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Case Report

Angiomatoid melanoma

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Abstract

Angiomatoid melanoma is a rare variant of malignant melanoma that is not currently recognized by the World Health Organization classification system. In this study, we present a case of primary angiomatoid melanoma in a 57-year-old man who presented to clinic with a complaint of a growing lesion on the frontal scalp for four months. Microscopic examination of the lesion revealed cavernous spaces filled with extravasated red blood cells. Immunohistochemical markers were positive for melanoma and negative for vascular endothelium. We also review the literature on angiomatoid melanoma, finding distinct morphological differences in previously reported cases. Owing to these differences, we propose new diagnostic criteria and offer a mechanism for formation of blood-filled cavernous spaces while cautioning against misinterpretation of CD31 expression by macrophages in zones of immune regression. Angiomatoid melanoma is a diagnostic challenge because of its rarity, signaling a need for further histopathological evaluation and more complete awareness of its features.



Figure 1. A) On the midline of the frontal scalp there is a firm, crusted, dark brown, exophytic nodule with some overlying mild erosion and extensive background actinic damage. **B)** Anterior to the primary midline lesion and left of midline there is a crusted, brown, flat papule.

quently reported in the literature.⁴⁻⁸ In addition, Ambrogia recently reported a case of “melanoma with pseudo-angiomatous features.”⁹

We report a new case of angiomatoid melanoma and review the literature. In our review, we find substantial differences between cases reported as angiomatoid melanoma and suggest criteria for the diagnosis. Further, we suggest a mechanism for the formation of the characteristic blood lakes and document the potential diagnostic pitfall of CD31 expression by macrophages in zones of immune regression.

Introduction

The current World Health Organization classification of melanoma includes nine families, separated into two groups by their relation to UV irradiation.¹ There are rare histopathologic variants of melanoma not recognized by the World Health Organization.² Angiomatoid melanoma was first described in 1997 as a lesion “composed of nodular aggregates of cavernous spaces, containing red blood cells and lined by a flattened layer of cells.”³ The authors noted the potential for clinicians and pathologists to confuse the tumor with a vascular lesion. Six more cases of angiomatoid melanoma were subse-

Case Synopsis

A 57-year-old man presented with a four-month history of a growing lesion across the midline of the frontal scalp. He had no prior history of skin cancer. He had no significant other medical history besides hypertension. Physical examination demonstrated an ulcerated 1.5cm violaceous nodule with two sub-centimeter satellite lesions (**Figure 1**). The clinical differential diagnoses included angiosarcoma, scalp metastasis, basal cell carcinoma, squamous cell carcinoma, and seborrheic keratosis. The violaceous nodule and a satellite nodule were tangentially shaved for histopathology evaluation.

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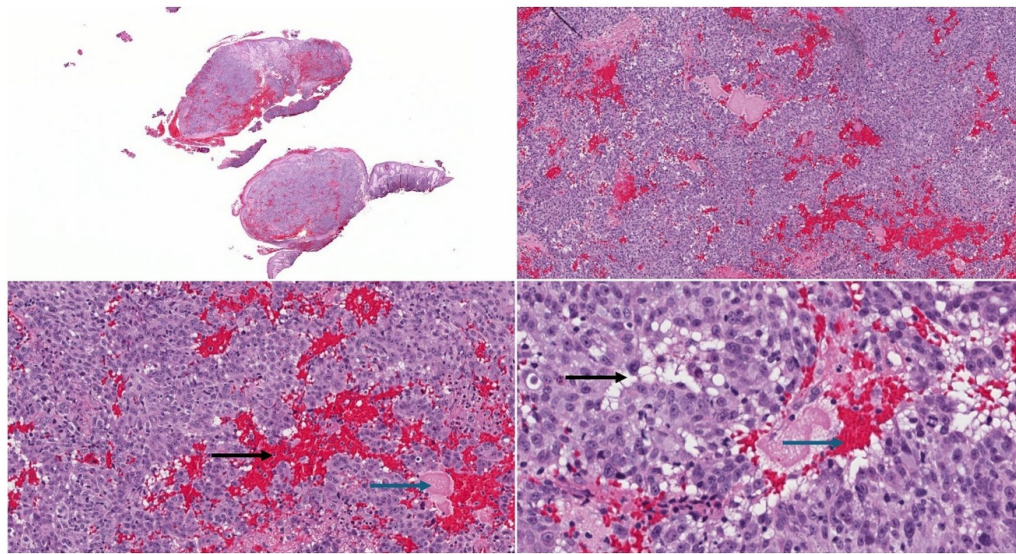


Figure 2. **A)** Scanning magnification demonstrates an ulcerated nodular tumor (H&E, 40X). **B)** The tumor contains conspicuous collections of erythrocytes (H&E, 100X). **C)** Collections of erythrocytes form blood lakes (black arrow), some with fibrin thrombus (blue arrow) (H&E, 200X). **D)** Smaller intercellular spaces consist of vacuolar tumor cell degeneration (black arrow) whereas larger intercellular spaces have blood elements circumscribed by vacuolated tumor cells (blue arrow). (H&E, 400X).

The findings in the primary and satellite lesion were identical. Hematoxylin-eosin histology demonstrated a hemorrhagic dermal neoplasm composed of epithelioid cells arranged in anastomosing cords and nests and surrounding blood lakes. The epidermis was secondarily involved and ulcerated. The tumor cells were amelanotic and epithelioid to slightly spindled. They exhibited cellular atypia with nuclear enlargement, pleomorphism, coarse chromatin, macro nucleoli, and 10 mitotic division figures per square mm with frequent atypical mitotic spindles. Tumor-infiltrating lymphocytes were abundant and mixed with extravasated erythrocytes. Irregular pseudo-vascular spaces containing pooled erythrocytes and organized fibrin peppered the tumor. Vacuoles separated pseudo-vascular spaces from adjacent tumor cells. Early spaces without erythrocytes consisted only of vacuoles ([Figure 2](#)).

Tumor cells expressed the melanocytic antigens SRY-related HMG-box gene 10, Melan-A, and preferentially expressed antigen in melanoma (*PRAME*, a marker expressed by melanoma cells), confirming the diagnosis of melanoma. *CD31* immunohistochemistry highlighted macrophages in an area of regression but was negative in tumor cells. *CD31* significance is discussed later in this manuscript. Tumor cells and the cells lining the cavernous spaces were negative for the vascular endothelial markers *ERG* and *CD34* (excluding a vascular neoplasm), the mesenchymal cell marker *CD10* (excluding atypical fibroxanthoma), the hematolymphoid marker *CD30* (excluding anaplastic large cell lymphoma), the lymphoid

marker *CD45* (excluding lymphoma), and the epithelial cell markers epithelial membrane antigen and *p63* (excluding carcinoma) ([Figure 3](#)). Tumor cells were negative for *BRAF* mutation by polymerase chain reaction and there was positive programmed death-ligand 1 expression (3% tumor proportion score, intensity 2+, programmed death-ligand 1 22C3).

Physical examination for lymphadenopathy was negative. Brain magnetic resonance imaging and full-body positron emission tomography were negative for metastatic disease. The patient underwent wide local excision and sentinel lymph node biopsy. Histopathology demonstrated residual melanoma with a final Breslow thickness of 7.0mm, tumor-induced ulceration, macroscopic and microscopic satellite metastases, medium vein invasion, frequent mitotic figures (8/square mm), and perineural involvement. Three sentinel lymph nodes from the right neck were negative for metastatic melanoma. We diagnosed angiomatoid nodular melanoma with satellite metastases, stage IIIC (pT4bN1cMX).

The patient was treated with nivolumab infusion (480mg/48ml over 30 minutes) planned to be once monthly for one year. One month after excision, the wound was reconstructed with split-thickness skin graft from the left anterior thigh. The patient is free of disease free at 7-months follow-up postexcision.

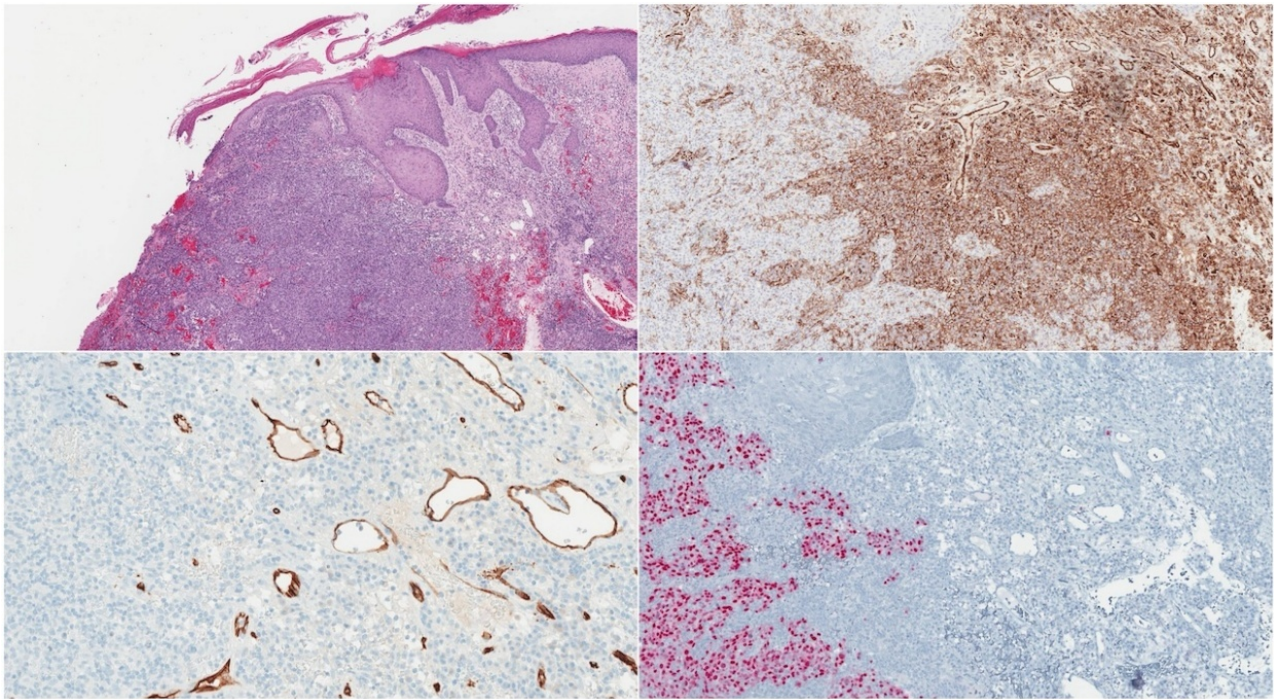


Figure 3. **A)** Viable tumor on the left, with immune-mediated regression on the right (H&E, 40X). **B)** CD31 highlights numerous macrophages in the zone of regression (CD31 IHC, 100X). **C)** Both the tumor cells and macrophages are negative for CD34, which highlights neovascularization within regression (CD34, 200X). **D)** SOX10 highlights melanoma and is negative in the area of regression (SOX10, 100X).

Case Discussion

Adler and coworkers coined the term angiomatoid melanoma in 1997 to describe a metastatic melanoma with cavernous spaces containing erythrocytes that mimicked a vascular neoplasm.³ Including the case reported herein, nine cases of angiomatoid melanoma have been reported in the literature. The term has been applied to both primary and metastatic lesions and different histopathologic variants of melanoma. Herein, we highlight the differences between these cases, suggest criteria for the histopathology diagnosis of angiomatoid melanoma, and discuss mechanisms behind the formation of the characteristic blood-filled spaces.

Table 1 summarizes the cases reported as angiomatoid melanoma. Five were primary cutaneous nodular melanomas⁶⁻⁹ [current case], three were metastatic melanomas,^{3,5} and the final case was a recurrent desmoplastic melanoma.⁴ Angiomatoid has been used to describe two different pathological patterns in these cases. In the classic form described by Adler et al, there are prominent cavernous spaces engorged with erythrocytes.³ The poor differentiation, abundant blood elements, and violaceous clinical appearance can lead to confusion with a vascular lesion. In 6 out of 7 tested cases,^{3,5-8} the cells lining these spaces were negative for vascular markers and they are best considered as pseudo-vascular spaces. The two other reported cases of angiomatoid melanoma describe a primary nodular melanoma and a recurrent desmoplastic melanoma which formed empty tubules.^{4,9} Unlike the other cases,

these did not form cavernous spaces engorged with blood and did not mimic vascular lesions clinically. Given the disparate features of cases reported as angiomatoid melanoma, we suggest the following criteria for diagnosis: 1) primary melanoma of the skin, usually of the nodular type, 2) formation of cavernous blood-filled spaces, and 3) clinically violaceous or vascular appearance.

The pathogenesis of the characteristic blood-filled cavernous spaces is unknown. Vasculogenic mimicry and tumor/stromal instability are two leading theories. Vasculogenic mimicry is the formation of patterned vascular channels lined by basement membrane-forming melanoma cells.¹⁰ Maniotis et al hypothesize that vascular mimicry enables tumor microcirculation in the absence of neo-angiogenesis. Vascular channels in vasculogenic mimicry are very narrow, lined by a basement membrane, and do not show evidence of necrosis, tumor degenerative changes, blood lakes, or thrombosis. Another theory is that stromal/tumor instability may cause formation of blood lakes. In our case, we identified acellular clefts formed by vacuolar degeneration within neoplastic cells at the periphery of cavernous blood-filled spaces, suggesting tumor cell degenerative changes may precede blood lake development. The pathogenesis of blood lakes in aneurysmal dermatofibroma may be instructive. Like angiomatoid melanoma, aneurysmal dermatofibroma may mimic a vascular lesion and forms blood filled spaces without endothelia which are identical to those in angiomatoid melanoma. Some investigators suggest mechanical trauma to dermatofibromas cause hemorrhage because of stromal instability, creating

Table 1. Cases reported as angiomatoid melanoma.

Author, year	Demographic	Histopathology	Studies	AJCC Stage	Follow-up
Adler, 1997	44 y/o male with metastatic disease to sacral vertebra and left forehead (unknown primary)	Metastatic melanoma with cavernous blood-filled spaces	Positive: S-100, HMB-45 Negative: CD31, CD34	Stage IV: TXN0M1	None
Baron, 2000	84 y/o male with multiple local recurrences of desmoplastic melanoma across right forehead	Recurrent desmoplastic melanoma with empty tubular spaces	Positive: S-100 Negative: HMB-45	Stage III: T4bN0M0	None
Zelger, 2004	51 y/o female with subcutaneous metastases across right thigh and paravertebral soft tissue from prior T2a melanoma of right arm	Metastatic melanoma with multifocal geographic hemorrhagic necrosis surrounded by an MFH-like reaction	Positive: S-100, Melan-A, HMB-45, CD56 in neoplastic cells; CD68 positive in MFH like reaction Negative: CD31, CD34, Factor VIII	Stage IV: T2aN0M1	Alive at nine years post diagnosis; multiple subsequent metastatic foci treated by excision
Zelger, 2004	61 y/o male with left axillary nodal metastasis from prior T1a acral lentiginous melanoma of subungual left middle finger	Lymph node remnant compressed by metastasis with multifocal geographic hemorrhagic necrosis surrounded by an MFH-like reaction	Positive: S-100, CD56 in neoplastic cells; CD68 positive in MFH-like reaction Negative: CD31, CD34, Factor VIII	Stage III: T1aN1M0	Alive at seven years post diagnosis; treated with lymph node dissection and adjuvant chemotherapy
Ramos-Rodriguez, 2015	59 y/o male with T2a melanoma of the right thigh	Nodular melanoma with cavernous pseudo-vascular spaces filled with erythrocytes	Positive: S-100, HMB-45, MiTF-1 in neoplastic cells; D2-40 in cells lining pseudo-vascular spaces. Negative: CD31	Stage IB: T2aN0M0	None
Fonda-Pascual, 2018	63 y/o female with T4b nodular melanoma of the right scapula and subsequent metastases to lungs, liver, and celiac lymph nodes	Nodular melanoma with cavernous pseudo-vascular spaces filled with erythrocytes, arising in association with a dermal nevus	Positive: S100, HMB-45, SOX-9, BRAF V600E Negative: D2-40, CD31, AE1-AE3	Stage IV: T4bN1M1	Alive at six months; treated with vemurafenib
Paolino, 2019	72 y/o male with T2a melanoma of the right temple	Nodular melanoma forming empty tubular spaces	Positive: S100, Melan-A, HMB-45 Negative:	Stage IB: T2aN0M0	None

Author, year	Demographic	Histopathology	Studies	AJCC Stage	Follow-up
			CD34, cytokeratin 5/6		
Ambrogio, 2023	87 y/o male with T4a primary cutaneous melanoma of unspecified anatomic site	Nodular melanoma with cavernous pseudo-vascular spaces filled with erythrocytes	Positive: S-100, Melan-A, HMB-45, SOX-10, BRAF V600E Negative: CD31, CD34, ERG	Stage IIB: T4aNXM0	None
Current case	57 y/o male with T4b nodular melanoma and macroscopic satellite metastases across scalp	Nodular melanoma with cavernous pseudo-vascular spaces filled with erythrocytes	Positive: SOX10, Melan-A, PRAME, PD-L1; CD31 positive in macrophages Negative: ERG, CD34, p63, EMA, BRAF, CD30, CD45	Stage IIIC: T4bN1cM0	Alive at three months

blood filled spaces.¹¹ A similar process may lead to the blood lakes in angiomatoid melanoma.

We noted with interest that Zelger et al reported a “malignant fibrous histiocytoma-like” reaction by *CD68*+ macrophages in their cases.⁵ In our case, there was a discrete zone of regression populated by large *CD31*+ macrophages that might represent a similar phenomenon. *CD31* is widely regarded as a marker for endothelial cells, but expression on cells of the macrophage-monocyte lineage is common.¹² Therefore, it is important to be cognizant of the histological and immunohistochemical features that distinguish *CD31*+ macrophages and neoplastic endothelial cells. Failure to do so may result in an inaccurate diagnosis, posing potential harm to the patient.

Conclusion

In summary, we report a new case of angiomatoid melanoma. There are profound differences between reported cases, and we suggest restricting the diagnosis to cases of primary cutaneous melanoma which form blood-filled cavernous spaces and clinically mimic vascular lesions. These blood-filled spaces may be the effect of mechanical trauma to melanomas predisposed to acute intratumoral hemorrhage by preexisting cellular and stromal degenerative changes.

Potential conflicts of interest

The authors declare no conflicts of interest.

References

1. WHO Classification of Tumours Editorial Board. Skin tumours. In: *WHO Classification of Tumours Series*. Vol 12. 5th ed. International Agency for Research on Cancer; 2023.
2. Cota C, Saggini A, Lora V, et al. Uncommon histopathological variants of malignant melanoma: Part 1. *Am J Dermatopathol*. 2019;41:243-263. PMID:30024414
3. Adler MJ, Beckstead J, White CR. Angiomatoid melanoma: A case of metastatic melanoma mimicking a vascular malignancy. *Am J of Dermatopathol*. 1997;19:606-609. doi:[10.1097/0000372-199712000-00010](https://doi.org/10.1097/0000372-199712000-00010). PMID:9415619
4. Baron J, Monzon F, Galaria N, et al. Angiomatoid melanoma: A novel pattern of differentiation in invasive periocular desmoplastic malignant melanoma. *Human Pathology*. 2000;31:1520-1522. PMID:11150378
5. Zelger BG, Zelger B. Angiomatoid metastatic melanoma. *Dermatologic Surgery*. 2004;30:336-340. doi:[10.1097/00042728-200402002-00018](https://doi.org/10.1097/00042728-200402002-00018). PMID:14871230
6. Ramos-Rodríguez G, Ortiz-Hidalgo C. Primary angiomatoid melanoma as an exceptional morphologic pattern in cutaneous melanoma. A case report and review of the literature. *Actas Dermosifiliogr*. 2015;106:e13-e17. PMID:25498159
7. Fonda-Pascual P, Moreno-Arrones OM, Alegre-Sanchez A. Primary cutaneous angiomatoid melanoma. *JDDG: Journal Der Deutschen Dermatologischen Gesellschaft*. 2018;16:345-347. doi:[10.1111/ddg.13437](https://doi.org/10.1111/ddg.13437). PMID:29389063
8. Paolino G, Muscardin LM, Buccini P, et al. Angiomatoid melanoma: A dermoscopic and pathologic challenge. *G Ital Di Dermatol Venereol*. 2019;154:718-719. PMID:29417796
9. Ambrogio F, Colagrande A, Cascardi E, et al. Partially dedifferentiated primitive malignant melanoma with pseudo-angiomatous features: A case report with review of the literature. *Diagnostics*. 2023;13:495. PMID:36766604
10. Maniotis AJ, Folberg R, Hess A. Vascular channel formation by human melanoma cells in vivo and in vitro: Vasculogenic mimicry. *Am J of Pathol*. 1999;155:739-752. PMID:10487832
11. Nishimoto A, Ito K, Usami S, et al. 168 cases of Aneurysmal Dermatofibroma and 29 cases of hemosiderotic dermatofibroma: A clinicopathologic study. *Am J of Clin Pathol*. 2024;161:232-244. PMID:37897209
12. McKenney JK, Weiss SW, Folpe AL. CD31 expression in intratumoral macrophages. *Am J of Surg Pathol*. 2001;25:1167-1173. PMID:11688576