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Conservative treatment of lentigo maligna with topical imiquimod 5% cream: a case report

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Abstract

The use of imiquimod 5% cream, a topical immunomodulator for the treatment of lentigo maligna (LM) was first described in 2000. Subsequent studies have indicated that imiquimod might be an effective nonsurgical treatment in patients who refuse to have, or are ineligible for surgery because of comorbidities, tumor size, or risk of cosmetic disfigurement. Herein, we outline our experience with treating LM on the nose in an 88-year-old skin cancer patient with significant comorbidities. Given our patient's strong preference against surgical intervention, he was treated with topical imiquimod cream applied once daily for a total of 12 weeks. A two-week treatment holiday was required for severe nausea and vomiting, treated effectively with ondansetron wafers. There were no clinical or dermoscopic signs of LM recurrence 12 months posttreatment. Topical imiquimod is an effective alternative to excision in nonsurgical candidates.

Keywords: lentigo maligna, melanoma in situ, imiquimod cream, treatment

To the Editor:

Lentigo maligna (LM) is considered a sub-type of melanoma in situ (MIS) that primarily affects elderly individuals and typically occurs on chronically sun-exposed skin, such as the head and neck region. There is a 2.2% to 4.7% lifetime risk of transformation into an invasive form known as lentigo maligna melanoma (LMM), [1]. Treatment of LM is therefore recommended in order to prevent this progression, with surgical excision being the treatment of choice [2]. The use of imiquimod 5% cream, a topical immunomodulator for the treatment of LM was first described in 2000 [3]. Subsequent studies have indicated that imiquimod might be an effective nonsurgical treatment in selected patients, such as those who refuse to have, or are ineligible for surgery because of comorbidities, tumor size, or risk of cosmetic disfigurement. The response rate to topical imiquimod for LM, however, varies greatly from 37.0% to 84.2%, possibly owing to differences in treatment regimens [4-8]. We describe our experience with treating LM on the nose in an 88-year-old skin cancer patient with significant comorbidities.

An 88-year-old man was referred to our skin cancer clinic for evaluation of an asymptomatic, slowly growing lesion appearing as a cluster of irregularly pigmented macules on the apex of the nose (**Figure 1A)**. The macule had been treated for cosmetic reasons with liquid nitrogen on at least two occasions over the past year and had recurred after initially disappearing. His past medical history was significant for a permanent pacemaker, atrial fibrillation, hyperlipidemia, hypertension, and numerous non-melanoma skin cancers. Dermoscopy showed an irregularly pigmented lesion with grey circles and dots and asymmetric pigmented follicular openings, suspicious for LM. A shave biopsy was performed and histopathology confirmed the diagnosis.

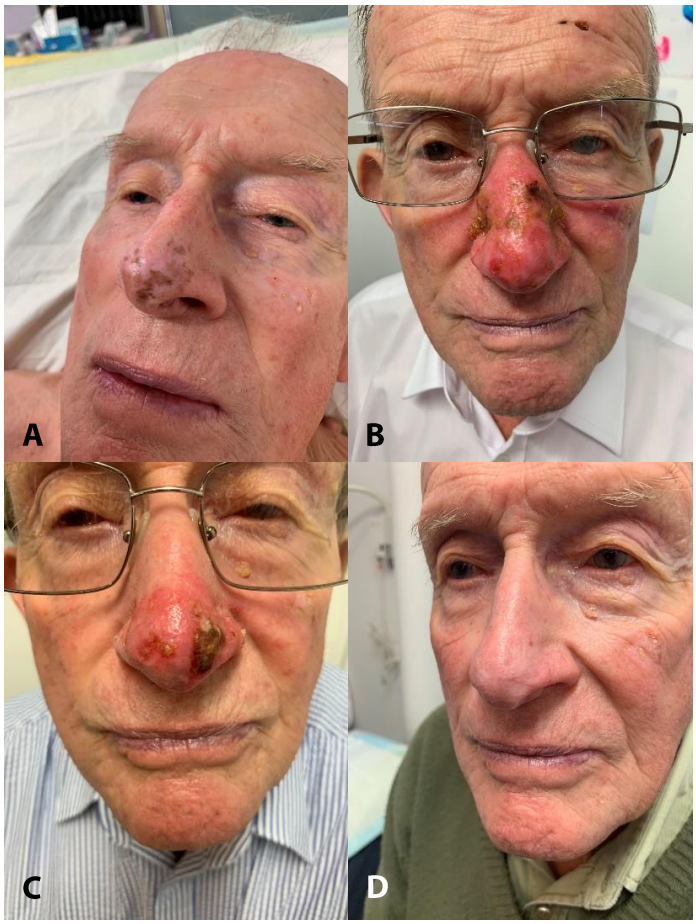

Figure 1. *Imiquimod clinical response.* ***A)*** *Biopsy-proven lentigo maligna on the apex of the nose prior to treatment with topical imiquimod.* ***B)*** *After three weeks, and* ***C)*** *12 weeks of treatment: local inflammatory response with scaling, crusting and ulceration is observed.* ***D)*** *Clinical response seen after treatment cessation, at the six-week follow-up visit. There is no residual pigmentation or other clinical signs of lentigo maligna recurrence.*

All treatment options were discussed with the patient. Given his strong preference against surgical intervention, he was treated with topical imiquimod 5% cream applied once daily for a total of 12 weeks and 84 applications. An adequate local inflammatory reaction consisting of scaling, crusting, and ulceration was observed and initially well tolerated (**Figure 1B**, **C)**. In week two of treatment, our patient experienced severe nausea and vomiting. Ondansetron wafers were prescribed and treatment was continued. Over the subsequent week, the inflammatory reaction and nausea became intolerable and treatment was paused. After a two-week treatment holiday, the nausea completely resolved and the inflammatory reaction settled. The patient desired to recommence therapy. The remaining treatment course was completed uninterrupted with ongoing use of ondansetron as required to control nausea. There was no residual pigmentation observed at the six-week (**Figure 1D)** and 12-month follow-up appointments, with no clinical or dermoscopic signs of LM recurrence. Patient satisfaction with the treatment and cosmetic outcome was high.

According to a systematic review by Tio et al. describing 471 patients with LM treated with topical imiquimod, rates of complete clinical clearance were achieved in almost 80% of patients, with a histological clearance of 77%. The odds ratio of achieving complete clinical and histological clearance, respectively was 6.4 and 7.1 times greater if imiquimod was applied 6-7 times per week compared to 1-4 applications per week [4]. Based on these findings, the optimal treatment schedule consists of a cumulative dose of greater than 60 applications and a treatment intensity of greater than five applications per week. Our patient applied topical imiquimod daily for a total of 84 applications over a period of 12 weeks. This more intense treatment regimen could explain the complete clinical clearance observed in our patient.

There is little published data on the long-term efficacy of imiquimod-treated LM, with considerable variability in results. Gautschi et al. and Kai et al. reported contrasting recurrence rates of 18% over a median of 4.8 years, and 0% over a median of 7.5 years, respectively [7, 9]. In a more recent nonrandomized retrospective study by Papanikolaou and Lawrence, the recurrence rate of LM among patients treated with topical imiquimod 5% cream was reported to be 0% over a median follow-up of 4.1 years [10]. Given the varying recurrence rates and relatively small sample sizes demonstrated in the literature, there is a need for larger, randomized studies assessing the long-term outcomes of LM treated with topical imiquimod.

Clinical assessment of clearance can be difficult and does not always correlate with histological clearance [7]. Histological assessment of tissue is therefore recommended [7]. Because lesions are usually large and poorly defined, multiple scout or broad shave biopsy specimens are needed to ensure adequate

sample collection [6]. Despite this, areas of disease recurrence may be missed on sampling error, leading to false negative results [6, 7]. Our patient was highly satisfied with the cosmetic outcome and opted against having further biopsies to evaluate for histological clearance.

The 12-week treatment course is long and can be challenging with significant adverse effects, such as the severe nausea and vomiting experienced by our patient. Furthermore, imiquimod therapy is likely associated with a higher recurrence rate than the current standard of surgical excision. Long-term follow-up is therefore essential. Care should also be taken in selecting the appropriate patient for this non-invasive treatment. Patients should be aware of, and willing to endure the lengthy treatment course and potentially severe local inflammatory and systemic adverse effects associated with the treatment.

Topical imiquimod is an effective and useful alternative to excision in nonsurgical candidates. Topical imiquimod has several advantages including being non-invasive, cheap and easy to use for elderly patients. It also provides a good cosmetic outcome. However, it does not come without its limitations including serious adverse effects and the potential for disease recurrence or invasive disease following treatment, requiring long-term follow-up. Both benefits and limitations of imiquimod and its role in the management of LM need to be considered, with a focus on proper patient selection. Further research is needed to assess the most effective treatment schedule and the long-term outcomes of LM treated with topical imiquimod.

Potential conflicts of interest

The authors declare no conflicts of interest.

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