Case report

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TREATMENT OF A LARGE LENTIGO MALIGNA AND LENTIGO MALIGNA MELANOMA WITHIN THE LESION WITH INCISIONAL BIOPSY AND 5% IMIQUIMOD

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Lentigo maligna melanoma (LMM) is an invasive melanoma most commonly occurring on the head and neck. The diagnosis is aided by specific dermoscopic criteria and confirmed by biopsy. The treatment of LMM is surgical excision. There are alternative therapies for its precursor lesion lentigo maligna (LM, also known as Hutchinson's melanotic freckle) – melanoma in situ, and they include the application of topical 5% imiquimod cream. Our patient had a 7 x 4 cm lesion with dermoscopic features of both LM and LMM. The diagnosis was confirmed by pathohistological examination of the incisional biopsy. The patient, concerned about the aesthetic outcome, refused surgical treatment and was treated by 5% imiquimod cream. Dermoscopy aided the clinical diagnosis, it allowed for a non-invasive follow-up and tailoring of the treatment in order to attain satisfactory results – evanescence of dermoscopic features suggestive of LM and LMM and an aesthetically acceptable outcome after treatment.

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Key words: *Hutchinson's melanotic freckle, melanoma, biopsy, dermoscopy, imiquimod*

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Introduction

The most common type of melanoma *in situ* is lentigo maligna (LM, also known as Hutchinson's melanotic freckle), a precursor lesion of the invasive lentigo maligna melanoma (LMM) (1, 2). The diagnosis of both entities is based on the clinical characteristics and dermoscopic features. The diagnosis is confirmed by a histopathologic examination of the excision or biopsy of the lesion. Dermoscopy aids in selection of the site of biopsy for an adequate diagnosis and in the complex management of LM and LMM (3). Surgical excision remains the standard treatment for all stages of primary cutaneous melanoma; however, when surgery is not a reasonable option because of the size of the lesion, patient comorbidities or preferences, the alternative therapies are considered for the treatment of LM (4). Alternative therapies supported by the results of a systemic review of non-surgical treatment of LM include radiotherapy and topical imiquimod cream (5). Still there are no review studies supporting alternative therapies in the treatment of LMM.

Case report

An 80-year-old female patient presented with an irregularly shaped, ill-defined, flat pigmented, two colored skin lesion on chronically sun-damaged skin. The lesion covered more than 60% of her right cheek at the time she was referred to our clinic. The lesion was 7 x 4 cm, the size had been reached by slow growing during the last ten years. The patient was otherwise healthy with no history of chronic or malignant disease. Dermoscopic examination revealed a pseudonetwork, presence of a number of colors – light brown, dark brown, black, grey, as well as structureless areas. Also some obliterated hair follicles, increased density of the vascular network and gray circles were among the key dermoscopic features for the dermoscopic diagnosis of lentigo maligna melanoma (Figure 1). The dermoscopic findings were suggestive of LMM within the lesion of LM. The part of the lesion that was suspicious for LMM was marked before the incisional biopsy (Figure

2). The pathologist report staged the melanoma with Breslow depth of 0.2 mm as stage I A. Also, apart from the LMM, there was a lentigo solaris on the lower part of the cheek.

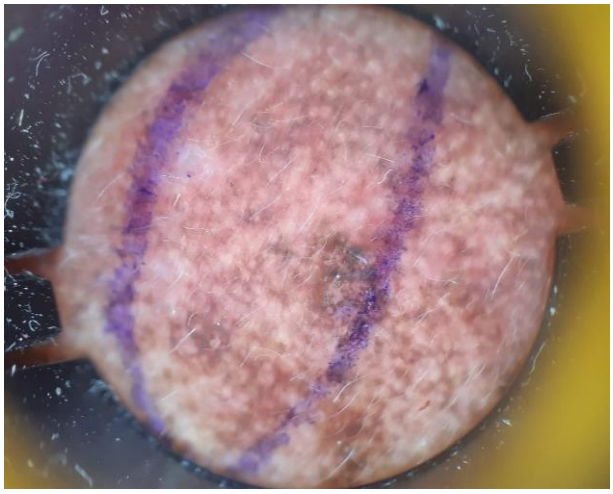

Figure 1. Dermoscopy of the part of the lesion marked up for the incisional biopsy.
The picture was taken by a smartphone camera lens leaned into a Derm Lite DL100 dermatoscope (10 x magnification).

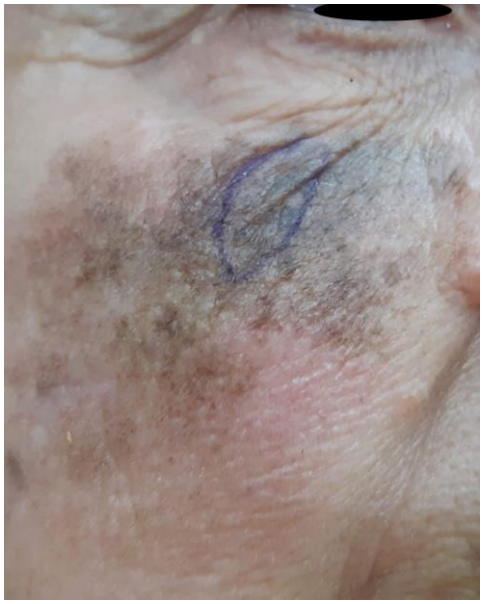

Figure 2. LMM of the cheek, the marked region is the planned site of biopsy.

The patient refused to undergo surgical treatment of the melanoma. After a detailed discussion of alternative treatments of LMM with the patient and the patient's family, the decision was made to start with the daily application of 5% imiquimod cream.

After the ninth month of the topical therapy a pinkish papule of 2 mm in diameter, located in the central part of the lesion in close proximity to the scar of the incision biopsy, was noticed. The papule had been present there for four weeks. It was excised at the follow-up and the pathologists report

showed hyperkeratosis with no atypical or malignant cells.

The last follow-up took place three years after the introduction of topical treatment. Upon clinical and dermoscopic evaluation, a mild erythema was seen in the upper part of the treated field, beneath the lower eyelid, indicating that there is still some ongoing inflammatory reaction to 5% imiquimod cream (Figure 3). Treatment is being continued, in order to be assessed at the next follow-up in a month.

Figure 3. Ongoing reaction to 5% imiquimod cream at 36 months of therapy.

Discussion

LM and LMM most commonly occur on the head and neck, on chronically sun-damaged skin (6). LM arises on the cheeks with a significant female predominance (7); this was the case with the LMM in our patient. LMM arising in the facial skin presents with a different dermoscopic pattern from those observed in melanoma on non-acral skin (8). Dermoscopy is an indispensable tool for the diagnosis and treatment, since it not only aids the diagnosis, but allows for a non-invasive follow-up during treatment, particularly for topical treatments (3). For an accurate and timely diagnosis, being up to date with dermoscopic features of LMM is a necessity (8). The Tiodorovic-Zivkovic et al. study from 2013, highlights that the presence of the gray color in facial lesions is the single most sensitive feature for the dermoscopic recognition of early facial melanoma. Its presence should always prompt the clinician to perform a biopsy (9). We were guided by this clinical thinking during the diagnosis, treatment and follow-up of our patient, too. The classical follicular invasion criteria defined by Stolz et al. were confirmed by Pralong et al. in the study "Dermoscopy of lentigo maligna melanoma: report of 125 cases". The study draws attention to the utility of original new features for the diagnosis of LMM: increased vascular density, red rhomboidal structures, target-like pattern and darkening at dermoscopic examination (8). One of the new original features was present in our patients' lesions – increased vascular density.

The final diagnosis of cancer is based on the pathologist's report, so a biopsy is a mandatory step after strong clinical suspicion. When the clinical diagnosis is cutaneous melanoma, one should ideally perform a narrow excisional biopsy that encompasses the entire breadth of the lesion with clinically negative margins to a depth sufficient to ensure that the lesion is not transected (4). Our patient refused excisional biopsy of the LMM, and consented to an incisional biopsy.

In our clinical case, the LMM was classified as stage IA melanoma. The alternative treatment modalities to surgical excision and their risks were discussed in detail with the patient. Therefore, the decision to start with the topical application of 5% imiquimod cream was made.

Topical imiquimod is a synthetic imidazoquinoline amine that has the ability to increase the production of inflammatory cytokines and chemokines; it induces tumor cell apoptosis and has an anti-angiogenic effect (10). There is no high-quality evidence supporting the use of imiquimod as a single therapy for LMM. However, the results of a systemic review study from 2017, might be of relevance to those patients with LM who refuse to undergo or are not eligible for surgery or radiotherapy. Evidence suggests complete clinical clearance rates of 78.3% and histological clearance rates of 77% after the application of imiquimod cream (11). The proposed

treatment schedule to achieve clinical and/ or histological clearance consisted of a cumulative dose of > 60 applications and a treatment intensity of > 5 applications per week (11). In our case the treatment lasted twelve times longer. No new clinical or dermoscopic features of LMM were observed and the final result was complete resolution of clinical and dermoscopic features of LM.

Conclusion

Being well-acquainted with the dermoscopic features for LM and LMM is the key to an accurate and timely diagnosis. Dermoscopy is a powerful tool for the diagnosis of LM and LMM, it aids biopsy such as selection of the site of biopsy, precise staging of cutaneous cancer and allows for non-invasive follow-up of patients during treatment.

The patient studied in our case refused the complete excision of the lesion fearing the potential facial damage to an aesthetically sensitive region. Based on our experience in this case, 5% imiquimod cream was an acceptable alternative to surgical excision. The treatment was tailored to the patient, and the response to treatment was satisfactory both in respect to the regression LMM, and in the aesthetic outcome after the treatment. Further studies should be performed in cases similar to this one in order to evaluate the effectiveness of the topical application of imiquimod on LMM lesions.

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Prikaz bolesnika

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TERAPIJA VEĆE LEZIJE LENTIGO MALIGNA I LENTIGO MALIGNI MELANOM U OKVIRU LEZIJE INCIZIONOM BIOPSIJOM I 5% IMIKVIMODOM

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Lentigo maligni melanom (LMM) je invazivni melanom koji se najčešće javlja na glavi i vratu, čija se klinička dijagnoza, potpomognuta specifičnim dermoskopskim karakteristikama, potvrđuje biopsijom. Lečenje LMM podrazumeva eksciziju lezije, dok za njegovu prekursorsku leziju lentigo maligna (LM, poznata i kao Hačinsonova melanocitna pega) – melanoma in situ – postoje alternativni terapijski modaliteti, kao što je lokalna primena 5% imikvimod kreme. Naša bolesnica imala je leziju veličine 7 cm x 4 cm sa dermoskopskim karakteristikama LM i LMM. Bolesnica je odbila hirurško lečenje, zbog potencijalne deformacije estetski osetljive regije. Dijagnoza je postavljena patohistološkim pregledom materijala incizone biopsije. Lečena je 5% imikvimod kremom. Dermoskopija je pomogla u postavljanju kliničke dijagnoze, omogućila neinvazivno praćenje i prilagođavanje treapije radi postizanja zadovoljavajućeg rezultata – nestanak dermoskopskih karakteristika, koje sugerišu na LM i LMM i estetski zadovoljavajući rezultat.

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Ključne reči: *Hačinsonova melanocitna pega, melanom, biopsija, dermoskopija, imikvimod*