealth, a lack of in-person visits, and topical treatments. It is an example of how to manage MIS remotely during a pandemic crisis until an in-person visit is possible.

HISTOPATHOLOGY

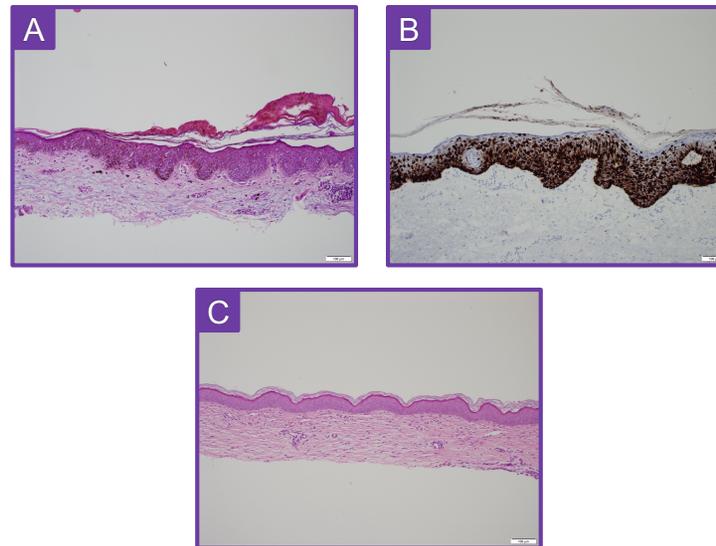


Figure 2. A) Hematoxylin and eosin staining of melanoma in situ of the left forearm. There is a mildly thickened epidermis with atypical melanocytes at all levels of the epidermis organized in a pagetoid pattern. Single cells have an expanded cytoplasm with a dusty tan pigment and enlarged nuclei. Some of the nuclei have a single nucleolus. There is no evidence of dermal invasion. B) Immunoperoxidase stain for Melan-A highlights the melanocytic cells of the melanoma in situ. C) Tangential biopsy of the left forearm post-treatment with imiquimod, 5-fluorouracil and tretinoin revealed only a dermal cicatrix.