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Case Report

Rethinking the management of pedunculated melanomas: A case and discussion of an amelanotic pedunculated melanoma

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Abstract Nodular melanomas are a common structural class of melanomas. Pedunculated melanomas constitute a rare and often aggressive variant of nodular melanoma. Pedunculated melanomas have often been grouped with other exophytic melanomas, not suspended from a free stalk, bringing controversy regarding staging and clinical management of such tumors. Due to the unique nature of pedunculated melanomas, we believe AJCC staging alone may not accurately reflect true prognosis. We present and discuss a case of pedunculated melanoma which exemplifies the key role that pathologic and genetic evaluation play in the current management of these challenging tumors.

Key words
Pedunculated melanoma, amelanotic melanoma, melanoma.

Introduction

Nodular melanomas are classically defined as melanomas that have an invasive component with a junctional component that does not extend more than 3 rete ridges beyond the invasive component.[1,2] Clinically, they present as papules or nodules that grow rapidly and may progress to ulcerate and/ or bleed. Over 50% of nodular melanomas do not have pigmentation.[3] Pedunculated melanomas are a subclass of nodular melanomas.

Pedunculated melanomas present as exophytic masses, with or without pigmentation and/or ulceration, and are classically defined as tumors with greater than 50% to 100% of their area above the epidermis, suspended from a free stalk, and lateral dissemination encompassing less than three intraepidermal crests.[2] Pedunculated melanomas have often been grouped with other exophytic melanomas, not suspended from a free stalk, bringing controversy regarding staging and clinical management of such tumors.

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Case Report

A 74-year-old white male presented to our clinic for skin tag evaluation and removal. The patient had multiple skin tags, possibly including one lesion on the left flank, which had been present for many years per the patient **(Figure 1)**. The patient stated that the lesion on the left flank had been slowly growing. On exam it appeared as a polypoid growth, 1.5x1 cm at the apex, pedunculated in nature, with a thin white fibrous stalk at the base. The lesion was soft, non-indurated, and freely movable along its stalk. On dermoscopy, the lesion exhibited a homogenous erythematous hue and had a few small central violaceous clods, but no clear globular or reticular network was appreciated. Of note, there

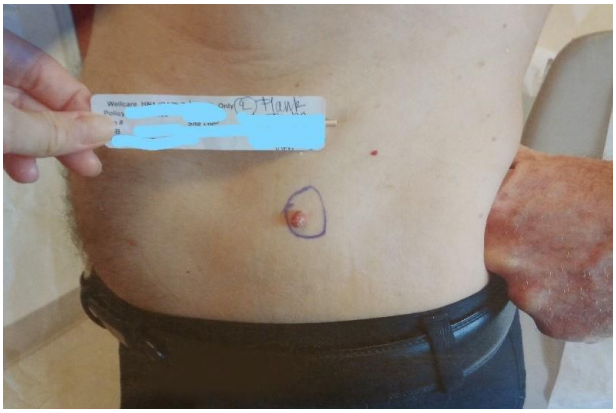

Figure 1 1.5 x 1cm erythematous, soft, non-indurated, freely movable, pedunculated polypoid growth with a thin white fibrous stalk at the base of the left flank

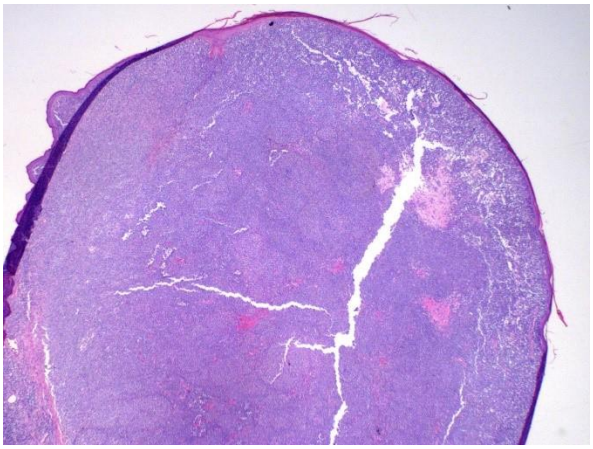

Figure 2 H+E staining demonstrating a polypoid pedunculated neoplasm with an aggregate of basophilic cells (20x).

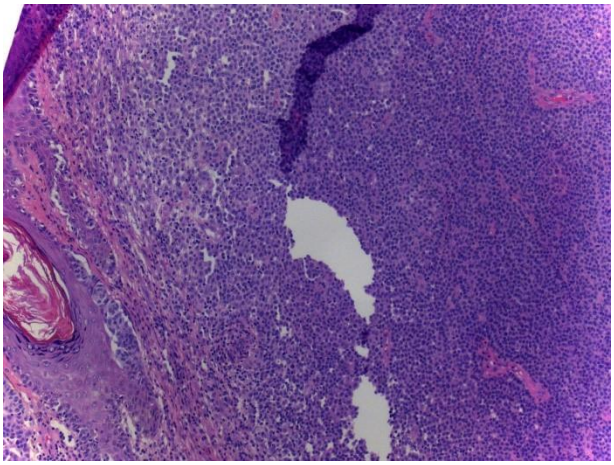

Figure 3 H+E staining within the neoplasm demonstrating multiple atypical cells with basophilic nuclei (40x).

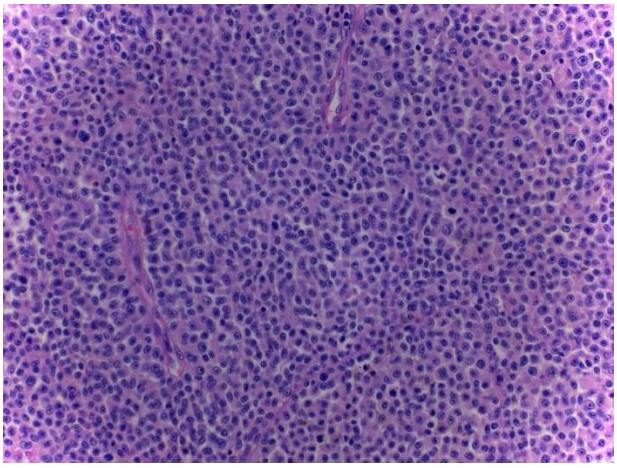

Figure 4 H+E staining on higher magnification demonstrating numerous mitotic figures (100x).

was an associated nevus just to the right of the lesion **(Figure 1)**.

It was not apparent as to if the lesion was growing out of the nevus or if it was adjacent to it. The nevus did not exhibit any atypical features by eye or dermoscopy. The nevus did exhibit a homogenous light brown reticular pigment network. Shave biopsy was performed on the lesion.

Histologic findings were consistent with an amelanotic pedunculated melanoma **(Figures 2, 3,** and **4)**.

Sections showed a polypoid neoplasm composed of atypical melanocytes. The tumor was assigned a Breslow depth of 6.5mm and a mitotic rate of 5/mm^2. The lesion extended to the peripheral margins and the base of each section. Ulceration, angiolymphatic invasion, and features of regression were not identified. A non-brisk lymphocytic host response was noted. Thus, an AJCC (American Joint Committee on Cancer) pathologic stage of T4a was assigned. Of note, S100 immunostaining was performed and supported the diagnosis of melanoma. In addition, an associated dermal melanocytic

nevus consistent with what was seen on exam was identified histologically.

After a detailed discussion with the patient, sentinel lymph node biopsy (SLNB) and excision were elected and performed. SLNB was negative for malignant melanoma cells. Surgical excision was performed with 2 cm margins, the patient tolerated the procedure well, and subsequent histologic review confirmed the margins were clear. Thus, per AJCC criteria, the tumor was T4aN0M0 and technically stage IIB. 31-Genetic Expression Profile testing (31-GEP test) was discussed with the patient and elected with the goal of an enhanced prognosis. 31-GEP testing revealed a result of class 2, sub-class 2B with a probability score of 61%. This subclass is associated with a 59-100% chance of recurrence within 5 years. GEP testing classifies the melanoma into class 1 or class 2. Class 1 has a low risk for metastasis with a 5-year distant metastasis-free survival (DMFS) of 90%. Class 2 has a high risk for metastasis with a 5-year DMFS of 63%. The classes are further sub-classified as A or B based on how close the result is to the crossover point between classes. Class 1A, 1B, 2A, and 2B have 5-year survival rates of 95%, 78%, 78%, and 57%, respectively.[4,5,6]

With these alarming results, detailed discussion with the patient regarding close follow-up, serial labs, and serial imaging was performed. Discussion regarding melanoma vaccine clinical trials and a hematology and oncology referral took place. The patient has followed up twice in the last 6 months with no signs of recurrence

Discussion

Data on the incidence, prognosis, and management of pedunculated melanomas in the literature is skewed; they are often grouped with sessile melanomas under the umbrella of polypoid melanomas. The pedunculated melanoma is characterized by its rapid vertical growth, with almost no radial growth. The tumor is located above the skin connected by a pedicle. This distinguishes the pedunculated form from the sessile form in which there is no pedicle.[3] Due to the disparate morphology between pedunculated and sessile melanomas, which may affect staging, prognosis, and management, we along with prior authors, agree that sessile and pedunculated melanomas be classified separately.

The majority of melanomas arise *de novo*. 23.7% of melanomas arise in association with melanocytic nevi, including our case. An associated nevus does not directly impact AJCC staging and is not known to affect the prognosis of a melanoma.[7]

The 5-year and 10-year survival rates for patients with AJCC stage IIB are 87% and 82%, respectively.[8] Due to the unique nature of our patient's tumor, we believe AJCC data may not accurately reflect our patient's true prognosis. Pedunculated melanomas grow above the epidermis; hence using Breslow depth may be inaccurate, as depth of pedunculated melanomas may not accurately reflect equivalent depth when compared to other non-pedunculated growths. Moreover, a multitude of other factors may be involved in the prognosis of pedunculated melanomas such as tumor genetic characterization.

Genetic mutations have been shown to be an independent predictor of prognosis for patients with primary melanomas. Only one out of three patients who ultimately develop metastatic disease demonstrate a positive sentinel lymph node biopsy at the time of diagnosis; two out of three patients are initially SLNB negative.[9] The genetic expression profile (GEP) test looks at 31 genetic markers and has been validated to

identify melanomas and metastasis risk. The test categorizes tumors into classes based on retrospective data obtained from patients with melanomas, and has been shown to accurately predict risk of metastasis in primary melanomas staged I or II by the AJCC.[4,5,6]

A limitation of these studies regarding our patient's case is a lack of pedunculated melanomas in the samples the test is based on. It is unknown if pedunculated melanomas, in comparison to non-pedunculated melanomas, tend to have a more aggressive genetic profile. Regardless, the genetics of our patient's tumor indicate a poorer prognosis than previously thought. Moreover, the genetic testing results changed our management. Based on this, we recommend discussing genetic profile testing with all patients with pedunculated melanomas as the results, as demonstrated in our case, may have significant prognostic impact. A limitation of current genetic testing is that although there is a clear prognostic impact, and closer management may be performed, there is no data indicating improved survival benefit. It will be interesting to see how future genetic testing and associated targeted therapies evolve and become utilized in the management of melanoma.

Conclusion

The pedunculated melanoma represents a rare and aggressive variant of the nodular type of melanoma. Pedunculated melanomas have previously been grouped with sessile melanomas; a distinction should be made between the two as this may affect patient prognosis and management. We suggest that patients with pedunculated melanomas are offered genetic testing, especially in cases with negative sentinel lymph node biopsies, as classic AJCC staging may not be accurate, impacting patient prognosis and management. We expect continued progress in the coming years pertaining to the reliability and accuracy of genetic testing for melanomas, which has already been shown to be a viable management tool. Moreover, in the near future we envision genetic testing will take on an even larger role in clinical utilization. Our case of a rare amelanotic non-ulcerated pedunculated melanoma with an associated nevus draws attention to the importance of diagnosis and management of unusual tumors, as the classic prognostic norm may not apply to all melanomas. Furthermore, the importance for clinicians to maintain a high index of suspicion for this rare variant of cutaneous melanoma could have significant implications in terms of early recognition, patient management, and prognosis.

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