Aggressive Amelanotic Melanoma Masquerading as Squamous Cell Carcinoma

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CASE PRESENTATION

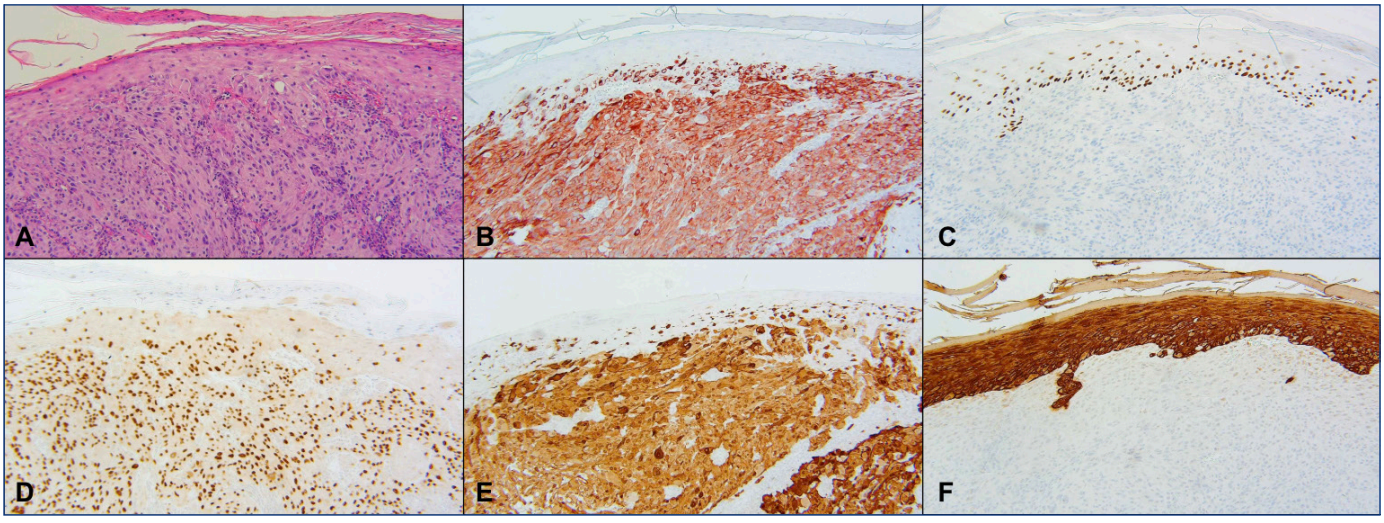
A 75-year-old man presented with a pruritic and intermittently bleeding mass on his right posterior shoulder, first noticed a few months prior. His medical history included coronary artery disease, abdominal aortic aneurysm, hypertension, hyperlipidemia, osteoarthritis, deep vein thrombosis with subsequent pulmonary embolism, and early-stage right renal cell carcinoma status post partial nephrectomy. On examination, the lesion appeared as a firm, slightly erythematous 1.2cm nodule with central crusting and telangiectasias [**Figure 1**]. A clinical diagnosis of squamous cell carcinoma (SCC) was considered, prompting a shave biopsy.

Pathology revealed atypical pleomorphic epidermal and dermal melanocytes, with pagetoid melanocytosis and rare dermal melanophages [**Figure 2**]. Immunohistochemistry highlighted the atypical melanocytes with S100, SOX10, and Melan A [**Figure 2**]. The immunophenotypic and morphologic findings confirmed nodular melanoma with a Breslow thickness of 2.7 mm, exhibiting both vertical and radial growth phases but lacking ulceration or other concerning histologic features. The melanoma was excised with 2 cm margins down to the fascia. The final excision pathology

Figure 1. Firm, skin-colored papule on the right upper posterior shoulder with telangiectasia and central crusting.

Figure 2. Malignant Melanoma

[**A**] H&E stain showing atypical pleomorphic epidermal and dermal melanocytes, 100x; [**B**] S100 immunostain 100x; [**C**] P40 immunostain highlighting epidermal keratinocytes; [**D**] SOX10 immunostain highlighting dermal and epidermal atypical melanocytes, 100x; [**E**] Melan A immunostain highlighting dermal and epidermal atypical melanocytes; [**F**] Keratin mix immunostain (AE1, AE3, and CAM5.2) highlighting the epidermal keratinocytes.



demonstrated residual malignant melanoma with a maximum Breslow thickness of 1.2mm. Sentinel lymph node biopsies were also performed at the time of excision, with localization to the right axilla and neck. The axillary node was negative, while the cervical node showed focal staining for Melan-A and SOX-10, confirming metastatic disease and staging at pT3a pN1a cM0.

TREATMENT COURSE/OUTCOME

The patient began adjuvant pembrolizumab. However, by the 10th cycle he developed immune-mediated colitis refractory to prednisone, leading to a 28-pound weight loss and ultimately requiring a fecal transplant. A total of 16 pembrolizumab cycles were completed.

Six months after initiating immunotherapy, recurrence was detected in the right axilla by PET CT. Ultrasound-guided fine needle aspiration confirmed metastatic melanoma. Ipilimumab with concurrent radiation therapy was initiated; however, after three cycles, his condition deteriorated, marked by recurrent colitis, chronic dehydration, weight loss, and rectal bleeding. Given his poor response and declining status, the patient was transitioned to hospice care where he eventually passed.

DISCUSSION

Melanoma is the deadliest form of skin cancer, accounting for the majority of skin cancer-related deaths.[1] Representing nearly 14% of melanomas, nodular melanoma (NM) is the second most common clinical subtype.[2] NMs are associated with rapid growth and early lymphatic spread, contributing to a poor prognosis.[2-4] Therefore, early and accurate diagnosis of NM is crucial to ensuring that patients receive appropriate treatment before the skin cancer progresses.

Given NM's aggressive nature, distinguishing it from other malignancies is essential for effective intervention. In this case, the diagnosis of amelanotic melanoma was confirmed through histopathology and immunohistochemistry, with SOX10, Melan-A, and S100 positivity distinguishing it from SCC.[2]

While educating patients about the ABCDE criteria (asymmetry, border irregularity, color variation, large diameter, and evolution) is effective for raising awareness of traditional melanomas,[1] NMs, especially the amelanotic variant, typically do not adhere to these early warning signs.[2,5] NMs tend to exhibit a high degree of border regularity, a more uniform color pattern, and can have a smaller diameter compared to other subtypes.[6] Classically, they present as a skin-colored/erythematous or hyper-pigmented round nodule, and can also be pruritic, friable, and/or tender.[7] These lesions often undergo rapid changes in appearance and become increasingly noticeable over the course of weeks.[7]

NM's ability to mimic benign or less aggressive skin cancers, such as SCC and basal cell carcinoma, contributes to its diagnostic challenge. A high index of suspicion, timely biopsy with morphologic and immunophenotypic evaluation, and improved patient awareness are crucial for early detection and treatment.

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