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Intraoperative Real-Time Reflectance Confocal Microscopy for Guiding Surgical Margins of Lentigo Maligna Melanoma

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Lentigo maligna melanoma (LMM) represents a diagnostic and therapeutic challenge because of its heterogeneous nature with poorly defined borders, subclinical extension, and location on sun-damaged skin. Reflectance confocal microscopy (RCM) has advanced the authors' ability to better diagnose and manage these lesions through noninvasive examination of skin on a cellular level. Herein, the authors report the first case of RCM used intraoperatively, in a multidisciplinary approach involving dermatology and head and neck surgery to manage a challenging LMM.

A 77-year-old woman was referred for treatment of an LMM on the left malar cheek approaching the lower eyelid. The lesion had been present for 2 years and previously treated with cryotherapy. On examination, there was an ill-defined 2-cm patch with irregular contour and variegated shades of brown–gray bordering the left lower eyelid (Figure 1). A biopsy revealed spindle cell–type melanoma with a depth of 1.25 mm. Preoperative mapping with RCM identified 2 surrounding areas suspicious for melanoma with epidermal disarray, dendritic hyperreflective melanocytes, and rounded pagetoid cells (Figure 2). Biopsies found invasive melanoma and melanoma in situ. Wide excision in the operating room assisted by RCM with rush pathology and delayed reconstruction was planned.

Preoperatively, surgical 1 cm margins were defined under Wood lamp. Because of the poorly defined borders, RCM imaging was performed under an institutional review board–approved protocol using a commercially available handheld RCM (VivaScope 3000; Caliber ID, Rochester, NY). The lesion was imaged at the clinical and surgical margins from the stratum corneum down to inside the papillary dermis. Scanning confocal video microscopy was performed to rapidly inspect the border. Reflectance confocal microscopy examination allowed enhanced delineation of the borders and subsequently increased the resection

margins. An area around the 9-o'clock margin was suspicious for positivity under RCM because of the presence of sheets of atypical cells and epidermal disarray, but it was not excised for possibility that it was a false positive because it encompassed a separate cosmetic subunit. It was decided to not increase the surgical margin in this area because of the experimental nature of this technology and instead wait for rush permanent hematoxylin and eosin pathology confirmation. Excision of the lesion and margins down to subcutaneous fat was performed. Then, RCM was used to re-evaluate the periphery of the area of resection. The same region of concern, showing dendritic processes and round pagetoid cells around the 9-o'clock position, was highlighted. A video captured intraoperatively was converted into a mosaic by stitching together individual frames to provide a detailed overview of the peripheral margin, highlighting the atypical findings (Figure 3).

Pathology revealed residual invasive and in situ melanoma within the lesion and melanoma in situ extending to the 9-o'clock margin as suspected on confocal microscopy. The patient returned for re-excision along this margin and closure with a cervical facial flap and full-thickness skin graft. No further melanoma was seen on pathology.

Discussion

The diagnosis of facial LMM can be challenging, even with dermoscopy and Wood lamp. As LMM is often a lesion occurring on cosmetically sensitive areas, taking random, blind scouting biopsies and performing wide local excisions can be disfiguring. The cellular-level resolution afforded by RCM allows for noninvasive examination of the skin for distinct cytomorphological and architectural features unique to LMM, including epidermal disarray, atypical melanocytes with pagetoid spread, and aggregates of atypical melanocytes surrounding adnexal structures. This technology offers the advantage of assessing large areas of the skin in a nontraumatic manner, improving diagnostic accuracy of difficult melanocytic lesions.

Reflectance confocal microscopy assists in the management of LMM through identifying optimal biopsy sites for early diagnosis, presurgical mapping,¹ assessing response to nonsurgical therapies,² and monitoring for recurrence.³ The capability to delineate facial LMM margins can help dictate surgical versus nonsurgical treatment.¹ However, until now, the ability to use this technology intraoperatively to provide the surgeon with real-time assessment of tumor margins in vivo has not been explored.

In this patient, the size and location of the lesion with its subtle borders warranted further examination with RCM. The patient's history of cryotherapy further obscured the clinical margins. The findings on RCM resulted in expansion and improved accuracy of the surgical margins and potentially could have resulted in the need for only 1 surgical excision had the area of suspicion been excised at that time.

As surgery remains the standard of care for LMM, it is important to optimize surgical methods. Mohs micrographic surgery is used for surgical management, providing tissue sparing and total margin control. However, facial LMM may require larger margins for clearance.⁴ At present, there is a need for better pretreatment margin evaluation in LMM,

allowing for healthy tissue to be spared while ensuring clearance of the lesion. Reflectance confocal microscopy is currently used as an adjunct to existing therapies to better delineate borders, with the goal of conserving tissue and lowering recurrence rates. This can aid in surgical planning to help define the extent of subclinical spread before surgery, informing both the surgeon and patient. Furthermore, although RCM was used to increase the margins in this case, it can also verify narrower surgical margins to facilitate reconstruction and decrease patient morbidity. Thus, RCM provides valuable clinical information to potentially guide surgical management and may lead to favorable cosmetic outcomes and a better prognosis. Currently, initial cost and the associated learning curve are limitations to widespread use of this technology.

Conclusion

This case demonstrates the utility of RCM in augmenting the management of a challenging LMM. To date, this is the first reported case of the use of intra-operative RCM for a multidisciplinary approach to LMM. The improved accuracy of diagnosis and treatment of skin cancers provided by RCM improves patient management and could potentially reduce morbidity and mortality. Although the sensitivity and specificity of RCM findings in cases of LM have been defined,⁵ identifying normal background atypical melanocytes versus pathological atypia in these large atypical lesions has yet to be elucidated. Further studies are planned to evaluate the efficacy of intraoperative RCM and better define its clinical applications.

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Figure 1. Clinical photograph showing the ill-defined hyperpigmented patch on the left malar cheek approaching the lower eyelid outlined in green. The yellow circles mark areas outside of the clinical lesion where RCM showed suspicious findings, later confirmed to be melanoma in situ and invasive melanoma.

Figure 2.
(A) Reflectance confocal microscopy showing dense areas of hyperreflective, atypical dendritic processes with adnexal tropism. (B) Reflectance confocal microscopy showing pagetoid infiltration within the epidermal layer surrounding the hair follicles.

Figure 3.

Representative section from the mosaic created to assess outside of the surgical margin. Area in the blue rectangle represents normal-appearing tissue architecture. The area within the red circle highlights large atypical hyper-reflective cells at the dermoepidermal junction. Within the green ellipse are 2 sheets of large cells and an area of perifollicular infiltration by dendritic cells (green arrowheads) and inflammatory cells. These areas correlated with the positive margin seen on pathology.