

**Original contribution**

Melanoma coexisting with solar elastosis: a potential pitfall in the differential diagnosis between nevus and melanoma^{☆,☆☆}



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Summary Melanomas, like nonmelanoma skin cancers, are known to be causally related to sun exposure. It is therefore not surprising to see benign nevi and melanomas in a background of solar damage, which at times may complicate their distinction. Because of their long-standing nature, nevi often occur before the development of solar elastosis and as such are intimately associated with the solar elastosis. In contrast, visible solar elastosis often occurs before the development of melanoma, in which case the band of solar elastosis is displaced downward from the overlying invasive melanoma and/or its host response. We describe 4 cases in which invasive melanoma cells were intimately admixed with actinically damaged elastin fibers in the absence of a prominent host response. In each case, melanoma cells were admixed with prominent solar elastosis and lacked a significant host response, suggesting that they were either histiocytes or an associated melanocytic nevus. Recognition of this potential pitfall may be helpful in the diagnosis of primary/in-transit/satellite/metastatic melanoma as well as when evaluating marginal status and determining Breslow thickness.

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1. Introduction

The distinction between nevus and melanoma is a common challenge in dermatopathology, often necessitating the careful integration of numerous individual histologic criteria to discriminate benign from malignant. Because some melanocytic lesions are causally related to sun exposure, they may be accompanied by histologic evidence of actinic damage in the form of solar elastosis. For melanocytic lesions occurring on sun-damaged skin, analysis of the relationship of the lesion to the solar elastotic band (SEB) has been suggested to aid in the differential diagnosis. Horenstein et al [1] described

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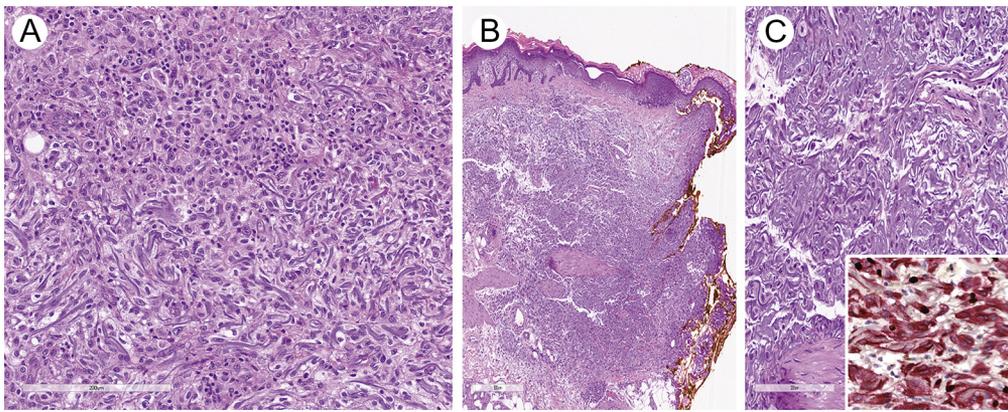


Fig. 1 A, Melanoma cells intimately associated with solar elastosis with only occasional scattered lymphocytes (hematoxylin and eosin, original magnification $\times 200$). B, Lateral en face margin (hematoxylin and eosin, $\times 40$). C, Lateral en face margin ($\times 100$) showing atypical epithelioid cells. A pan-melanocytic cocktail (inset) is positive in these cells, consistent with melanoma.

downward displacement and superficial attenuation of the SEB as an attribute of melanoma and its accompanying host response. In contrast, in long-standing benign lesions, the position and thickness of the SEB match that of perilesional dermis; in addition, nevus cells are seen intercalating among individual degenerated elastic fibers. Herein, we describe 4 cases of melanoma in which melanoma cells permeate the SEB and lack a prominent host response, challenging the convention that melanoma cells typically do not infiltrate, but rather displace the SEB deeper into the dermis. These cases illustrate a potential diagnostic pitfall in the initial diagnosis of melanoma. Furthermore, they highlight potential challenges for margin evaluation and determination of Breslow thickness in such cases.

2. Case Series

2.1. Case 1

A 74-year-old white man underwent a wide local reexcision for a melanoma of the right forearm (Fig. 1A). Both of the 2 sentinel lymph nodes biopsied were positive for metastatic melanoma. All margins of resection were negative, with the exception of the lateral en face margin (Fig. 1B). Upon initial examination of this margin, there were epithelioid cells intimately associated with solar elastosis that resembled histiocytes, with no prominent overlying melanoma in situ (Fig. 1B). However, these cells were large with irregular nuclear contours and prominent nucleoli (Fig. 1C), similar to the patient's melanoma (Fig. 1A). An immunohistochemical study with MART1/Ki67 cocktail revealed these atypical cells to be diffusely positive for MART1 with a high Ki67 proliferative index, consistent with melanoma, and thus diagnostic of a microsatellite lesion (Fig. 1C, inset). The patient underwent a completion lymphadenectomy of the left axillary and epitrochlear basins, showing metastatic melanoma in additional 8 of 27 lymph nodes. The

patient subsequently received local radiation without systemic therapy due to his comorbidities, including end-stage renal disease and Crohn disease. Approximately 3 months after surgery, the patient developed metastases to the lungs and liver (pT4bN3bM1) and died of pulmonary complications. The clinicohistologic features are summarized in the Table.

2.2. Case 2

A skin shave biopsy from the right upper arm of a 63-year-old man revealed a contiguous intraepidermal proliferation of large spindled and epithelioid melanocytes arranged singly and in large nests along the dermal-epidermal junction with pagetoid spread. Similar-appearing cells were seen in the dermis in association with actinically damaged elastin fibers and minimal host response. In addition, one dermal mitotic figure per square millimeter was noted. The findings were diagnostic of malignant melanoma, superficial spreading type (pT1b, per the American Joint Committee on Cancer eighth edition). The patient underwent a wide local excision and biopsy of 2 sentinel lymph nodes, which were negative for residual and metastatic melanoma, respectively. The patient is currently alive with no evidence of disease, 40 months after diagnosis. The clinicohistologic features are summarized in the Table.

2.3. Case 3

A 68-year-old man underwent a wide local excision and sentinel lymph node biopsy of a left cheek melanoma (lentigo maligna type, Breslow thickness at least 0.7 mm). The excision revealed healing biopsy site changes, scar formation, and associated melanoma in situ (Fig. 2A). The SEB underlying the scar contained a variably dense mononuclear infiltrate resembling histiocytes (Fig. 2B). At that time, the primary melanoma from the previous biopsy specimen was not available to review for comparison. A pan-melanocytic immunohistochemical cocktail (MART1, HMB45, and tyrosinase)

Table Summary of demographic and clinicohistologic features of melanoma cases intimately associated with solar elastosis

	Cases			
	1	2	3	4
Presenting history				
Age (y)	74	63	68	75
Sex	M	M	M	F
Ethnicity	White	White	White	White
Anatomic location	Right forearm	Right upper arm	Left cheek	Right lower leg
Family history of malignancy	Melanoma/colon and breast cancer	Breast cancer	NA	NA
Personal history of malignancy	SCC of skin	NA	NA	NA
Histopathology				
Type	Nodular	Superficial spreading	Lentigo maligna	NA
Breslow thickness (mm)	6.8	0.9	1.7	NA
Mitotic rate (/mm ²)	21	1	2	2
Ulceration	Present (10 mm in width)	Not identified	Not identified	NA
Perineural invasion	Present	Not identified	Present	Present
Lymphovascular invasion	Present	Not identified	Not identified	Not identified
Clark level	IV	IV	IV	NA
Associated nevus	Not identified	Not identified	Not identified	Not identified
In situ component	Present	Present	Present	Not identified
Molecular alterations (mutation)	<i>EGFR, RET, CDKN2A</i>	NA	<i>CCND3, RET, ALK, TERT</i>	NA
Management and follow-up				
Margin status after wide local excision	Positive, lateral en face	Negative	Negative	Positive
Lymph node status	2/2 SLNs positive; 8/27 RLN positive	0/2 SLNs positive	1/2 SLNs positive, 1 additional clinically positive node	NA
Distant metastasis	Yes (lungs and liver)	No	No	Present
Follow-up	Died 13 mo after diagnosis	Alive 40 mo after diagnosis	Alive and exploring treatment options	Alive and exploring treatment options

Abbreviations: F, female; M, male; NA, not available; RLN, regional lymph node; SLN, sentinel lymph node; SCC, squamous cell carcinoma.

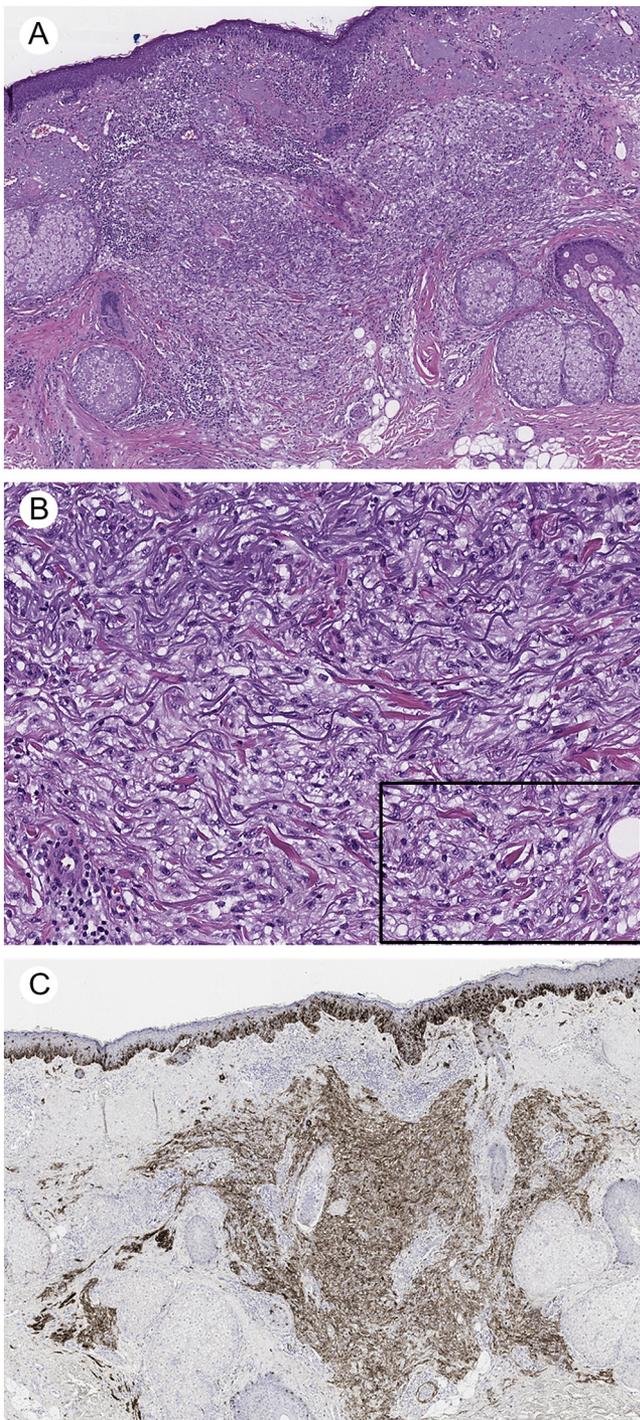


Fig. 2 A and B, Melanoma cells intimately associated with prominent solar elastosis with underlying previous biopsy site changes and melanoma in situ (hematoxylin and eosin, original magnifications $\times 20$ [A] and $\times 200$ [B]). C, A pan-melanocytic cocktail highlights overlying in situ melanoma and epithelioid cells underlying a scar, consistent with invasive melanoma (pan-melanocytic immunohistochemical cocktail, $\times 100$ [C] and $\times 200$ [B, inset]).

stained the aforementioned bland mononuclear cells within the SEB (Fig. 2C). Perineural invasion of small nerve fibers and 2 dermal mitotic figures per square millimeter were identified.

The overall findings were diagnostic of residual melanoma (pT2aN2bMx). The patient is alive with disease and currently exploring personalized treatment options. The clinicohistologic features are summarized in the Table.

2.4. Case 4

Skin shave biopsies from 2 pigmented papules on the right lower leg of a 75-year-old woman revealed similar histologic features. Each biopsy showed a dermal proliferation of cytologically atypical epithelioid and nevoid cells in a single-cell growth pattern without epidermal involvement. These atypical cells were found in association with the actinically damaged elastin fibers with only minimal host response. MART1/Ki67 immunohistochemical cocktail highlighted the epithelioid/nevoid cells and showed a high proliferative index. The patient had a history of melanoma approximately 20 years ago; however, prior pathology materials were not available for review. Based on the reported history of melanoma and presence of 2 papules with similar clinicopathological features and high Ki67-proliferative index, a final diagnosis of metastatic melanoma was rendered. She is currently alive with disease and exploring available therapeutic options. The clinicohistologic features are summarized in the Table.

3. Discussion

Ultraviolet radiation is a major causative factor for many cutaneous malignancies and, when received in a sufficient cumulative dosage, is demonstrated histologically by perilesional solar elastosis and actinic keratosis. A case-control study of 100 difficult-to-diagnose melanocytic neoplasms deemed the presence of solar elastosis to be an important contributor to a melanoma diagnosis, with a sensitivity of 35% and a specificity of 93% when considered in isolation [2]. In addition, a cross-sectional study of pathologists' clinical practices found that for 57%, the presence of solar elastosis would influence them toward a more severe diagnosis, with that number rising to 73% among dermatopathologists [3]. However, chronic sun exposure is not required in the pathogenesis of all melanomas, as evidenced by those which lack evidence of solar elastosis or those that arise in sites without sun exposure. Several studies have found that melanomas adjacent to marked solar elastosis are strongly associated with increased age, locations on the head and neck, and self-reported sun exposure [4-7]. Although melanomas occurring in a background of solar elastosis are associated with increased copy numbers of *CCND1* and predominately wild-type *BRAF* and *NRAS* genes, those melanomas occurring in skin without chronic sun-induced damage are associated with frequent *BRAF* or *NRAS* mutations [8].

Despite the above associations of melanoma with solar elastosis, nevi may also occur in association with solar elastosis and thus pose a diagnostic challenge. It is believed that

most nevi, due to their long-standing nature, predate the development of solar elastosis. Consequently, the nevus cells may be seen either dispersed among the basophilic fibers of the SEB, without fibrosis or inflammation, or are visible below the SEB. Melanoma associated with solar elastosis causes downward displacement and attenuation of the SEB. In melanoma in situ, this alteration is produced by the host inflammatory response, whereas both the host inflammatory response and melanocytes are responsible for the alterations in invasive melanoma.

All cases in our series comprised predominantly male patients (male-to-female ratio, 3:1) with advanced age. Despite their various pathologic stages, all cases demonstrated at least focally atypical cells admixed with actinically damaged elastin fibers, without a significant host inflammatory response, which are typical in benign nevi arising in sun-exposed skin. In case 1, this finding was focal and limited to the lateral en face margin (Fig. 1B and C), which showed extensive solar elastosis and appeared hypercellular on low power, without an overlying in situ melanoma. High-power examination revealed cytologic atypia with morphologic semblance to the main melanoma mass. This case illustrates the point that careful analysis of the SEB should be performed even at locations far from the main lesion so as to not miss microsatellites and/or positive margins. In addition, the finding of such cytologically atypical melanocytes among the solar elastosis fibers should not be assumed to represent an incidental nevus. Cases 2 and 3 showed somewhat bland melanocytes in the dermis intimately associated with solar elastosis and a minimal host inflammatory response with an overlying melanoma in situ component. In case 4, there were similar findings but no melanoma in situ component. In addition, there is no deeper displacement of the SEB. For these reasons, the cells may be mistaken for nevus cells, potentially resulting in an underestimation of the Breslow thickness or misdiagnosis as benign melanocytic lesions. The exact mechanism causing the peculiar relationship of invasive melanoma to solar elastosis described herein remains unknown. The lack of a significant inflammatory host response may be related, but further studies are needed to explain our findings.

In conclusion, contrary to prior understanding, melanoma does not always cause downward displacement of solar elastosis. Furthermore, the relationship of melanocytic nevi and melanoma to solar elastosis cannot be used reliably to distinguish between the 2. In a patient with a history of melanoma, special attention should be paid to the solar elastosis, especially when it appears more cellular than usual; in these cases, evaluation for atypia, mitotic figures, a high proliferation index by immunohistochemistry, perineural invasion, and other indicators of malignancy would be prudent. Our cases show the importance of this pitfall not only in initial diagnosis of a primary or metastatic melanocytic neoplasm but also in evaluation of excision specimens, where dermal melanocytes dispersed among solar elastosis may represent the only evidence of residual melanoma. Knowledge of this rare pitfall may also avoid potential discrepancies in measuring the Breslow thickness.

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