# Lymph Node Melanosis in a Patient With Metastatic Melanoma of Unknown Primary

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**• Tumoral or nodular melanosis in the skin is considered a variation of completely regressed melanoma, presenting clinically as a suspicious pigmented papule or nodule. Microscopically, the lesion consists of a nodular accumulation of heavily pigmented melanophages in the dermis, staining positive for immunohistochemical markers of histiocytic lineage (CD68) and negative for those of melanocytic lineage (S100, HMB-45, Melan-A). This process is rarely described in lymph nodes. We present a report of a patient with melanosis involving multiple lymph nodes of an axillary dissection, done for metastatic melanoma with an unknown primary, and discuss possible prognostic and treatment factors.**

**(*Arch Pathol Lab Med.* 2009;133:1332–1334)**

Regression is a well-known and described entity in malignant melanoma, exhibiting a spectrum of clinicopathologic features. Partially regressed melanomas most often present clinically as either variably pigmented or hypopigmented, flat lesions, a histologic picture of focal papillary dermal fibrosis, and a variably cellular infiltrate of melanophages and lymphocytes.[1,2] Residual melanoma cells are present at the periphery of the fibrosis in the epidermis, dermis, or both.[2]

Rarely, regressed melanomas present as pigmented papules or nodules that are biopsied to rule out a malignant process. Microscopically, these lesions consist of nodular collections of dermal melanophages positive with CD68 and negative for melanocytic markers (S100, HMB-45, Melan-A).[3] This process, known as tumoral or nodular melanosis, is considered and treated as a variant of *completely* regressed melanoma.[4]

Only a small number of cases of tumoral melanosis have been reported. In addition, Satzger et al[5] seem to be the first, to our knowledge, to describe a case of tumoral melanosis involving sentinel lymph nodes in a patient with a history of malignant melanoma. We present a case of tumoral melanosis involving multiple nodes of an axillary dissection done for metastatic melanoma of unknown primary.

## REPORT OF A CASE

A 36-year-old, male soldier presented with a self-palpated, left axillary mass. A computed tomography scan revealed a large, left axillary mass, which led to excision of a solitary 4.5-cm lymph node that was histologically consistent with malignant melanoma. The patient was referred to a larger medical center, where a staging workup was done, including a positron emission tomography scan demonstrating a 4-cm left axillary lymph node with a standard uptake value of 13.1 (>3 is considered hypermetabolic) and an adjacent 1.5-cm lymph node. The patient underwent a left axillary lymph node dissection.

A total of 24 lymph nodes were identified, ranging in size from 0.5 to 4 cm. On histologic examination, the majority of the lymph nodes (n = 13; 54%) contained heavily pigmented cells in a subcapsular and focally sinusoidal pattern. The degree of pigmentation obscured many of the nuclear features, but, when visible, most of the nuclei were bland, with vesicular nuclear chromatin and inconspicuous eosinophilic nucleoli. The largest lymph node (4 cm) displayed an effaced architecture by wildly pleomorphic epithelioid cells with bizarre nuclei; large, cherry-red macronucleoli; occasional nuclear pseudoinclusions; and variable amounts of dusty cytoplasmic pigment, consistent with metastatic melanoma (Figure 1, A). In addition, an extracapsular focus of pigmented cells, admixed with multinucleated giant cells, was noted in the extranodal soft tissue (Figure 1, B). This latter focus, the 4-cm node, and several of the smaller nodes were stained with CD68, S100, HMB-45, and Melan-A immunostains. Because of the heavy pigmentation, a melanin bleaching step with potassium permanganate/oxalate was performed before staining. In addition, immunostains were performed on the 4-cm node with and without a preliminary bleaching step.

The malignant-appearing cells in the largest node stained positive with S100, HMB-45, and Melan-A (nonbleached), and negative with CD68 (Figure 2, A through D). The extranodal focus of the pigmented cells and the subcapsular pigmented cells in the malignant node and remaining nodes were positive with CD68 and negative for the melanocytic markers, consistent with melanophages. A total of 1 of 24 lymph nodes (4%) was positive for metastatic melanoma, with the remainder displaying nodular melanosis (n = 13; 54%) or normal histologic features (n = 10; 42%).

The patient underwent further workup with a magnetic resonance imaging scan of the brain, which revealed a 1-mm, nonenhancing lesion in the midadenohypophysis, and a whole-body computed tomography scan that revealed no evidence of further metastatic disease.

## COMMENT

Tumoral or nodular melanosis is a rare manifestation of fully regressed melanoma and, unless proven otherwise,

Accepted for publication October 8, 2008.

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The authors have no relevant financial interest in the products or companies described in this article.

The views expressed in this article are those of the authors and do not necessarily reflect the official policy of the US Navy, Department of Defense, or the US government.

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# Report Documentation Page

*Form Approved*
*OMB No. 0704-0188*



| 1. REPORT DATE | 2. REPORT TYPE | 3. DATES COVERED |
|---|---|---|
| **AUG 2009** | | **00-00-2009 to 00-00-2009** |

| 4. TITLE AND SUBTITLE | 5a. CONTRACT NUMBER |
|---|---|
| **Lymph Node Melanosis in a Patient With Metastatic Melanoma of Unknown Primary** | 5b. GRANT NUMBER |
| | 5c. PROGRAM ELEMENT NUMBER |
| 6. AUTHOR(S) | 5d. PROJECT NUMBER |
| | 5e. TASK NUMBER |
| | 5f. WORK UNIT NUMBER |
| 7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) **Department of Pathology and Laboratory Services,National Naval Medical Center,Bethesda,MD** | 8. PERFORMING ORGANIZATION REPORT NUMBER |
| 9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES) | 10. SPONSOR/MONITOR'S ACRONYM(S) |
| | 11. SPONSOR/MONITOR'S REPORT NUMBER(S) |

12. DISTRIBUTION/AVAILABILITY STATEMENT
**Approved for public release; distribution unlimited**

13. SUPPLEMENTARY NOTES

14. ABSTRACT

15. SUBJECT TERMS

| 16. SECURITY CLASSIFICATION OF: | | | 17. LIMITATION OF ABSTRACT | 18. NUMBER OF PAGES | 19a. NAME OF RESPONSIBLE PERSON |
|---|---|---|---|---|---|
| a. REPORT | b. ABSTRACT | c. THIS PAGE | | | |
| **unclassified** | **unclassified** | **unclassified** | **Same as Report (SAR)** | **3** | |

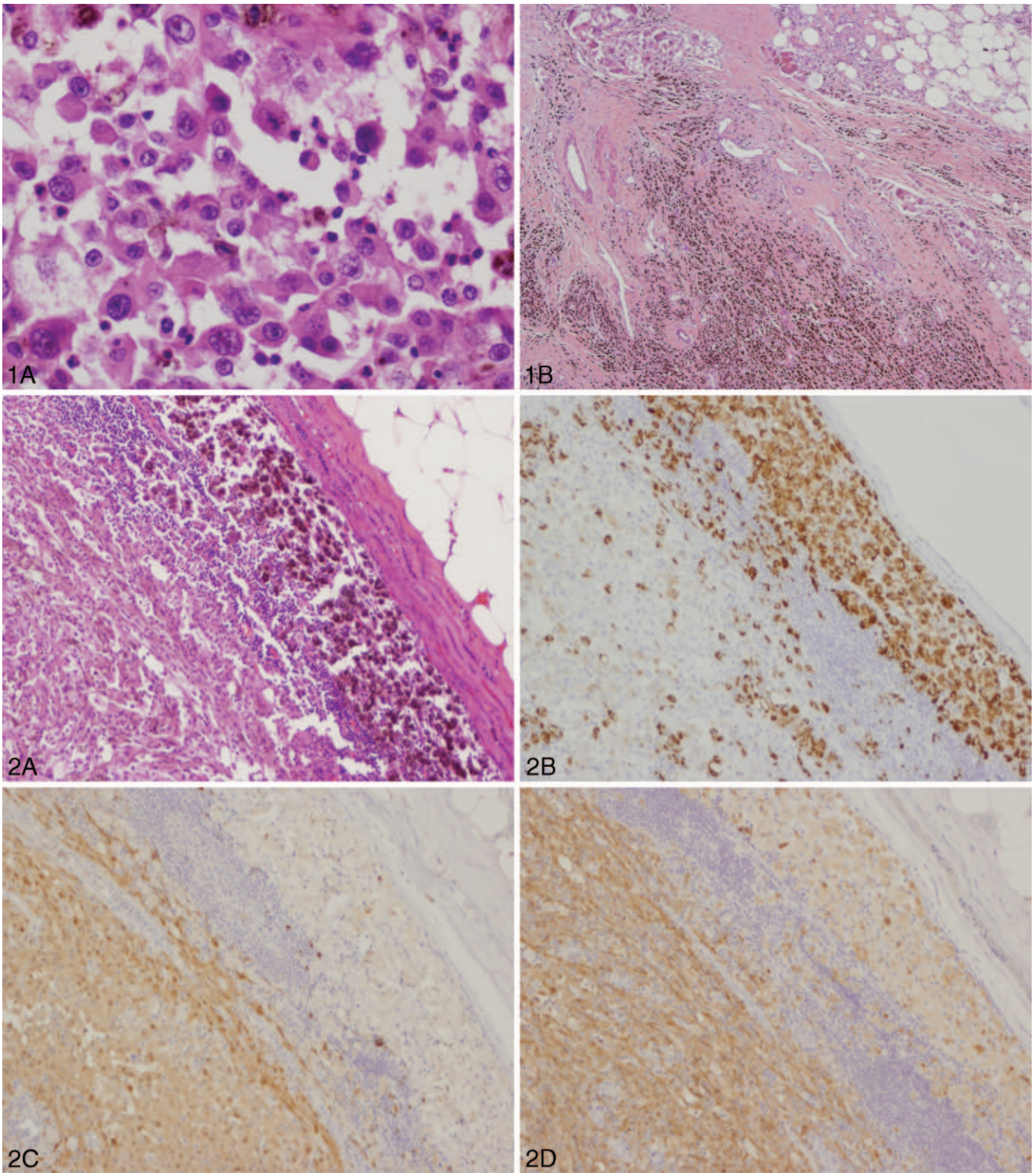


**Figure 1.** *A, Largest node with subcapsular pigmented cells as well as effaced architecture with cytologically malignant cells. B, Focus of heavily pigmented histiocytes in extranodal soft tissue in the setting of foreign-body giant cells (prior biopsy site changes; hematoxylin-eosin; original magnifications ×40 [A] and ×4 [B]).*

**Figure 2.** *A, Largest node with subcapsular pigmented cells as well as effaced architecture with cytologically malignant cells (hematoxylin-eosin; original magnification ×20). B, The subcapsular cells were positive for CD68 (postmelanin bleach; original magnification ×20), whereas the malignant cells were negative for CD68 and positive for (C) HMB-45 and (D) S100 (C and D: postmelanin bleach; original magnifications ×20).*

is managed as such, even though no residual melanoma cells are identified in the lesion.[1–3,5–9] Occasionally, tumoral melanosis occurs secondary to regressed epithelial neoplasms, basal cell carcinomas, benign nevi,[3] and mycosis fungoides.[6]

Because of the unknown identity of the initial lesion, the prognosis of tumoral melanosis is not well known. One study followed 7 patients with tumoral melanosis, all of whom developed metastatic melanoma in regional lymph nodes. The average time from discovery of the regressed lesion to pathologic diagnosis in the nodes ranged from 12 months to 4 years.[8]

To our knowledge, only one case of tumoral melanosis involving sentinel lymph nodes has been described.[5] In that report, unlike ours, the patient had a known primary melanoma of the skin. We report here on a patient presenting with metastatic melanoma in axillary lymph nodes associated with extensive nodal and focal extranodal melanosis. The etiology of the melanosis is not understood. Although the location of the melanophages might suggest a regressed focus of metastatic melanoma, the possibility also exists that the melanophages migrated to the lymph node from the primary lesion.[5] In our case, the extent of nodal involvement, in addition to the extranodal focus of melanosis, would support the former theory.

This uncertainty raises various questions. Should nodes involved with melanosis in patients with a diagnosis of melanoma be considered regressed metastatic deposits, or should they be considered uninvolved by tumor? How does this influence clinical and pathologic staging? How does this finding affect treatment options for the patient? In our case, the patient was offered systemic interferon therapy and was initially persuaded against adjuvant radiation because the nodes involved with melanosis were considered uninvolved. After the possibility of regressed nodal metastasis was discussed by pathology at tumor board, however, the radiation oncologists changed their initial opinion, finally persuading the patient to pursue adjuvant radiation.

Tumoral melanosis involving lymph nodes, which may be better termed *nodal melanosis* because it doesn't form a tumor per se in the node, is a seldom-described entity associated with many unanswered questions concerning etiology, incidence, and prognostic significance. The paucity of cases precludes adequate evaluation of long-term outcome and treatment implications. However, given that the appearance of new skin nodules, microscopically consistent with tumoral melanosis in patients with known primary melanoma, has been considered by some as regressed metastasis, it seems fitting that the same status be given to lymph nodes with melanosis present in similar patients.

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