SKIN

BRIEF ARTICLE

Epithelioid Angiosarcoma: A Diagnostic Dilemma with Clinically and Histopathologically Overlapping Features

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ABSTRACT

Cutaneous angiosarcoma is a rare malignancy of endothelial cell origin that commonly presents in the head and neck region of elderly individuals and is known for high rates of lymph node metastasis and mortality. There is significant variability in the histopathologic features, and immunohistochemistry is necessary to help differentiate epithelioid angiosarcoma from lesions it may clinically mimic. Here, we report a rare case of poorly differentiated epithelioid angiosarcoma on the trunk initially diagnosed as poorly differentiated squamous cell carcinoma (SCC) on shave biopsy. A 56-year-old man presented for a full-body skin examination significant for a 5.6 x 2.8 mm brown-black macule on the left superomedial posterior trunk and a 5.0 x 2.7 mm pink, ulcerated papule on the right inferior posterior trunk. On histopathology, one lesion was found to be melanoma in situ, and the other showed ulcerated and infiltrative, poorly differentiated SCC. Post-excision histologic analysis of the right inferior back lesion revealed tumor cells immunoreactive to vimentin, ERG, and CD31 (PECAM-1). These findings suggested that the lesion previously diagnosed as SCC was an invasive, poorly differentiated epithelioid angiosarcoma. The patient underwent 40 sessions of radiotherapy. Epithelioid angiosarcoma occurring outside of the conventional epidemiologic profile is believed to portend higher mortality rates. This case highlights the importance of thorough clinical evaluation and appropriate histopathologic diagnosis of an aggressive neoplasm unlikely to present in this location. Further studies are required to explore potential risk factors, effective treatments, and long-term outcomes in patients with epithelioid angiosarcoma.

INTRODUCTION

Angiosarcoma is a rare malignant tumor of endothelial origin that accounts for less than 1% of all soft tissue sarcomas.[1] Its incidence is estimated at 0.4 to 1.0 per million people per year, and it has a poor prognosis due to its high rate of recurrence and metastasis.[2] Epithelioid angiosarcoma, a subtype of angiosarcoma, is even rarer and often presents a diagnostic challenge due to its varied clinical presentation and resemblance to other skin conditions. Here, we present a case of a 56-year-old patient who was diagnosed with an invasive, poorly differentiated epithelioid angiosarcoma on the back that mimicked, and was initially

diagnosed as, poorly differentiated squamous cell carcinoma.

CASE REPORT

A 56-year-old man with a past medical history of type 2 diabetes, hyperlipidemia, and major depressive disorder presented to an outpatient dermatology clinic for a full-body skin examination. Physical examination was significant for a 5.6 x 2.8 mm brown-black macule on the left superomedial posterior trunk (**Figure 1**) and a 5.0 x 2.7 mm pink, ulcerated papule on the right inferior posterior trunk (**Figure 1**), both of which were present for approximately 4 years and were biopsied via shave method. On histopathology, one of the lesions was found to be melanoma in situ, and the other showed ulcerated and infiltrative, poorly differentiated squamous cell carcinoma (SCC). Both lesions were subsequently excised with a 1-cm margin. Post-excision histologic analysis of the right inferior back lesion via immunohistochemistry revealed tumor cells immunoreactive to vimentin, ERG, and CD31 (PECAM-1); there was no reactivity for cytokeratins CK5/6 or CK20. These findings suggested that the lesion previously diagnosed as SCC was actually an invasive, poorly differentiated epithelioid angiosarcoma. The patient underwent computed tomography (CT) of the head, chest, abdomen, and pelvis to evaluate for systemic involvement. The patient's CT head resulted with abnormal findings including "asymmetric of left side of sella turcica with large abnormal enhancing left sellar and parasellar mass," prompting further investigation with MRI brain. This then led to discovery of a "large abnormal enhancing left sellar and parasellar heterogenous mass likely representing a pituitary macroadenoma."

The patient was referred to radiation oncology for radiotherapy (RT) for poorly differentiated epithelioid angiosarcoma, and underwent 40 sessions of RT. The patient was also referred to endocrinology and neurosurgery for evaluation of pituitary gland function, as well as serial MRI of the brain every 3 months for an incidentally discovered pituitary macroadenoma.

DISCUSSION

Cutaneous angiosarcoma is a rare malignancy of endothelial cell origin that commonly presents in the head and neck region of elderly individuals and is known for high rates of lymph node metastasis.[1] While the etiology of angiosarcoma is largely unknown, it has been associated with radiation and chemical exposure and chronic lymphedema.[1] Epithelioid angiosarcoma is a subtype characterized by epithelioid cells with a large nucleus and abundant eosinophilic cytoplasm.[1,3,4] It accounts for almost 30% of all angiosarcomas.[1] Furthermore, whether epithelioid angiosarcoma portends a worse prognosis when compared to conventional cutaneous angiosarcoma has yet to be conclusively established.[1] There exists significant variability in the histopathologic features seen in epithelioid angiosarcoma.[4] As such, immunohistochemistry (IHC) should be performed to help differentiate epithelioid angiosarcoma from lesions it may clinically mimic, including carcinomas, adenocarcinomas, certain lymphomas, and amelanotic melanoma, among others.[5] In our case, the initial diagnosis based on shave biopsy stained with hematoxylin and eosin stain was poorly differentiated SCC that, after excisional biopsy and IHC, showed epithelioid angiosarcoma (**Figure 2**). IHC post-shave biopsy revealed positive ERG (**Figure 3a**) and CD31 (**Figure 3b**), and

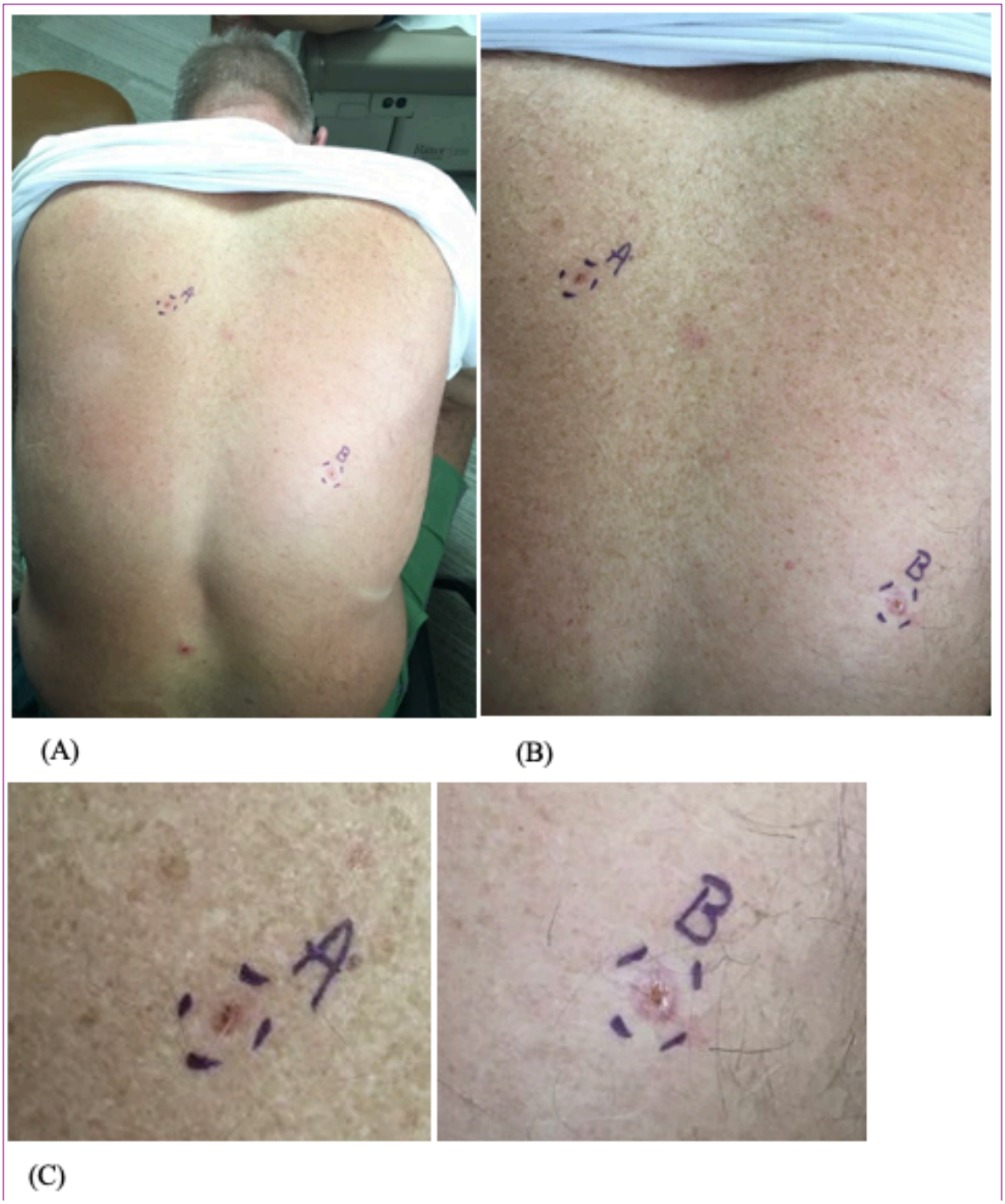

Figure 1. (a) 5.6 x 2.8 cm brown-black macule labeled “A” on the left superomedial back and 5.0 x 2.7 mm pink, ulcerated papule labeled “B” on the right inferior back. (b) Lesion A was biopsy-proven “Melanoma in Situ.” Biopsy result of Lesion B initially labeled “poorly differentiated Squamous Cell Carcinoma” but post excisional histopathology and immunostaining was re-described as “Poorly Differentiated Epithelioid Angiosarcoma.”

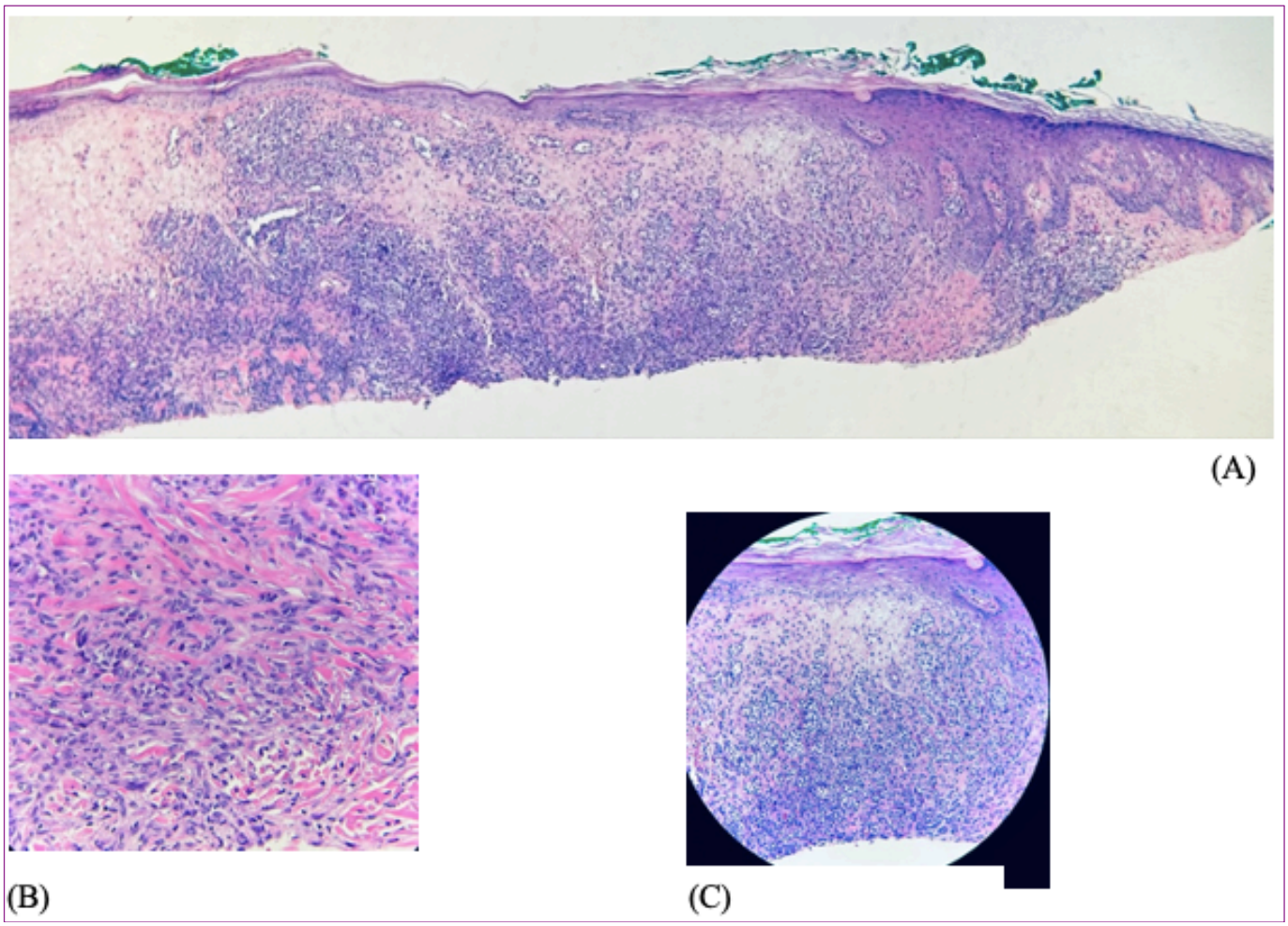

Figure 2. Original biopsy H&E slides from (a) low-power to (b) high-power field showing a morphologically ambiguous specimen with an initial differential diagnosis of carcinoma, melanoma, lymphoma. On high-power field (c), there are minimal mitotic figures but variable cytologic atypia.

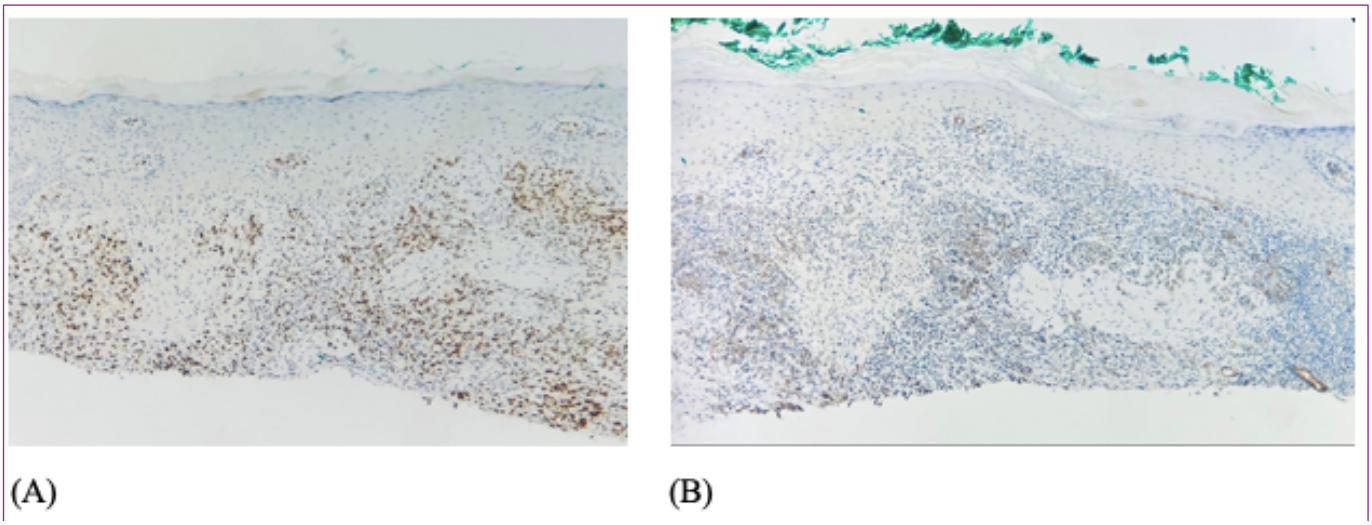

Figure 3. Specimen reassessed following subsequent re-excision with immunostains showing reactivity in the tumor cells for (a) ERG and (b) CD31.

weakly positive EMA. The specimen had a moderately high proliferative index, with greater than 50% Ki-67 staining. S100, HMB-45, melan-A, PRAME, CD3, CD20, CD30, bl-6, pankeratin, and p40 were negative. Thus, with IHC post-excisional analysis revealing positivity with ERG (**Figure 3a**), CD31, (**Figure 3b**) and vimentin, and negative CK5/6 and CK20, these findings altered the diagnosis to epithelioid angiosarcoma. None of the aforementioned markers alone are highly sensitive or specific for epithelioid angiosarcoma.[4]

Epithelioid angiosarcoma occurring outside of the conventional epidemiologic profile – in the head and neck, post-radiation – is believed to result in higher mortality rates.[6] This is particularly alarming given the preponderance of cases on the trunk or limbs.[3,4,5,6,7,8] Our case proved unique in that although the location of the epithelioid angiosarcoma was on the patient's trunk, it was located on the patient's back. While there are no definitive guidelines, treatment typically involves surgical excision with wide margins and adjuvant RT.[6] The high mortality rate associated with this diagnosis drives individualized treatment decisions based on factors such as tumor location, size, and grade, as well as patient factors such as age and overall health.[6] Treatment may include surgery, radiation therapy, chemotherapy, and/or targeted therapy, but a multimodal approach may be necessary for the successful treatment of epithelioid angiosarcoma.[6]

CONCLUSION

This case highlights the importance of thorough clinical evaluation and presentation of an aggressive neoplasm unlikely to present in this location. Thus, appropriate histopathologic diagnosis of skin lesions is imperative. The high mortality rates associated with epithelioid angiosarcomas warrants further studies to analyze potential risk factors and a standardized treatment regimen based on patient outcomes and longevity.

Consent: Consent for the publication of all patient photographs and medical information was provided by the authors at the time of article submission to the journal stating that all patients gave consent for their photographs and medical information to be published

in print and online and with the understanding that this information may be publicly available.

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