Research Letter

Effectiveness Of Topical Tirbanibulin For Lentigo Maligna: A Case Series Of Eight Patients And Biological Insights

Andrea Agostini[1], Martina Merli[1], Paola Calamaro[2], Paolo Broganelli[1]

1 Department of Medical Sciences, Dermatology and Venereology, Mauriziano Umberto Hospital, Turin, Piedmont, Italy
2 Department of Medical Sciences, Anatomical Pathology, Mauriziano Umberto Hospital, Turin, Piedmont, Italy

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Corresponding author: Andrea Agostini, Department of Medical Sciences, Dermatology and Venereology, Mauriziano Umberto Hospital, Turin, Piedmont, Italy. E-mail: andreajr.agostini@libero.it

Introduction

Lentigo maligna (LM) is a subtype of melanoma in situ that typically affects chronically sun-exposed areas, especially the face and scalp of elderly patients. Surgical excision remains the

standard of care, but this may not be feasible due to lesion size, comorbidities, or patient refusal [1]. Topical imiquimod has been proposed as an alternative, although its efficacy is variable [2]. Tirbanibulin 1% ointment is approved for actinic keratosis and has shown antiproliferative and pro-apoptotic effects via inhibition of microtubule polymerization, blockade of Src kinase signaling, and p53 activation. Its off-label use in LM is still poorly documented [3,4].

Case Presentation

We retrospectively evaluated eight patients (aged 63–86; four women, four men) with histologically confirmed LM located on the face (n=6) or scalp (n=2). Surgery was not performed due to comorbidities, lesion size or location, or refusal. The first four patients had previously received imiquimod for three months without benefit. Based on their positive outcomes with tirbanibulin, this treatment was proposed as first-line therapy for the remaining four patients.

Tirbanibulin 1% ointment was applied once daily for ten consecutive days; three patients received a second cycle after two weeks. All LM lesions regressed spontaneously within approximately 14 days following treatment. Clinical and dermoscopic clearance was complete in five cases and near-complete (~90%) in three (Figure 1, figure 2). All patients experienced mild-to-moderate local inflammation (erythema, edema, pruritus, crusting), which resolved spontaneously.

In the three cases with minimal residual pigmentation, post-treatment biopsies confirmed the absence of melanocytic proliferation; the pigment was attributed to melanophages. No biopsy

was performed in cases of complete clinical and dermoscopic clearance. Follow-up ranged from less than 6 months to 3 years, with no signs of clinical or dermoscopic recurrence (Patient characteristics and treatment outcomes are summarized in Table 1).

Discussion

This case series highlights the potential of tirbanibulin as a non-invasive option for treating LM, particularly in elderly patients with large lesions or those unfit for surgery. The treatment was well tolerated, easy to apply, and induced a rapid and long-lasting response. The choice of tirbanibulin was guided by the clinical complexity of LM cases and by the failure of previous imiquimod treatment in half of the patients. Remarkably, histologic confirmation of tumor clearance supports the clinical results.

From a mechanistic perspective, the antiproliferative effect of tirbanibulin in LM cannot be explained solely by microtubule inhibition, since LM is a slow-growing tumor with rare mitotic figures. The additional roles of Src kinase inhibition and p53 activation deserve further exploration in this setting [5,6].

Conclusion

Topical tirbanibulin appears to be an effective and well-tolerated off-label therapy for LM. These preliminary results support further studies to explore its molecular mechanisms and to define standardized treatment protocols for this indication.

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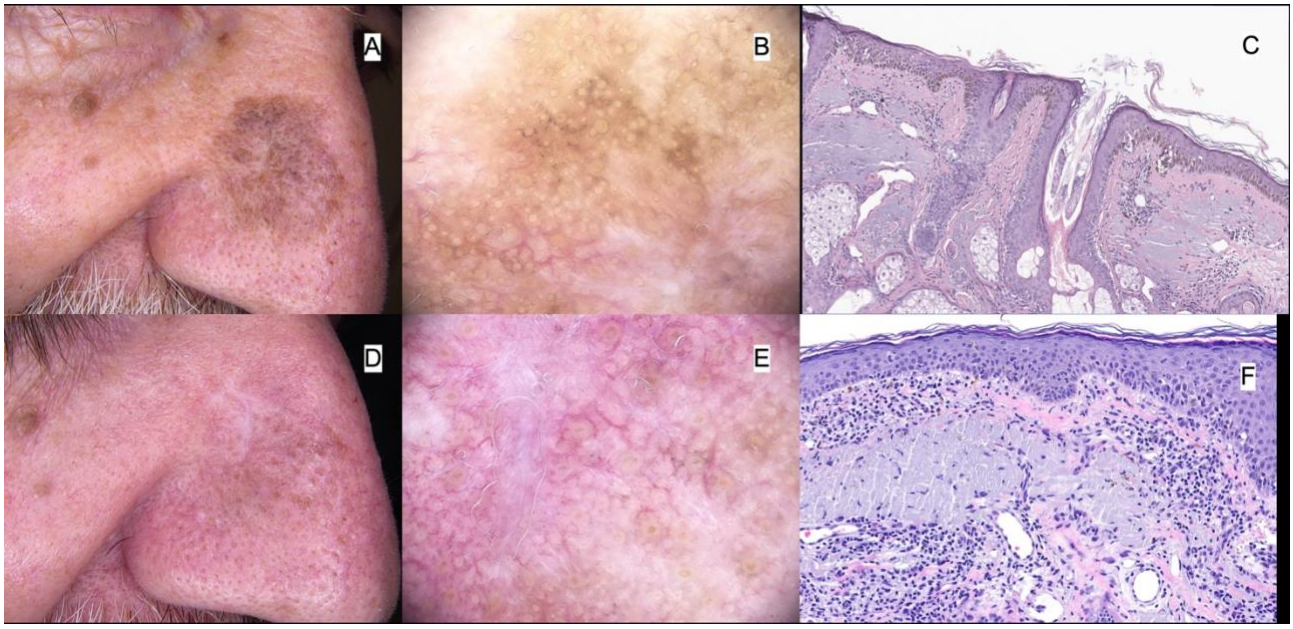

Figure 1. (A) Pigmented macule of the nose, previously treated with imiquimod without benefit and showing progressive growth; (B) dermoscopic examination at 20× magnification revealing irregular pigment distribution around the follicles; (C) haematoxylin and eosin stained sections of the incisional biopsy demonstrated a continuous proliferation of atypical melanocytes, with involvement of adnexal structures, in a severely sun-damaged skin (magnification 10x); (D) near-complete clinical resolution after two 10-day treatment cycles separated by a 2-week interval; (E) faint residual pigment in follicular areas with non-specific features on dermoscopic evaluation at 20× magnification; incisional biopsy post-treatment showing an inflammatory reaction in the dermis with diffuse infiltrate of small lymphocytes and melanophages. The melanocytic component was significantly vanished. (F) (Haematoxylin and eosin stained section, magnification 20x).

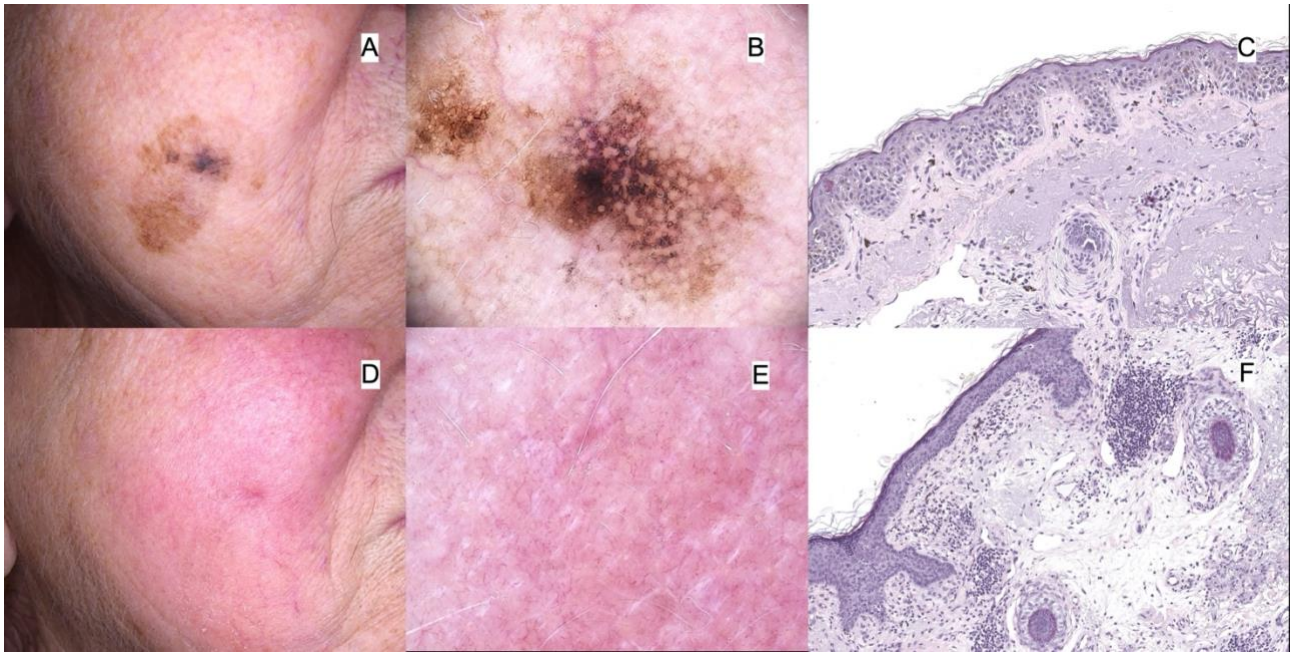

Figure 2. (A) Pigmented macule of the right cheek, previously treated with imiquimod without benefit and showing progressive growth; (B)dermoscopic examination at 20× magnification of the upper portion of the lesion revealing irregular perifollicular pigmentation and the presence of brown–slate gray granules; (C) incisional biopsy of the lesion showing a continuous proliferation of atypical melanocytes with pagetoid spread, in severely sun-damaged skin. (Haematoxylin and eosin stained section, magnification 10x) ; (D) complete resolution of the lesion with restitutio ad integrum; (E) disappearance of pigment on dermoscopic evaluation at 20× magnification; incisional biopsy post-treatment showing an inflammatory reaction in the dermis with nodular aggregates of small lymphocytes, melanophages and slight fibrosis. The junctional melanocytic component was vanished. (F) (Haematoxylin and eosin stained section, magnification 10x).

Table 1. Patient Characteristics and Outcomes Following Tirbanibulin Therapy for Lentigo Maligna.

Age	Sex	Site	Lesion size (mm)	Prior therapy	Regimen	Local reaction	Residual pigmentation	Post-treatment biopsy	Follow-up duration
63	M	Scalp	45	None	2 cycles of 10 days (2-week interval)	Mild	Yes	Negative	9 months
86	F	Face	40	IMQ	10 days	Mild-to-mid	Yes	Negative	9 months
79	M	Face	25	IMQ	2 cycles of 10 days (2-week interval)	Mild	Yes	Negative	9 months
85	F	Face	25	IMQ	10 days	Mild-to-mid	No	Not carried out	3 years
85	M	Face	15	None	10 days	Mild-to-mid	No	Not carried out	9 months
85	F	Face	20	Surgery	10 days	Mild-to-mid	No	Not carried out	9 months

75	F	Face	15	IMQ	10 days	Mild	No	Not carried out	9 months
70	M	Scalp	20	None	10 days	Mild	No	Not carried out	6 months

Abbreviations: IMQ: imiquimod.