

Lentigo Maligna: A Case Report on Off-Label Treatment with Imiquimod

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Abstract

Lentigo Maligna (LM) is a melanoma in situ on sun-exposed facial skin in the elderly. Although surgery is the standard treatment, anatomical and aesthetic concerns may limit its use: Imiquimod, a topical immune modulator, offers a non-surgical alternative. A 64-year-old woman with a 3 cm × 2 cm LM on the nasal dorsum refused surgery. Off-label treatment with 5% Imiquimod (five times weekly for 12 weeks) was started, and inflammatory reactions indicated an active immune response. Four weeks after finishing the treatment, a partial clinical improvement of the lesion was noted. At six months, no recurrence was observed, with excellent aesthetic and clinical outcomes. This case highlights Imiquimod's potential as a non-surgical alternative for LM in difficult-to-treat areas, emphasizing the importance of careful patient selection and close monitoring.

Keywords: *Lentigo Maligna; Imiquimod; Melanoma*

1. Introduction

Lentigo Maligna (LM) is a non-invasive melanoma in situ variant. Unlike the most common melanoma subtype, superficial spreading melanoma, which typically arises on areas intermittently exposed to intense UV radiation or previously sunburned skin, LM develops on chronically sun-exposed skin, primarily affecting the head and neck region [1].

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The gold standard treatment is surgical excision with histologically confirmed clear margins, ensuring complete removal [2]. Mohs micrographic surgery and staged excision are preferred in cosmetically and functionally sensitive areas, such as the face, to maximize tissue preservation [3].

For patients ineligible for surgery, alternative treatments include radiotherapy, which provides good local control but may result in hypopigmentation or fibrosis [4]. Topical therapies, such as Imiquimod 5% cream, represent an off-label option by stimulating a local immune response against tumor cells. Studies suggest its efficacy in selected cases, particularly in elderly patients or those refusing surgery [5]. Another off-label approach is photodynamic therapy (PDT), though its effectiveness is less established [6].

The Authors report the case of a patient with a LM successfully treated with off-label use of Imiquimod.

2. Case Report

A 64-year-old woman presented with an irregularly pigmented macule measuring approximately 3 cm × 2 cm on the nasal dorsum, which had progressively enlarged over the past few years. The lesion was found in a context of chronically sun-damaged skin. Dermoscopy revealed features consistent with Lentigo Maligna, including poorly defined margins, uneven coloration, asymmetric pseudo-reticular pattern, irregularly distributed pigment areas around hair follicles and obliteration of the follicular openings (FIG. 1).



FIG. 1. **A) Clinical before the treatment; B) Dermoscopy before the treatment.**

Although excisional biopsy is necessary for determining the Breslow score, we decided to perform incisional biopsy for confirming diagnosis and due to the patient's condition, also supported by dermoscopic characteristics of the lesion. The incisional biopsy confirmed the diagnosis of melanoma in situ type Lentigo Maligna, showing a proliferation of atypical melanocytes in a continuous intraepidermal pattern. The dermis exhibited fibrosis, elastosis, and chronic inflammation with

the presence of melanophages. The diagnosis was further supported by positive immunohistochemical staining for HMB-45 and S100 (FIG. 2).

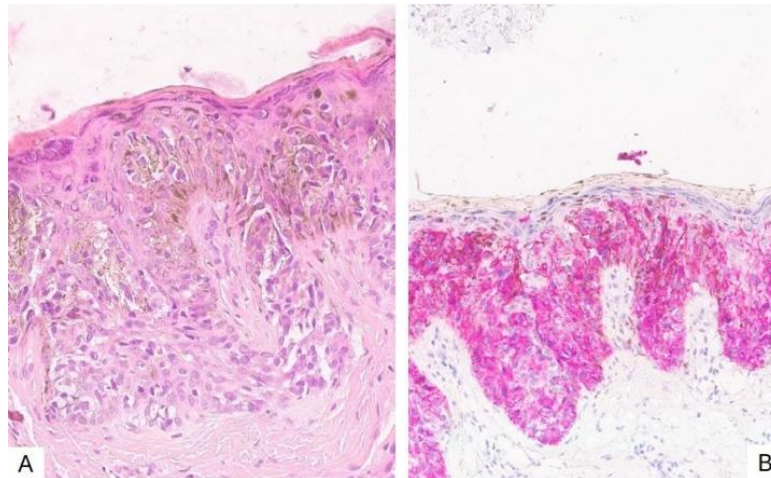


FIG. 2. A) Histology in hematoxylin-eosin; B) Histology with immunohistochemistry for HMB45.

Given the delicate anatomical location of the lesion and the patient’s desire to avoid invasive and potentially disfiguring surgery, off-label treatment with 5% Imiquimod cream was started, applied five times a week for 12 weeks on the lesion and 1 cm beyond the clinically healthy-appearing skin. During treatment, the patient developed a local inflammatory response characterized by erythema, edema, and desquamation, indicating an active immune reaction.

Four weeks after completing the treatment, a partial clinical response of the lesion was observed. At a six-month follow-up, the patient exhibited no recurrence, achieving good aesthetic results without significant complications (FIG. 3).



FIG. 3. A) Clinical after the treatment; B) Dermoscopy after the treatment.

After the treatment, a new histological examination was not performed, both for patient’s decision and dermoscopic features that left no doubt that the lesion was completely healed.

3. Discussion

This case highlights the effective use of Imiquimod in treating LM, a condition that typically poses significant challenges due to its anatomical location and the potential for surgical complications. Imiquimod acts primarily by stimulating the local immune system to recognize and attack atypical melanocytes. It activates toll-like receptor 7 (TLR7), leading to the production of pro-inflammatory cytokines (INF-alpha and TNF-alpha), activating Natural Killer (NK) cells, and ultimately enhancing the body's immune response against the tumor cells [7]. Its effectiveness can vary based on lesion size, depth, and the degree of atypicality of the melanocytes. Clinical studies report clearance rates for LM ranging from 37% to 97%, with higher success rates generally seen in smaller lesions [8-10].

The assessment of treatment response can be challenging; however, it typically induces clinical inflammation, which is often linked to a positive outcome [11].

Moreover, Imiquimod may serve as a neoadjuvant therapy, especially in cases where surgical excision is not immediately feasible. By reducing tumor burden prior to surgery, it can facilitate more effective and aesthetically favorable surgical outcomes [12].

Imiquimod can be also combined with other modalities, such as cryotherapy, to enhance treatment efficacy. Cryotherapy can induce additional local tissue destruction, potentially allowing for better penetration of Imiquimod into the lesion. This combination approach could also help to manage larger or more resistant lesions [13].

In conclusion, Imiquimod represents a valuable non-surgical treatment option for Lentigo Maligna, particularly in patients seeking to avoid invasive procedures. Its mechanism of action, which stimulates the local immune response, can lead to favorable clinical outcomes, often indicated by associated inflammatory reactions. Continued research and careful patient selection will be crucial in optimizing the use of Imiquimod, ensuring that it remains a relevant and effective option in the management of Lentigo Maligna. Overall, this case underscores the importance of personalized treatment strategies tailored to individual patient needs and preferences.

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