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Case Report
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Collision Tumors of Malignant Melanoma *in situ* and Basal Cell Carcinoma: A Rare Case Report and Review of Literature

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Abstract

Collision tumors are two or more distinct neoplasms coexisting at the same anatomical location. The pathogenesis and nomenclature of cutaneous collision tumor is still ambiguous. We reported a case of 0.3 cm cutaneous lesion on the nose of an elderly female patient. Histological examination released a collision tumor of malignant melanoma in situ and basal cell carcinoma, which were adjacent to each other. Immunohistochemistry staining of SOX-10 and MOC31 confirmed the morphological findings. This case is consistent with the current literature that coexistent malignant melanoma and basal cell carcinoma is the most frequent combination of collision tumors.

Introduction

Various primary cutaneous neoplasms may derive from one or multiple different types of cells and coexist at one anatomical location. This type of tumor was originally named as "collision tumor" regardless of whether the two populations of neoplastic cells admixed together or not. A retrospective study of approximate 40,000 cutaneous biopsy cases reveals only 69 cases (0.17%) with two or more contiguous neoplasm [1]. Despite being extremely rare the coexistence of Malignant Melanomas (MM) and Basal Cell Carcinomas (BCC) are the most frequently seen coexistent cutaneous malignancies. Pierard et al. reviewed about 78,000 cutaneous tumors and identified only 11 tumors with both malignant melanoma and basal cell carcinoma [2].

The exact pathophysiology of coexistent cutaneous tumors is still unknown. Further investigation classify the coexistent cutaneous tumors into different subtypes according to histopathological patterns, including collision, combination, and colonization [3]. These subtypes of tumors advocate the theory that coexistent tumors are differentiated from different lineages of progenitor cells. However, another theory states that some coexistent tumors share the same type of stem cells and further differentiate into two or more morphologically distinct tumors, thus named biphenotypic tumor [3-5]. Although coexistent cutaneous tumors have been reported over four decades [6], the ambiguous pathogenesis limits clinical management and prediction of prognosis for these patients. Therefore, we reported a case of coexistent MM and BCC from our institute, which is most consistent with a collision tumor.

Case Presentation

The patient presented to the dermatologist for a 0.3 cm ill-defined, irregular, and red, macule at the tip of her nose for 2 months. She denied any bleeding or symptoms related to this lesion. Patient has a history of cutaneous basal cell carcinoma. Biopsy of this lesion at an outside institute revealed an invasive malignant melanoma adjacent to basal cell carcinoma. Breslow thickness of melanoma is at least 0.5 mm with the deep surgical margin involved by invasive melanoma.

Patient was referred to the surgeon in our institution for wide excision. Microscopic examination of the specimen revealed nests of atypical melanocytes with pagetoid spread along the dermal-epidermal junction (Figure 1A, 1B), consistent with malignant melanoma in situ. The closest distance to free margin of melanoma in situ is 1.5 mm. Atypical melanocytes also extended into hair follicles but did not invade the underlying dermis. Additional nests of atypical large basaloid cells with palisading architecture of the peripheral border, consistent with BCC, present adjacent to but not attached to melanoma in situ (Figure 1C, 1D). Immunohistochemistry staining of the atypical melanocytes show positive expression of SOX-10 (Figure 1E). Atypical basaloid cells

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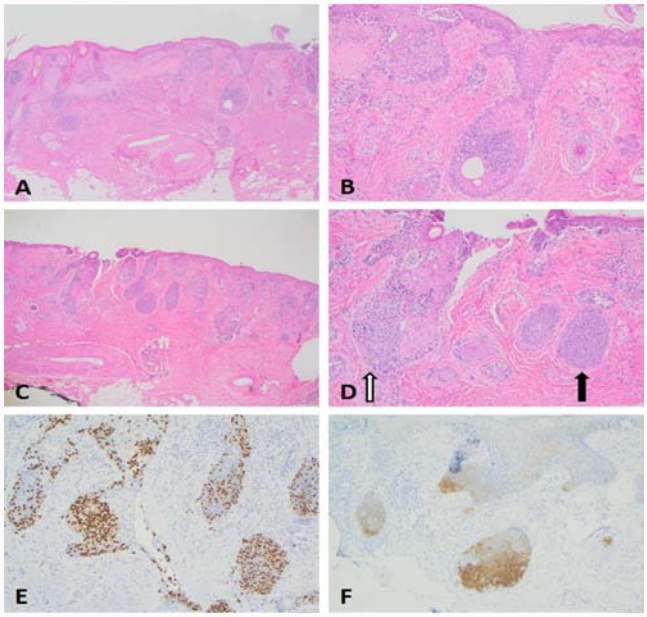

Figure 1: Microscopic examination of the lesion with H&E stain demonstrates melanoma in situ (A, 4x), involving hair follicles (B, 10x). Nests of basal cell carcinoma (C, 4x, and D, 10x, black arrow) are adjacent but not attached to melanoma in situ (C and D, open arrow). Immunostains with SOX10 (E, 10x) and MOC31 (F, 10x) confirm each component of melanoma in situ and basal cell carcinoma in this lesion.

showed positive expression of MOC-31 (Figure 1F). These findings are consistent with collision tumor of malignant melanoma in situ and basal cell carcinoma.

Discussion

A variety of nomenclatures have been employed to characterize the tumors consisting of two or more neoplastic cell populations, including collision, combination, colonization, and biphenotypic tumors [3,4,7]. Multiple skin neoplasms at one site (MUSK IN A NEST) is the most recently proposed nomenclature to describe this group of tumors to avoid the inconsistency of the various terminologies [8]. Current nomenclatures classify coexisting neoplasms according to the histological patterns and clonalities. A collision tumor refers to two or more distinct neoplasms that occur within close proximity of each other but maintain clear boundaries. A combination tumor refers to two distinct but admixed neoplasms without distinguishable borders. A colonization tumor refers to one distinct neoplasm, such as melanoma in situ, infiltrating into a second distinct neoplasm, but is confined to the second neoplasm with no invasive component extending to the underlying dermis. Neoplastic cells of collision, combination, and colonization tumors may be derived from multiple different clones. On the contrary, neoplastic cells of a biphenotypic tumor originate from the same clone but further differentiate into two or more phenotypically distinctive neoplasms [3,4,7]. In current case, the melanoma component infiltrates into and intermingled with BCC, but does is not confined to the BCC. In addition, immunohistochemistry stains demonstrate separated staining profile of melanoma from BCC without co-expression of melanocytic or basaloid makers. It is mostly consistent with a combination tumor.

There is still lack of consensus regarding the exact nomenclature of coexistent tumors, most likely due to the disagreement on the pathogenesis among investigators. “Interaction theory” believes that the presence of the first tumor creates a pro-oncogenic environment, which facilitates the second tumor to develop [1,9]. “Field cancerization theory” states that certain anatomical sites of skin that exposes to carcinogens or environmental damages, such as UV light, have higher risk to develop dual or more neoplasms [2,10]. Another theory, which is associated with “biphenotypic tumor”, suggests that neoplastic cells of coexistent tumor originates from the same stem cells and further differentiate into two or more lineages [3,5,10]. In our opinion, the problem with the above theories is that you might expect coexistent tumors to be much more common however they are extremely rare. Finally, the coexistent tumors could be explained by pure coincidence: The two most common cutaneous tumors account for the most common coexisting cutaneous tumors.

In current literature, there are approximately 34 case reports and series investigating coexistent MM and BCC including the present case. MM associated with BCC are most commonly reported malignant tumors together although the incident is low at 0.014% [2]. The documentation of coexistent MM and BCC started in mid-1980s [6,11-13]. Bhawan et al. published 2 cases with coexisting superficial spreading MM *in situ* and BCC for the first time in 1984. Cornejo et al. [ ] in 2013 and Blum et al. 2017 reported 17 and 3 respectively [10,14]. There is limited information regarding the management and prediction of prognosis for these tumors. Breslow thickness of invasion for the melanoma component is the best prediction factor of prognosis for coexistent MM and BCC. When the presence of invasive melanoma is clearly outside coexistent BCC, such as in collision or combination tumors, the standard guideline should be followed to measure the Breslow thickness. However, the challenge to determine the Breslow thickness for melanoma colonized with BCC--whether it should be treated as *in situ* or invasive. Most authors agree that melanoma in colonized tumor should be evaluated as in situ [15,16]. However, one study suggests that melanoma in colonized tumor is more indolent than melanoma in situ, indicating that atypical melanocytes may depend on the epithelial component to grow and invade [17]. Considering the origin of the atypical melanocytes, the coexistent melanoma could be a new rare variant in the histological classification of melanoma.

Conclusion

The etiology, prognosis, and management of coexistent tumors are still unclear due to limited cases reported. Current literature suggests utilizing case-by-case approach with careful clinical correlation and appropriate ancillary techniques to manage the collision tumors. It requires multi-institutional collaboration and long-term follow up to investigate the outcome of these coexistent tumors. Thus, a standard terminology to categorize these tumors is important for pathologists from different institutes to share knowledge of these tumors.

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