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Case Report

# Complete remission after imiquimod Monotherapy Treatment of LM: A Case Report

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## Introduction

Lentigo maligna (LM) is an epidermal melanoma without dermal invasion irrespectively to LMM. The incidence increased over the last few years [1-3]. LM and LMM originate mostly on the head and neck i.e. in chronic sun-exposed area and are categorized as high cumulative solar damage [4]. Currently, the way to monitor and manage lentigo maligna (LM) by the gold standard procedure is only surgery with 1 cm-margins [5]. It can be very damaging especially on the face and some patients have potential functional and aesthetic surgical sequelae. Moreover, some patients are too weak or the lesion area and spreading cannot allow the surgeon to take 1 cm margins. In these cases, the care could be challenging. Imiquimod (Aldara®) has been proposed as a neoadjuvant treatment for LM before surgery to reduce the size of the lesion and decrease the margins [6,7]. There are currently no official recommendations. Currently, Aldara® is codified for the management of superficial basal cell carcinoma with application 5 days a week for 6 weeks, multiple actinic keratosis with application 3 days a week for 4 weeks and condyloma with application 3 days a week for 16 weeks [8]. A recent presentation in ASCO 2021 reported efficiency of Aldara® in LM is used as neoadjuvant therapy 5 days a week for 4 weeks then therapeutic window for 4 weeks before surgery with margins reduced to 5 mm [9]. We report a complete response of LM treated by imiquimod monotherapy without any completion surgery.

### Observation

A 90-year-old patient presented a clinically suggestive lesion of LM in November 2018. No significant disease was reported except high blood pressure. He presented a 4 cm left polychrome inhomogeneous-pigmented temporal lesion, with two very dark areas (Figure 1, A-B).

The diagnosis of LM was confirmed performing a biopsy (Figure 2, A-B). The patient was old and refused surgery. As an alternative, it has been decided to start topic treatment with Aldara® 3 days a week in May 2019 and the patient was followed up.

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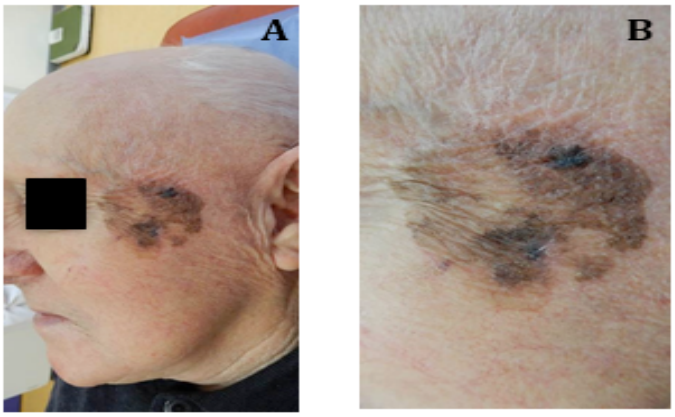


**Figure 1 A, B:** Pigmented inhomogeneous polychrome temporal lesion.

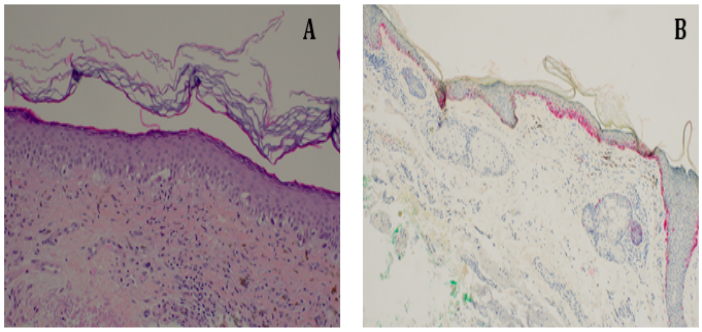


**Figure 2:** Histopathologic findings. A, melanocytic cells proliferation in the basal layer. B, melanocytic cells Melan-A positive in immunohistochemistry.

## Results

During the follow-up visit in July 2019, i.e. 2 months after Aldara® initiation, progressive depigmentation of the lesion is observed. Treatment is well tolerated. We decide to continue for another 3 months because of encouraging result. In September 2019, LM keeps on declining both size and colour. In November 2019, i.e. 6 months after treatment initiation, persisted only a 5 mm light brown -area with dermoscopic wrecks of pigment. . There is no more visible lesion in August 2020 (Figure 3) and dermoscopic examination was normal. . The patient reports no adverse events. In order to ensure the absence of residual lesion, 3 biopsies are performed in different areas of the initial lesion. . No melanocytic residual lesion is reported in all the biopsies but only fibrous scarring secondary to Aldara® (Figure 4).

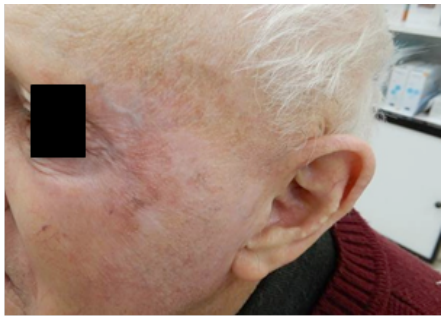

**Figure 3:** No visible evaluative lesion in August 2020.

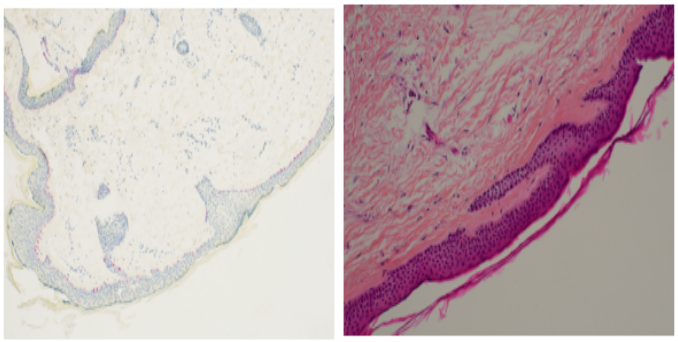

**Figure 4:** Histopathologic findings after imiquimod. No residual melanocytic lesion, only fibrous tissue secondary to imiquimod treatment.

## Discussion

We report a special clinical case lightening that Aldara® permit to obtain a complete remission and to postpone the cloture surgery as shown by the biopsy one year after treatment. Literature is lacking about complete response with imiquimod without any surgery, but some authors report similar benefits. Several studies have already reported the efficacy of imiquimod treatment in LM. It is used as an alternative therapeutic option when surgery is not feasible [10-12] (in elderly patients, in case of non-resecable tumors) as well as adjuvant [13] or neoadjuvant therapy [6,7]. Indeed, adjuvant imiquimod treatment may decrease LM recurrence rates [14,15]. Currently, the gold standard procedure to monitor and manage LM is only surgery with 1 cm-margins. When these margins cannot be respected for anatomical and functional limitations, clinical margins of 0.5 cm could be acceptable under strict histological control of the margins [16]. We would like to underline that our result is only applicable with LM with pure intraepidermal invasion, and our result cannot be extrapolated to LMM i.e. a melanocytic lesion with vertical phasis (i.e. Breslow

is available). Imiquimod is a topical immunomodulatory of the imidazoquinoline family with antiviral and antitumor activities [17,18]. It is a topical immune response modifiers and Toll-like receptor 7 (TLR7) agonist that induce the immunological destruction of SCC and other skin cancers [19]. It enhances the increasing of interferon gamma production in the tumoral lesion and the effector function of T lymphocytes [20,21]. Several factors are associated with an increase clearance rate like an inflammatory response during treatment and an intensified imiquimod regimen [22-24]. One of the limitations is that we use imiquimod less frequently than in ASCO, 3 days a week versus 5 days a week. In our case, the patient was treated during 6 months but only 3 days a week, which may improve the tolerance. This difference could underline that Aldara® is efficient even at low frequency as expected and that drug delivery is quite Flexible without negatively affecting clinical result. To conclude, we confirm that Aldara® can be very efficient way to treat LM in monotherapy or if needed as a neoadjuvant therapy. It would be interesting to include Imiquimod in the treatment recommendations for lentigo maligna in addition to, or instead of 5 mm-margins stipulated in the PNDS.

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