Rapid resolution of recalcitrant basal cell carcinoma of the ear with topical tirbanibulin

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INTRODUCTION

Actinic keratoses are precancerous lesions that may progress to invasive squamous cell carcinoma (SCC) in 0.1% to 20%.[1] Current treatment options are limited by poor cosmetic outcomes, intolerable side effects, or poor patient compliance. Tirbanibulin 1% ointment is a synthetic antiproliferative agent approved by the Food and Drug Administration in 2020 for the treatment of actinic keratoses in a contiguous area of 25 cm^2 as a once-daily topical treatment for 5 days. We recently reported the case of a periungual SCC that resolved with once-daily tirbanibulin 1% ointment application for 5 consecutive days. The lesion resolved on day 5 of application, with no perceived recurrence at 1 year.[2]

Abbreviation used:

SCC: squamous cell carcinombasal
BCC: basal cell carcinoma
LSR: local skin reactions

CASE REPORT

A 72-year-old Fitzpatrick type III male with biopsy-proven basal cell carcinoma (BCC) of the left ear measuring 9 mm (Fig 1) had been treated with topical imiquimod, 2 sessions of photodynamic therapy, and liquid nitrogen for 7 months with no evidence of improvement but dreaded surgery. Both sessions of photodynamic therapy included a 90-minute incubation period with plastic film occlusion. The patient then opted for off-label topical treatment with tirbanibulin 1% ointment once daily for 5 consecutive nights followed by no application for 2 weeks. He was treated with a light application of liquid nitrogen on the morning prior to the first night of tirbanibulin application to help facilitate deeper delivery of the antiproliferative agent. He was instructed to apply one-fifth of a sachet to the lesion each night without occlusion. The patient tolerated the treatment well with no local irritation (Fig 2). Clinical resolution of the BCC was noted at follow-up on day 21 (Fig 3), with no evidence of recurrence at 6 months (Fig 4). Persistent clinical resolution without dermoscopic examination was noted at follow-up 11 months after treatment.

DISCUSSION

Off-label treatment with tirbanibulin 1% ointment in this case was initiated based on the previous eradication of a periungual SCC in which the patient only experienced mild desquamation and no other adverse effects.[2] In phase 3 trials, topical tirbanibulin demonstrated complete clearance of actinic keratoses in 44% of patients in trial 1 and 54% in trial 2 with an estimated incidence of recurrence of 47% at 1 year. Local skin reactions (LSRs) included mild to moderate erythema, desquamation, application-site pruritus, and application-site pain that resolved spontaneously.[3] Studies have shown that apoptosis, with much less of an inflammatory response, rather

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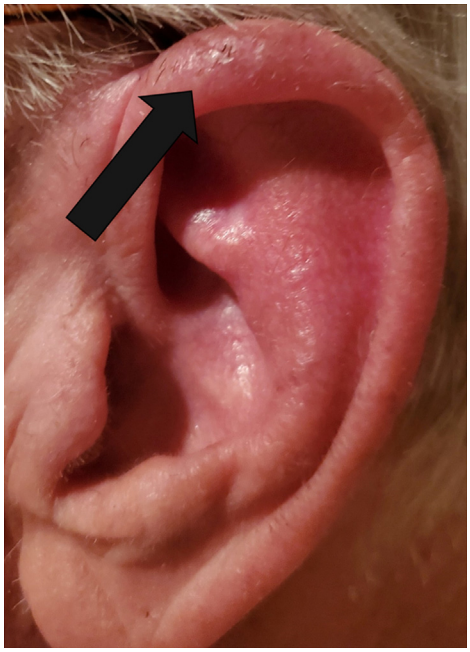

Fig 1. Basal cell carcinoma of the left ear before treatment with tirbanibulin 1% ointment.

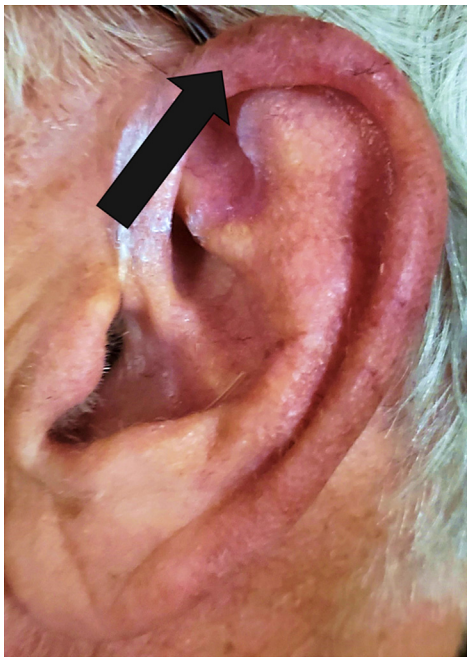

Fig 2. Basal cell carcinoma of the left ear on day 6 after treatment with tirbanibulin 1% ointment.

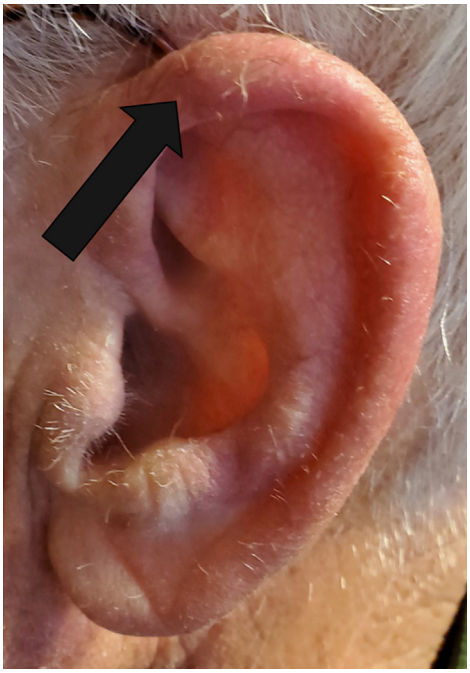

Fig 3. Eradicated basal cell carcinoma of the left ear on day 21 after treatment with tirbanibulin 1% ointment.

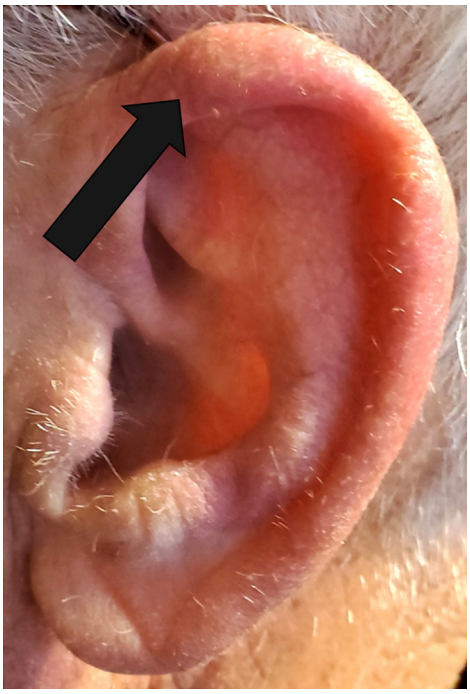

Fig 4. Persistent resolution of basal cell carcinoma of the left 6 months after treatment with tirbanibulin 1% ointment.

than necrosis may be the pathway to cell death with tirbanibulin; this may account for the decreased LSR with tirbanibulin. No irritation was seen in this reported case. Current topical medications used for the treatment of BCC including imiquimod and fluorouracil are usually associated with more significant LSRs including vesiculation or pustulation and erosion or ulceration and thus often have poor patient compliance.[3]

Tirbanibulin has demonstrated a dual mechanism of action via the inhibition of tubulin polymerization

and the disruption of Src kinase, an intracellular nonreceptor tyrosine kinase.[4] Downstream effects of tirbanibulin include induction of p53 expression, arrest of cell division at interphase Gap 2 and mitosis in proliferating cells, and subsequent stimulation of apoptosis.[3] Src family kinases including c-Src and c-Yes are involved in various signaling pathways and are believed to play an integral role in human epithelial cancers through overexpression or inappropriate activation. Continuous activation of Src family kinases have been shown to contribute to the proliferation and invasiveness of colon and breast cancers.[5]

Current data support upregulated c-Src activity in hyperproliferative skin disorders including malignant melanoma, SCC, and BCC.[5] Src kinase activity is reported to be higher in SCC than BCC.[4,5] Both the inhibition of microtubules and the disruption of Src kinase signaling likely play a role in the effectiveness of topical tirbanibulin in the treatment of nonmelanoma skin cancer as BCC and SCC follow different oncogenic pathways. The Hedgehog signaling pathway is an important factor in the pathogenesis of BCC, with nearly all BCCs showing amplified Hedgehog pathway.[6,7] It has been demonstrated that core components of Hedgehog signaling colocalize in the primary cilium, a microtubule-based organelle.[7] This could potentially be implicated in the mechanism for tirbanibulin effectively treating BCC.

Tirbanibulin 1% ointment has demonstrated good efficacy without severe LSR in our report of a periungual SCC and in this case of a BCC of the ear.[2] Larger retrospective and prospective studies of topical tirbanibulin for the treatment of nonmelanoma skin cancer are warranted to assess both efficacy and tolerability.

Conflicts of interest

Moore has received honoraria and/or research funds from Almirall, LLC.

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