Gray-black macules in a patient with melanoma

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A 39-year-old male presented for evaluation of newly developed pigmented macules on his left upper arm. He was diagnosed with stage IIIA, BRAF-negative malignant melanoma 2 years prior and underwent multiple wide local excisions, skin grafting, radiation, and immunotherapy. Despite extensive treatment, he developed recurrent melanoma at the site of the scar three times and metastasis to his liver, spleen, and right hip. The patient then began pembrolizumab therapy during which a cluster of gray-black macules developed at the inferomedial aspect of the melanoma scar on his left upper arm (Fig 1). A punch biopsy was performed with histopathologic findings shown in Fig 2.
Question 1: The clinical and histopathologic findings are most consistent with which diagnosis?

A. Agminated spitz nevus
B. Pigmented basal cell carcinoma
C. Tumoral melanosis
D. Malignant melanoma recurrence
E. Epithelioid blue nevus

Answer:

A. Agminated spitz nevus – Incorrect. Agminated spitz nevi are rare melanocytic lesions arising in childhood and adolescence and may be difficult to distinguish from malignant melanoma. Histologically, melanocytic nests are present.
B. Pigmented basal cell carcinoma – Incorrect. Pigmented basal cell carcinoma may clinically resemble melanoma or, in this case, tumoral melanosis; however, histopathologic examination would reveal a tumor containing basaloid cells with melanin deposits.
C. Tumoral melanosis – Correct. Tumoral melanosis is a rare cutaneous response associated with partial or complete regression of melanoma. Tumoral melanosis presents as darkly pigmented macules, papules, or nodules and often mimics the appearance of melanoma warranting biopsy. Histologically, densely grouped melanophages, but not melanocytes, are present in the dermis and correlate with the pigmented lesions observed clinically. Though not yet fully elucidated, the proposed pathophysiology involves a robust immunologic response in the setting of an aggressive tumor, like melanoma. Prognostic significance seemingly depends on the extent of the underlying malignancy; thus, a complete workup is prudent in close follow-up. Unfortunately, no treatment guidelines exist due to paucity of existing literature.
D. Malignant melanoma recurrence – Incorrect. Though alarming in appearance, tumoral melanosis can be evidence of partial or complete regression of melanoma rather than recurrence. Moreover, no melanocytes were present in the examined specimen.
E. Epithelioid blue nevus – Incorrect. Epithelioid blue nevus is a rare, solitary melanocytic lesion. Histologically, proliferations of variable-sized melanocytes are present.

Question 2: Which of the following immunohistochemistry stains would be positive?

A. SOX10
B. CD68
C. S100
D. Melan A
E. HMB45

Answer:

A. SOX10 – Incorrect. SOX10 is a neural crest marker expressed by melanocytes and schwann cells. Tumoral melanosis is characterized by the presence of melanophages but not melanocytes.
B. CD68 – Correct. CD68/macrosialin is a marker of macrophages. Melanin-laden macrophages in the dermis correlate with the pigmented lesions observed clinically in tumoral melanosis. Because melanocytes are not present in this phenomenon, melanocytic markers are negative.
C. S100 – Incorrect. S100 is a protein expressed by melanocytes and schwann cells. Melanocytes are not present in tumoral melanosis.
D. Melan A – Incorrect. Melan A (also known as MART1) is a melanocytic marker. Because melanocytes are absent in tumoral melanosis, melan A staining would be negative.
E. HMB45 – Incorrect. HMB45 is a marker of melanocytes. Melanophages, not melanocytes, are the cells present in tumoral melanosis.

Question 3: This phenomenon has not been described in which of the following cutaneous lesions:

A. Pigmented basal cell carcinoma
B. Solar lentigo
C. Malignant melanoma
D. Actinic keratosis
E. Mycosis fungoides

Answer:

A. Pigmented basal cell carcinoma – Incorrect. Reports of tumoral melanosis arising from completely regressed pigmented basal cell carcinoma have been described.
B. Solar lentigo – Incorrect. Regression of solar lentigo or seborrheic keratosis may result in residual
blue-gray granules on dermoscopy and grouped melanophages on histopathology.3,4

C. Malignant melanoma — Incorrect. As demonstrated in the case described, tumoral melanosis can be evidence of a partially or completely regressed malignant melanoma.1,2

D. Actinic keratosis — Correct. Tumoral melanosis has been described in cases of pigmented Bowen’s disease but has not been reported to occur from actinic keratosis.5

E. Mycosis fungoides — Incorrect. Rare reports of tumoral melanosis arising from mycosis fungoides plaques have been described.5

Conflicts of interest
None disclosed.

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