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p-16: immunohistochemical staining to differentiate an inflamed atypical nevus

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p-16 immunohistochemical staining to differentiate an inflamed atypical nevus from metastatic melanoma

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Clinical Challenge

- A 45-year-old white female with a history of metastatic melanoma to the left supraclavicular lymph node from an unknown primary melanoma on nivolumab presented to clinic
- There was a new pink papule with irregular vascularity on her right upper arm. (Fig 1)
- Histopathology revealed small nests of melanocytes in the dermis with a brisk lymphocytic infiltrate and rare dermal mitotic figures, (Fig 2) consistent with either an inflamed atypical intradermal nevus secondary to immunotherapy or a cutaneous metastatic melanoma site.
- Although histopathology is the gold standard for melanoma diagnosis, distinguishing between these two entities in this clinical setting requires further investigation.

Physical Exam

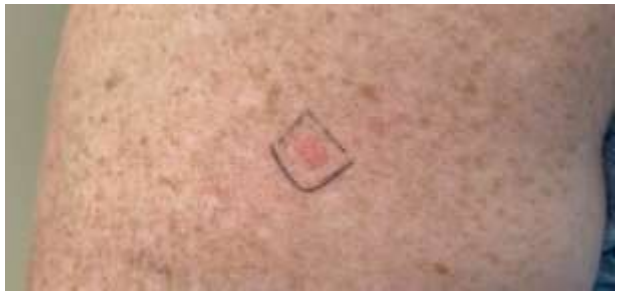

Figure 1: Pink papule on the right upper arm

Solution

- To help differentiate an inflamed melanocytic nevus with atypical features from a cutaneous melanoma metastasis in this setting, immunohistochemical staining for the tumor suppressor p16 can be utilized.
- One of the major genetic defects linked to melanoma pathogenesis is a mutation or deletion of the CDKN2A gene, which encodes for p16.[1]
- Loss of p16 expression results in unregulated cell-cycle progression.
- Several studies have demonstrated a frequent reduction in p16 expression in primary sporadic melanomas, and an even higher frequency of reduction in melanoma metastasis.[2]
- Given this, the patient's original lymph node melanoma sample and the biopsy from the right upper arm were stained for p16 (Fig 2).

Histopathology

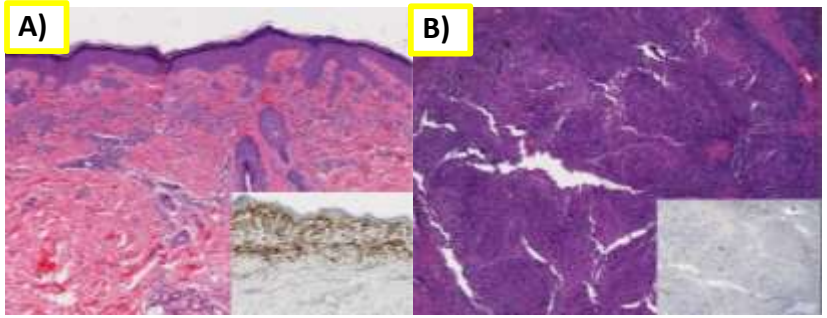

Figure 2. A) Inflamed melanocytic nevus with atypical features with positive p16 staining. B) Initial lymph node with metastatic melanoma of unknown primary with negative p16 staining

Solution Continued

- The new papule on the arm demonstrated preservation of p16, while the previous melanoma showed a loss of p16.
- Thus, this helped confirm that the new lesion was an inflamed melanocytic nevus secondary to treatment with nivolumab.

Discussion

- In the monitoring of patients who have had metastatic melanoma, repeat skin exams at specific intervals is a crucial screening tool to prevent recurrence.
- At many of these visits, suspicious melanocytic lesions are biopsied to determine if they represent a return of the patient's melanoma.
- Here, we present a case of a suspicious atypical melanocytic nevus discovered during a skin exam following diagnosis of metastatic melanoma to a lymph node from an unknown primary lesion.
- To determine whether this lesion was melanoma, p16 immunohistochemical staining was performed of both the lymph node biopsy and the nevus, and provided a reliable means for determining the nature of the nevus.
- This information would be helpful to readers who care for patients with a history of melanoma who require differentiation of atypical nevi from recurrence of melanoma.

References

1. Piepkorn M. Melanoma genetics: An update with focus on the CDKN2A(p16)/ARF tumor suppressors. Journal of the American Academy of Dermatology. 2000.
2. Straume O, Sviland L, Akslen LA. Loss of Nuclear p16 Protein Expression Correlates with Increased Tumor Cell Proliferation (Ki-67) and Poor Prognosis in Patients with Vertical Growth Phase Melanoma. Clinical Cancer Research. 2000.