Ingenol Mebutate 500 µg for Treatment of the Scalp in Refractory Field Cancerization

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Key Words

Ingenol mebutate · Field cancerization · Immunosuppression · Actinic keratosis · LLC · Scalp

Abstract

Patients suffering from chronic lymphocytic leukemia often develop actinic keratosis (AK) and squamous cell carcinoma in sun-exposed areas. In these particular patients, who have a suboptimal immune function, AK treatment can be particularly challenging. We report the case of a patient who failed to respond to most AK treatments, including 5-FU, imiquimod and photodynamic therapy, but responded to ingenol mebutate. We started with 3 applications of 150 µg/g (registered treatment of the scalp) and also 2 applications of 500 µg/g (registered in for trunk and extremities). Both treatments were well tolerated, but only the latter led to significant clinical success. This suggests that 500 µg/g of ingenol mebutate may represent an interesting therapeutic option in patients with mild immunosuppression.

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Case Report

The 68-year-old patient had a history of intense sun exposure that lasted most of his adult life. Together with a fair skin, this led to the development of many actinic keratoses (AKs) on the bald

part of his scalp, as well as several squamous cell carcinomas and basal cell carcinomas, which were treated by surgery. The AKs had been treated on numerous occasions with cryotherapy. According to the patient, imiquimod had also been tried, but with little significant effect. We were initially surprised by the notion of lack of success of imiquimod. We, therefore, conducted a new set of applications of imiquimod 5%, once daily for 12 days. To our surprise, there was no noticeable erythema or other sign of inflammation, even after 12 days of continuous application. This lack of inflammatory/immune response probably explains the lack of improvement of the AK he had previously observed. Taking a second look at the patient history, with a special accent on his immune function, we realized that the patient had chronic lymphocytic leukemia (CLL). We deduced that this could account for the lack of response to imiquimod, despite reports that this treatment is efficient in immune-deficient patients [1–4].

We decided to try other agents and focused our treatment on 5-FU and classic photodynamic therapy (PDT). Unfortunately, both modalities failed to improve the situation significantly. Daylight PDT and 5-FU failed to induce any observable response, while conventional PDT had to be discontinued early due to intense pain, which may explain why it did not induce a net clinical response either. Looking for new tools to treat this field carcinogenesis, we decided to employ ingenol mebutate. A course of ingenol mebutate as registered with 3 days of daily application of 150 µg/g resulted in a mild inflammation of the treated area (not shown), the first ever observed in this patient. The scalp was smoother after therapy, but 3 months later, the AK count had risen back to the initial level. Since the inflammation had been quite moderate, we switched to 500 µg/g of ingenol mebutate as an off-label treatment, starting on a hemi-scalp. This led to a more robust inflammation at day 4, well within the normal response we routinely observe with the 150 µg/g regimen (fig. 1). The AK response

Fig. 1. **a** Initial stage showing numerous AKs. **b** Day 4 after initiation of ingenol mebutate 500 mcg/g on the left side of the scalp. **c** Day 4 after initiation of ingenol mebutate 500 mcg/g on the entire scalp. **d** Skin after 3 cycles of ingenol mebutate 500 and excision of a squamous cell carcinoma of the vertex.

was much better, and using ingenol mebutate 500 at regular intervals of 6 months has allowed us to stabilize the scalp situation, with a net decrease in the number of SCC excision on the scalp.

The CLL slowly worsened during the few past years, prompting our patient's hemato-oncologist to start chemotherapy. The patient has responded well to this therapy, and we now hope that the increased function of his immune system will better keep AKs under control and favor a more prolonged response.

Discussion

In summary, we report the case of a patient responding neither to 5-FU nor imiquimod nor daylight PDT and not tolerating conventional PDT either, but who responded

well to a maximized regimen of 500 µg/g ingenol mebutate as an off-label treatment. We think that ingenol mebutate can be a useful option for dermatologists dealing with slightly immune-compromised patients.

Statement of Ethics

Informed consent to use images was provided by the patient.

Disclosure Statement

We have no conflict of interest to declare.

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