

Sentinel Lymph Node Melanosis: A
Report of Two Cases of Regressed
Melanoma MetastasesSteven H Sun¹, Sara B Peters² and J Harrison Howard^{1*}¹Department of Surgery, Division of Surgical Oncology, The Ohio State University Wexner Medical Center and James Cancer Hospital and Solove Research Institute, USA²Department of Pathology, The Ohio State University Wexner Medical Center, USA

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*Corresponding author

J Harrison Howard, Department of Surgery, Division of Surgical Oncology, The Ohio State University Wexner Medical Center and James Cancer Hospital and Solove Research Institute, Columbus, Ohio, USA,
Email: John.Howard@osumc.edu

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Abstract

Tumoral melanosis is found on histopathologic evaluation of a primary melanoma and is typically caused by regression of the tumor. The prognostic value of regression related to primary cutaneous melanoma has been controversial. Very few cases of melanosis in the sentinel lymph node have been described. We present two patients who presented with cutaneous melanoma and were found to have completely regressed metastatic melanoma present within the sentinel lymph node. One patient underwent completion lymph node dissection whereas the other opted for observation. Based on the outcomes of our two cases as well as review of other case reports of this phenomenon we discuss the biologic significance of sentinel lymph node melanosis and how it should be interpreted in relation to adjuvant therapies, staging, and follow up. Based on the unpredictable course associated with this finding we recommend that these patients be treated in a multidisciplinary fashion with treatment decisions influenced by the patient's goals of care.

Introduction

Regression of a primary melanoma is a well-known and well-described phenomenon. On histopathology, regression is identified via a combination of fibrosis and melanophages with residual melanoma cells that appear at the periphery [1]. The effect regression has on prognosis remains controversial. Several studies have reported worse 5-year survival in patients with regression [2-4]. Conversely, other studies have shown no difference and even improved 5-year survival for patients with regression [5-6]. Regression is often associated with other markers of worse prognosis such as male gender, older age, and truncal anatomic location. However, the same group of patients was shown to have lower risk of progression despite the other negative factors [7]. Gualano et al, performed a recent meta-analysis which reported that histological regression was associated with a lower relative risk and thus protective for survival [8]. Based on such mixed findings related to regression in primary melanoma, it is difficult to know the true prognostic significance of this finding.

Tumoral melanosis has been described as a rare variant of fully regressed melanoma [1], which appear as a nodular collection of dermal melanophages with nuclei that are obscured by melanin, stain positive for CD68, but negative for melanocytic markers such as S100, HMB-45 and Melan-A [9]. Nodal melanosis, where completely regressed melanoma is identified in the lymph nodes, is a much rarer occurrence. To date, there are only a few case reports describing the presence of nodal melanosis [10-13]. We present two cases of nodal melanosis in two patients and discuss strategies for management and follow up.

Patient 1

A 57-year-old woman noticed a mole on her left posterior shoulder. Biopsy revealed a 2 mm non-ulcerated melanoma with no mitotic figures and 1.5 mm of regression. She had no other signs of regional or distant metastases and was recommended to have wide local excision and sentinel lymph node biopsy. Pathologic evaluation revealed melanosis in the capsule in one of two sentinel lymph nodes. No evidence of viable melanoma was identified but the presence of melanophages in the lymph node capsule was compatible with melanocytic regression (Figure 1). Immunoperoxidase stains for Melan-A, HMB-45, and tyrosinase were negative further pointing toward regression. Based on the findings from her sentinel lymph node biopsy, a Positron Emission Topography (PET) was performed which showed no signs of distant metastatic disease. The patient was offered a completion axillary lymph node dissection given the presence of tumoral melanosis in the lymph node but she opted for observation. She remains without evidence of disease one year removed from her initial surgery.

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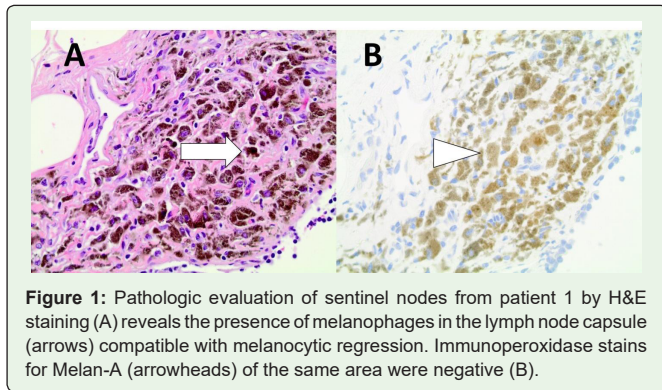


Figure 1: Pathologic evaluation of sentinel nodes from patient 1 by H&E staining (A) reveals the presence of melanophages in the lymph node capsule (arrows) compatible with melanocytic regression. Immunoperoxidase stains for Melan-A (arrowheads) of the same area were negative (B).

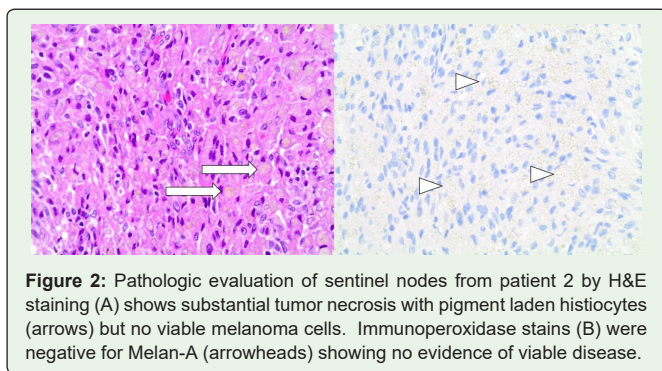


Figure 2: Pathologic evaluation of sentinel nodes from patient 2 by H&E staining (A) shows substantial tumor necrosis with pigment laden histiocytes (arrows) but no viable melanoma cells. Immunoperoxidase stains (B) were negative for Melan-A (arrowheads) showing no evidence of viable disease.

Patient 2

A 74-year-old man found a mole on his left upper arm which was proven to be a 17 mm, non-ulcerated melanoma with 14 mitoses. He also had no clinical evidence of regional or distant metastatic disease on physical exam and was offered wide local excision and sentinel lymph node biopsy. Pathologic evaluation of his sentinel nodes showed substantial tumor necrosis with patchy positive staining for Melan-A, HMB-45, and tyrosinase but no evidence of viable disease (Figure 2). A full body PET scan and brain MRI were obtained to complete staging which confirmed no additional detectable disease. Based on the evidence that he likely had viable metastatic disease in his sentinel node at some point a completion axillary lymph node dissection was offered and performed. Twenty-three additional lymph nodes were obtained and were all negative for evidence of melanoma. Immunoperoxidase stains were negative for Melan-A and HMB-45. He was not offered any additional adjuvant therapy. He is currently three years removed from his initial surgery and remains without evidence of disease.

Discussion

There is limited literature describing nodal melanosis. Several case reports have described the classic pathologic findings of tumoral melanosis and/or nodal regression but with varying interpretations of etiology [10-13]. Satzger et al, reported melanosis found concurrently in both the primary lesion and the sentinel nodes suggesting regressed melanoma, but could not exclude possibility of migration of melanophages from the primary lesion to the sentinel nodes [10]. The patient in Malafrente et al, underwent an axillary lymph node dissection which showed thirteen lymph nodes with melanosis, ten

negative nodes, and one lymph node positive for metastatic melanoma in the setting of an unknown primary [11]. Rongioletti et al, described a completely regressed primary melanoma that arose from a congenital nevus, and found regressed melanoma on sentinel lymph node biopsy [12]. From the few case reports available, it is our opinion that nodal melanosis is most likely due to regional lymph node metastases from the primary cutaneous tumor that subsequently regressed within the lymph node. It should be noted that there have been descriptions of melanosis that arise from non-melanoma sources such as pigmented epithelial neoplasms [14]. However, when melanosis is found in a sentinel node biopsy from a known primary melanoma, the etiology being from a second neoplasm seems unlikely.

The appearance of regression on pathologic evaluation has been described to include three phases - early, intermediate and late. The early phase is characterized by dense lymphocytic infiltration, transitioning to increasing number of melanophages, ending with deposition of fibrotic tissue, arranged in a structure similar to normal scar formation [15]. If sentinel lymph node melanosis does involve regressed, metastatic disease, then the role of the native immune system should be considered as a cause for regression. It is thought that melanoma-associated antigens are recognized by cytotoxic T lymphocytes resulting in spontaneous regression; interestingly this is also the basis for targeted immunotherapies [16]. Martin et al described 3 cases of spontaneous regression of melanoma without treatment, thought to be caused by an efficient systemic host immune response against melanocytes. The patients in this study were shown to have multiple subcutaneous nevi that progressively faded on dermoscopy with signs of regression on pathologic evaluation [17].

The clinical challenges that nodal melanosis presents include the need for staging, benefit of completion lymph node dissection, and the need for adjuvant therapies. Do we treat these patients similar to those who are histologically node positive? In our two cases, evidence of previous lymph node involvement on sentinel lymph node biopsy was identified but no active melanoma cells were present; one patient underwent a completion axillary lymph node dissection, whereas the other opted for observation. In the setting of the recently released data from the Multicenter Selective Lymphadenectomy Trial - II (MSLT-II), we believe that it is difficult to recommend completion lymph node dissection for a sentinel node with evidence of tumoral melanosis or regression. MSLT-II showed no difference in melanoma specific survival for patients with a positive sentinel node that were treated with either observation or lymphadenectomy [18]. If additional surgery did not help patients with active disease in their sentinel node, it is hard to imagine that it would benefit patients without active disease.

Both of our patients are over a year out from treatment and without evidence of recurrence. Satzger et al, also described a case where their patient remained without evidence of recurrence [10]. Rongioletti et al, reported a patient who after wide local excision and sentinel lymph node biopsy opted for observation refusing completion lymphadenectomy or adjuvant therapy. The patient was reported to have expired from metastatic melanoma 2 years later. The details of this patient's recurrence pattern were not reported but if melanoma was the cause of death, it is very likely the patient developed distant metastases [12]. Solano-Lopez described local recurrence and distal metastases over 5 years after initial diagnosis and identification of lymph node melanosis [13]. Unfortunately, there is not enough data

on sentinel lymph node melanosis to extrapolate its true prognostic significance.

Based on the outcomes described in the case reports, we suggest that these patients should be discussed in a multidisciplinary tumor board and followed as a stage III melanoma patient with regular physical examinations and staging scans to evaluate for regional and distant recurrence. Including our patients, 2 out of 5 reported patients (40%) with sentinel lymph node melanosis have succumbed to the disease. This mortality rate is consistent with the natural history of stage III melanoma. Given the side effects from additional surgery and adjuvant therapy, it is difficult for us to recommend these therapies based on current data but each patient should be educated on their treatment options and treated based on their individual goals of care.

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