Neurotropism detected during Mohs micrographic surgery for melanoma in situ

Matthew R. Donaldson, MD, Travis J. Morrell, MD, MPH, and L. Arthur Weber, MD

Key words: lentigo maligna; MART-1; melanoma; Mohs; neurotropic melanoma.

CASE REPORT

A 70-year-old man was referred for Mohs micrographic surgery (MMS) to treat a melanoma in situ, lentigo maligna type of the left nasal ala. Biopsy showed irregularly spaced nests and single melanocytes, pagetoid spread, and adnexal extension consistent with melanoma in situ arising in a severely dysplastic nevus. Clear margins were achieved with MMS using intraoperative MART-1 (melanoma antigen recognized by T cells) immunohistochemistry (IHC). In the vertically-sectioned debulk specimen, atypical melanocytes were found to involve the perineurium and endoneurium of large caliber nerves extending through the subcutis directly underlying the biopsy scar to a depth of 3.4 mm (Figs 1-3). No residual in situ tumor or desmoplastic component was identified. Tissue was submitted for formalin processing and dermatopathology consultation concurred with the finding of neurotropic melanoma (NM). The preoperative tumor size was 1.0 cm × 1.5 cm and postoperative defect was full thickness at the alar rim and measured 2.2 cm × 2.6 cm. The defect was reconstructed with a cartilage strut and paramedian forehead flap. Because of the depth of nerve involvement, the patient was sent for sentinel lymphadenectomy, the result of which was negative. Postadjuvant radiation to the site was performed. There was no evidence of recurrence at 2 years. MMS practitioners should be aware of the potential of neurotropism with melanoma—even when initially described as in situ. Identification of neurotropism in this case was facilitated by use of intraoperative MART-1 IHC.

Abbreviations used:

IHC: immunohistochemistry
MMS: Mohs micrographic surgery
NM: neurotropic melanoma

DISCUSSION

NM is characterized by perineural or endoneural spread of melanoma. Neurotropism is usually associated with desmoplastic melanoma but is rarely seen with nondesmoplastic, invasive melanoma. In the largest series of NM to date, 28% of desmoplastic cases were found to have neurotropism compared with just 0.8% of nondesmoplastic cases.[1] A single case of neurotropism associated with melanoma in situ, lentigo maligna type (in addition to 196 nondesmoplastic cases of NM in the literature) has been reported.[2]

The NM observed in our patient was the first out of 376 in situ and 137 invasive consecutive MART-1–stained nondesmoplastic melanomas treated with MMS in our practice. Neurotropism was unexpected as this was referred as an in situ tumor arising in a severely dysplastic nevus and no nerve involvement was noted on original biopsy. Dermatopathology review of the initial biopsy in the context of Mohs debulk specimens suggested reclassification of the original biopsy (initially called severely atypical compound lentiginous nevus with regression) as lentigo maligna melanoma extending to a depth of 0.2 mm.

The prognostic significance of NM is uncertain. Initial reports suggested NM was associated with a higher risk of recurrence.[3] However, multivariate

From the Mountain West Dermatology, Grand Junction, Colorado.
Funding sources: None.
Patient consent: The authors attest that they have obtained written consent from patient/s, their legal guardian/s or person/s with legal authority, for their photographs and medical information to be published in print and online and with the understanding that this information may be publicly available. Patient consent forms were not provided to the journal but are retained by the authors to be made available upon request.
IRB approval status: Not applicable.

Correspondence to: Matthew R. Donaldson, MD, Mountain West Dermatology, 2655 Little Bookcliff Dr, Grand Junction, CO 81501. E-mail: mrdonaldson@hush.com.
JAAD Case Reports 2024;52:74-6.
2352-5126

https://doi.org/10.1016/j.jdcr.2024.07.022

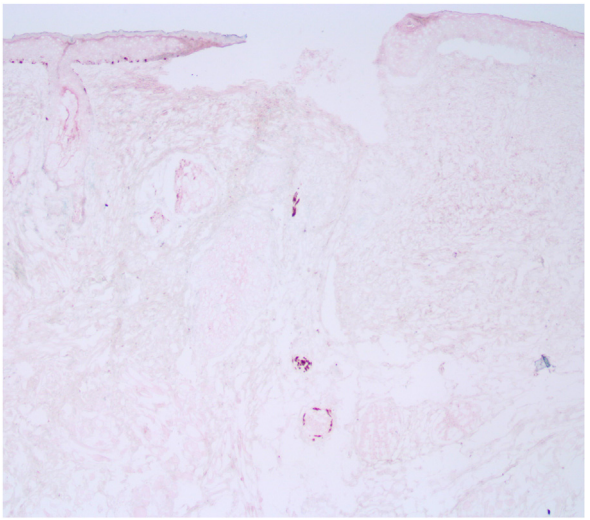

Fig 1. Neurotropism of large caliber nerve underlying biopsy site. (MART-1 stain; original magnification: ×4.)

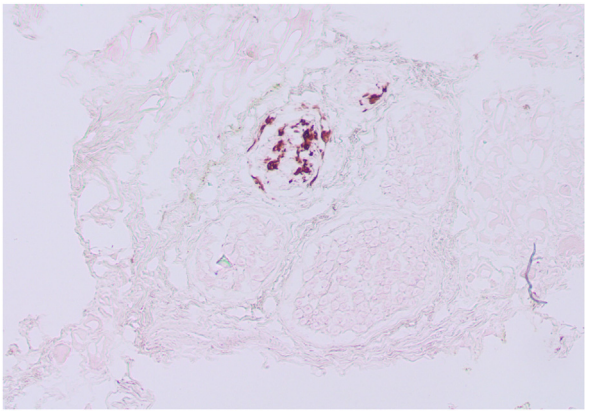

Fig 2. Endoneural and perineural melanoma seen with MART-1. (Original magnification: ×40.)

analysis of the largest series to date (671 cases with 718 nonneurotropic matched melanoma controls) suggested no difference in local recurrence or melanoma-specific survival.[1] Multivariate analysis of this cohort found that a pathologic margin >8 mm was statistically less likely to recur than a margin <2 mm (hazard ratio, 0.46; 0.31-0.68; $P < .001$). The precision of MMS margin evaluation with intraoperative IHC may reduce the risk of recurrence and allow sparing of normal tissue. Because of the rarity of this phenomenon in nondesmoplastic NM, prospective comparisons will be difficult.

The depth of nerve involvement in the context of original in situ diagnosis was striking. Without intraoperative MART-1 IHC, it may have been overlooked as findings were subtle on hematoxylin and eosin-stained sections and no overlying dermal or in situ component was seen. Nerve involvement in this case

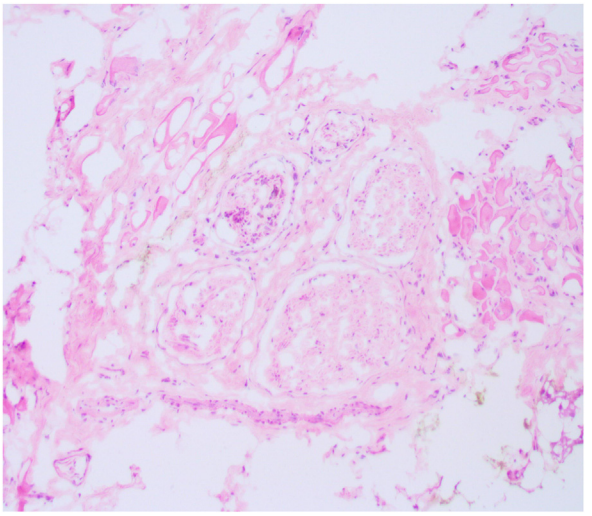

Fig 3. Nerve bundle involved with melanoma seen on hematoxylin and eosin. (Original magnification: ×40.)

extended below the follicular bulbs. The utility of reporting a Breslow depth of perineural extension is unknown.

Varey et al[1] found sentinel node positivity less likely when neurotropism was present. Univariate analysis supported attribution of this finding to overrepresentation of desmoplastic tumors among NM cases. Sentinel lymph node biopsy was performed in our patient given the deep extension and unusual clinical scenario of possible regressed melanoma.

Although it did not affect survival, Varey et al[1] reported a statistically significant reduction in recurrence in NM (hazard ratio, 0.51; 0.29-0.87; $P = .01$) after postadjuvant radiation. Subgroup analysis found no difference in recurrence between desmoplastic and nondesmoplastic cases. Postadjuvant radiation was more effective at reducing recurrence in the narrow-margin (<8 mm) than large margin (>8 mm) groups (hazard ratio, 0.48; 0.27-0.87; $P = .02$). Whether radiation would be indicated or beneficial after the narrow, precise removal with MMS is uncertain. As radiation appeared to be beneficial in narrow-margin NM regardless of histologic subtype, it was performed in our patient. Postadjuvant PD-1 inhibitor therapy was not considered in our patient because of lack of available literature for this indication and no evidence of metastatic disease.

NM may rarely be encountered during MMS—even on routine in situ referrals. In our case, intraoperative IHC was critical to identify neurotropism as findings on hematoxylin and eosin-stained sections were subtle. Limited data suggest sentinel lymph node biopsy is of uncertain utility and postadjuvant radiation may reduce recurrence risk with questionable margins in these cases.

Conflicts of interest

None disclosed.

REFERENCES

1. Varey AHR, Goumas C, Hong AM, et al. Neurotropic melanoma: an analysis of the clinicopathological features, management strategies and survival outcomes for 671 patients treated at a tertiary referral center. *Mod Pathol*. 2017;30(11):1538-1550. https://doi.org/10.1038/modpathol.2017.76
2. Occidental M, Shapiro R, Jour G. Lentigo maligna melanoma in situ with neurotropism. *J Cutan Pathol*. 2020;47(12):1155-1158. https://doi.org/10.1111/cup.13778
3. Croker J, Burmeister B, Foote M. Neurotropic melanoma: the management of localised disease. *J Skin Cancer*. 2012;2012: 706452. https://doi.org/10.1155/2012/706452