The Hidden Threat of Low Breslow Depth Melanomas

by Alyssa Iurillo, MS4

Melanoma is the deadliest form of skin cancer, accounting for 75% of skin cancer deaths though it only accounts for 4% of skin cancer cases (1). According to the National Comprehensive Cancer Network (NCCN) Guidelines for Cutaneous Melanoma, melanomas with Breslow depths exceeding 1.0 mm are associated with an increased likelihood of sentinel lymph node positivity, and such melanomas are managed with more caution, including larger surgical margins and sentinel lymph node biopsy (2). However, thinner melanomas with Breslow depths under 1.0 mm can lead to unexpected mortality. As a medical student engaged in both clinical rotations and research, I have witnessed firsthand the devastating outcomes of these deceptively shallow lesions.

The Breslow depth, a critical prognostic factor in melanoma, measures the vertical thickness of the tumor from the granular layer of the epidermis to the deepest point of invasion. Thin melanomas, defined as less than 1.0 mm in depth, are cited to have an excellent prognosis with an observed 12-year survival of approximately 85% (3,4). However, this outlook does not account for the clinical reality for a subset of patients. Despite being categorized as "low risk," these thin melanomas can lead to aggressive metastatic disease and death, a phenomenon I have observed in patients who initially seemed to have a manageable condition.

The patient was a middle-aged individual who presented with a pigmented lesion that, upon biopsy, revealed a melanoma with Breslow depth of 0.5 mm. Standard management according to NCCN guidelines is wide excision with a 1-cm margins and routine follow-up (2). Despite adherence to these guidelines, the patient returned months later with metastases in regional lymph nodes and distant organs. This tragic progression raises critical questions about our understanding and management of thin melanomas.

Emerging research highlights that thin melanomas can possess high-risk features that transcend their shallow depth. These include ulceration, a high mitotic rate, lymphovascular invasion, and certain molecular signatures, such as BRAF or NRAS mutations (2,5). Such features may not always be apparent on initial histopathological analysis but can drastically alter the clinical outcome.

As a future physician, these cases underscore the need for a shift in how we approach "thin" melanomas. Enhancing public and professional awareness is essential. Clinicians should be conscious about identifying and documenting high-risk features, even in lesions with a shallower Breslow depth.

Research must also prioritize identifying biomarkers that can stratify risk among patients with thin melanomas. Advances in genomic and proteomic profiling hold promise for distinguishing indolent lesions from those with metastatic potential. These resources could guide clinical decision-making and provide patients with more accurate prognostic information.

The experience of witnessing patients pass away to what was initially deemed a "low risk" melanoma has greatly shaped my understanding of the disease and how to approach and view shallower melanomas. This serves as a reminder that melanoma, irrespective of its depth, remains a grave and potentially fatal disease.

This information is not just for researchers and specialists but for all clinicians who encounter melanoma. Shallow melanomas may not appear life threatening at first glance, but their potential for devastation is real.

References:
1. Davis LE, Shalin SC, Tackett AJ. Current state of melanoma diagnosis and treatment. Cancer Biol Ther. 2019;20(11):1366-1379. doi: 10.1080/15384047.2019.1640032. Epub 2019 Aug 1. PMID: 31366280; PMCID: PMC6804807.

2. National Comprehensive Cacer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Cutaneous Melanoma. Version 3.2024. September 23, 2024. Available from: https://www.nccn.org/guidelines/category_1

3. Maurichi A., Miceli R., Camerini T. Prediction of survival in patients with thin melanoma: Results from a multi-institution study. J Clin Oncol. 2014;32(23):2479–2485. doi: 10.1200/JCO.2013.54.2340

4. Hieken T.J., Grotz T.E., Comfere N.I., Inselman J.W., Habermann E.B. The effect of the AJCC 7th edition change in T1 melanoma substaging on national utilization and outcomes of sentinel lymph node biopsy for thin melanoma. Melanoma Res. 2015;25(2):157–163. doi: 10.1097/CMR.0000000000000143.

5. Thomas NE, Edmiston SN, Aleander A, et al. Association Between NRAS and BRAF Mutational Status and Melanoma-Specific Survival Among Patients With Higher-Risk Primary Melanoma. JAMA Oncol. 2015;1(3):359–368. doi:10.1001/jamaoncol.2015.0493