SM Journal of Sarcoma Research

Case Report

Epithelioid Angiosarcoma in the Inguinal Canal Region of an 81-year-old man. Case Report of a Rare Tumor with Challenging Diagnosis and Review of the Literature

Christian Green*, Malina Mohtadi, Joseph Russo, Brandon Watkins, Siovan Hope-Ross, Zachary Elder, Jacqueline Nicholas, Mohamed Aziz

Department of Pathology- American University of the Caribbean, School of Medicine, USA

Abstract

Angiosarcomas, which are endothelial in origin, make up less than 1% of all soft tissue sarcomas. For every million people in the United States, one will be diagnosed with an angiosarcoma. Most angiosarcomas are found in the breast, deep soft tissue of the head and neck, and skin, though they may rarely arise within other soft tissue sites. Epithelioid angiosarcomas represent a diagnostically challenging subset of angiosarcomas due to their non-specific imaging features, non-specific clinical presentation and rarity of the neoplasm. Epithelioid angiosarcomas should always be included in the differential diagnosis in patients with vascular neoplasms. Early detection combined with complete resection of the mass, as well as adjuvant therapy if possible, yields the highest favorable prognosis for patients with EAs.

Keywords: Epithelioid, angiosarcoma, carcinoma, Immunohistochemistry, vascular

ABBREVIATION

EA: Epithelioid angiosarcoma, AS: Angiosarcoma, IHC: Immunohistochemistry, EM: electron microscopy

INTRODUCTION

Angiosarcomas (ASs) are endothelial in origin and make up less than 1% of all soft tissue sarcomas [1,2]. Endothelial malignancies are derived from mesenchymal origin, which can undergo blood vessel or lymphatic differentiation, though they may follow both endothelial cell lines [26].

Classically, angiosarcomas develop in the breast, head, neck or skin of patients who are 60-70 years of age [1,12,15]. The range of primary sites is credited to the universality of lymphatics and blood vessels throughout the body. Deep soft tissues have an extensive lymphovascular supply and thus are at the highest risk for developing ASs. Angiosarcomas vary and involve varied patterns of growth, including spindled, papillary and epithelioid morphology [4]. Epithelioid angiosarcomas (EAs) typically form spongy, hemorrhagic masses due to their vascular characteristics [8]. Angiosarcomas can develop at any age, however the median age is reported to be between 60 and 71 years old [15,12]. The head and neck account for the majority in location [16,12]. Risk factors for epithelioid angiosarcoma include toxic chemical exposure, Thorotrast exposure, use of Dacron vascular grafts, chronic lymphedema, and previous irradiation, though the etiology has not been completely confirmed [4]. Certain familial syndromes are associated with AS such as neurofibromatosis type-1, Maffucci syndrome, bilateral retinoblastoma, von Recklinghausen syndrome, hemochromatosis, and Klippel-Trenaunay syndrome and appear with other lesions like port-wine stains, and hemangiomas [11,17,10,18].

EAs represent a problematic subset of endothelial neoplasms due to non-specific radiological signs of malignancy, as well as an ambiguous clinical presentation, rarity of the neoplasm, and histomorphologic resemblance when compared to more prevalent benign and malignant neoplasms. Immunohistochemistry (IHC) is paramount in diagnosing EA. In conjunction with IHC, electron microscopy (EM) can provide further identifying information for EAs [23]. Patients usually experience pain and the presence of a mass, followed by fever, weakness, and weight loss [7]. In some studies, up to one-third of patients with EA experience a hypocoagulable state, including ecchymosis, gastrointestinal and peritoneal bleeding, and persistent hematomas [10].

Preventative measures for EA include avoiding Thorotrast exposure or use of Dacron vascular grafts, though most patients develop EA without an association with these risk factors [4]. Complete resection is considered the current standard of care in patients with EA, though the complexity of the small area of the head and neck make negative margins difficult to achieve. Paclitaxel and Bevacizumab used in conjunction with surgical intervention has been shown to improve prognosis [24,25]. We present a case of epithelioid angiosarcoma in the inguinal canal region in an 81-year-old man and we review the literature.

Submitted: 20 August, 2021 | **Accepted:** 12 September, 2021 | **Published:** 15 September, 2021

***Corresponding author(s):** Christian Green, Department of Pathology, American University of the Caribbean School of Medicine, 1 University Drive at Jordan Road Cupecoy, St. Maarten, Tel: +16013071393

Citation: Green C, Mohtadi M, Russo J, Watkins B, Hope-Ross S, et al. (2021) Epithelioid Angiosarcoma in the Inguinal Canal Region of an 81-year-old man. Case Report of a Rare Tumor with Challenging Diagnosis and Review of the Literature. SM J Sarcoma Res 5: 4.

CASE PRESENTATION

An 81-year-old man presented with a large painful soft tissue mass at the left inguinal region. He also reported a weight loss of 15 Ib during the year before current presentation. Physical examination noted two adjacent large soft tissue masses in the left groin region. CT scan studies revealed two soft tissue masses with irregular enhancement and decreased heterogeneous density infiltrating the surrounding soft tissue structures. MRI scan demonstrated a heterogeneous enhancement of the two masses, with ill-defined demarcation with infiltrated surrounding structures and non-enhanced necrosis inside the lesions. Patient reported history of controlled type-II diabetes, controlled hypertension and controlled hypercholesterolemia. The tumor masses measured 5.5x 3.5x 3 cm and 4X 3x 2.5 cm. He also reported localized prostatic adenocarcinoma treated by prostatectomy 10 years prior to current presentation.

A fine needle aspiration and core biopsy were obtained from the larger inguinal mass. Microscopic examination demonstrated a tumor composed of solid sheets of high-grade pleomorphic epithelioid neoplastic cells with abundant amphophilic to lightly eosinophilic cytoplasm, large vesicular nuclei, and prominent nucleoli. The tumor was set in fibrotic stroma with scattered complex anastomosing vascular channels and abundant abnormal mitosis exceeding 15 mitosis/10 HPF. Prominent tumor necrosis was also noted (Figure 1 A-B-C). The histomorphologic features were non-specific and could be seen in various carcinomas, epithelioid variants of mesenchymal tumors, anaplastic tumors as well as other malignant tumors. Although the tumor displayed prominent epithelioid features, immunohistochemistry studies were essential to determine the line of cell differentiation. The tumor cells were negative for numerous lineage specific markers including Cam5.2, EMA, P63, CK 5/6, 34 BE12, CK19, HMB45, S100, CD21, CD35, LCA (CD45), SMA, PAX-2, B-Catenin, CD34, WT-1, CD68, and CD99. Additional negative IHC studies included Desmin, H-Caldesmon, Myogenin, PLAP, AFB, CD138, PSA, Synaptophysin and Chromogranin. This negative IHC studies were sufficient to rule out epithelial, myoepithelial, lymphoid, dendritic, histiocytic, mesothelial or melanocytic origin. The tumor cells were, however, strongly and diffusely positive for Vimentin, which in absence of other specific markers supported mesenchymal origin of the tumor. As muscle and neural mesenchymal origin were also ruled out, vascular IHC markers were tested. The tumor cells were strongly positive for CD31, Fli-1, and Cytokeratin AE1/AE3 (Focal scattered positive cells), in addition to Vimentin (Figure 1 D-E-F).

The histomorphologic features and the IHC profile were consistent with the diagnosis of epithelioid angiosarcoma in the Inguinal canal region. Patient underwent staging investigations, and none were shown to have distant metastasis. The case was discussed in a multidisciplinary tumor board and it was recommended to undergo total surgical excision followed by adjuvant radiotherapy. Patient refused surgery or radiation therapy and chemotherapy was initiated with six courses of combination chemotherapy with paclitaxel, epirubicin and carboplatin. Patient tolerated the treatment well and showed no evidence of recurrence or metastasis for 8 months after which he was lost to follow up.

DISCUSSION

Angiosarcomas, which are endothelial in origin, make up less than 1% of all soft tissue sarcomas.1,2 Angiosarcomas have a propensity for breast, deep soft tissue of the head and neck, and skin, accounting for 5.4% of all skin sarcomas.1,3 Rarely, angiosarcomas may arise within other soft tissue malignancies.6

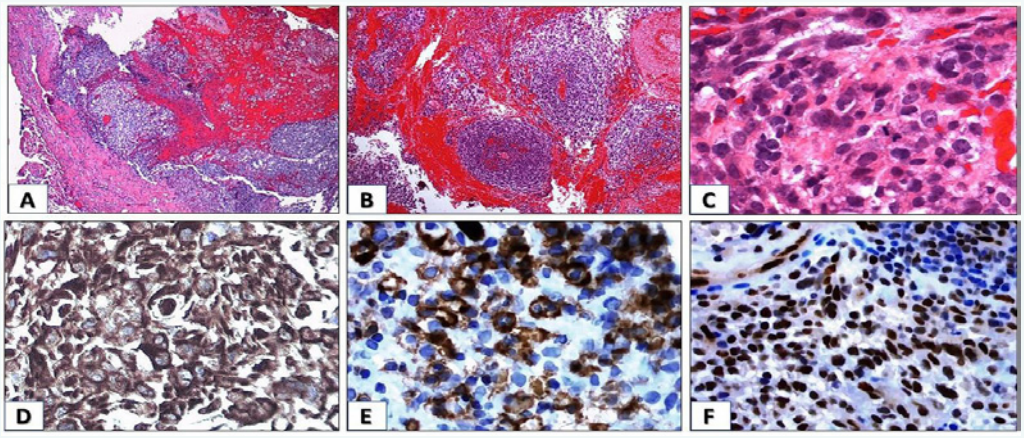

Figure 1 Histomorphology and immunohistochemistry profile of the excised angiomatoid angiosarcoma
1A: The tumor is set in fibrotic stroma with scattered complex anastomosing vascular channels (H&E stain X20 magnification)
1B: Low power view of the tumor showing masses of cellular epithelioid tumor cells (H&E stain X40 magnification)
1C: High power view of the tumor showing high-grade pleomorphic epithelioid neoplastic cells with abundant amphophilic to lightly eosinophilic cytoplasm, large vesicular nuclei, prominent nucleoli and multiple abnormal mitosis (H&E stain X60)
1D: Tumor cells positive for Vimentin
1E: Tumor cells positive for CD-31
1F: Tumor cells positive for Fli-1

EAs can resemble many types of neoplasms: metastatic melanoma, anaplastic large cell lymphoma, epithelioid sarcoma, epithelioid hemangioma, epithelioid hemangioendothelioma, metastatic carcinoma, proximal-type epithelioid sarcoma, epithelioid rhabdomyosarcoma and epithelioid-variant nerve sheath tumors. Low grade EA tumors often resemble a hemangioma, and high grade EA tumors may appear as various anaplastic neoplasms [14,10,12]. On contrast CT soft tissue EA can be seen as an irregular enhanced mass, occasionally with underlying bone or organ invasion [13,12]. EA tumors, such as those in the soft tissue of the extremities, abdomen, chest wall, and peritoneum or retroperitoneum are found to display differing characteristics [10,12]. EAs in the extremities are fast growing and palpable, compared to those in the peritoneum which are associated with increased pain due to mass effect [11,12]. Epithelioid hemangiomas are generally found in a younger patients, usually does not express factor VIII, and demonstrates normal nuclei well-formed vascularity, demonstrating its benign nature.21 Negative staining for S-100 and HMB-45 excludes melanoma from the differential diagnosis.4 Carcinoma will not stain positive for endothelial markers, including CD31, CD34, Fli-1 or factor VIII. Anaplastic large cell lymphomas express lymphocytic antigens, such as CD45 and CD30, which are absent in most EAs.21 Malignant nerve sheath tumors do not stain with vascular markers and will be S-100 positive.4 Analysis of EA cells by electron microscopy (EM) also proves to be helpful in the diagnosis of these tumors. Classic findings on EM include presence of pinocytotic vesicles, presence of red blood cells in vascular channels, presence of Weibel-Palade bodies, and desmosome attachments [23].

Immunohistochemistry (IHC) is immensely supportive in diagnosing EA.4 Vimentin is almost always positive in EA, as it is a marker for mesenchymal differentiation. The most sensitive markers for EA include CD31 and Fli-1, though less sensitive makers such as CD34 and Factor VIII-related antigen may also be useful in identifying endothelial cells [4,12]. Advances of surgical pathology techniques as well as further development of immunohistochemistry have enabled the recognition of malignant sarcomas with epithelioid cells since the original description in 1986 [5].

The current standard of care includes surgery, radiotherapy or chemotherapy, or a combination of the three. Paclitaxel-based chemotherapy has been shown to improve survival [24]. Neoadjuvant combination of radiation therapy and Bevacizumab is being studied as a potentially modality prior to surgical intervention [25]. Wide excision is recommended, when possible, though the head and neck area is a relatively complex small space to achieve negative margins. The possibility of adjuvant therapy is determined on an individual basis [9].

Prognosis of angiosarcoma is dependent on primary tumor site, size, mitotic activity, stage and cellularity. Poor prognostic factors include lesions larger than 5 centimeters in size and bleeding [22]. Generally, EAs have a poor prognosis due to the ability to grow quickly and metastasize to brain, bone, lung, lymph nodes and soft tissue [23]. The prognosis of angiosarcoma is found to have a 5-year survival rate ranging from 12%-35% [19,12]. The overall mean survival was seen to be 36 months with adjuvant radiotherapy versus a 9 months survival without adjuvant therapy [20,12]. This case report and literature review seek to shed light on the variability and diagnostic challenges in patients with epithelioid angiosarcoma. The non-specific radiological signs of malignancy, as well as an ambiguous clinical presentation, rarity of the neoplasm, and histomorphologic resemblance when compared to more prevalent benign and malignant neoplasms pose a threat to epithelioid angiosarcomas being mis-diagnosed. The definitive diagnosis of EA is made through biopsy and meticulous evaluation through histological and specific immunohistochemical analysis, and possibly EM studies. Epithelioid angiosarcomas should always be included in the differential diagnosis in patients with vascular neoplasms.

ACKNOWLEDGMENT

Special thanks to Grecia Corrada, Jacob Selph, and Lorenzo Russo, MD candidates, American University of the Caribbean for their assistance in reviewing the final version of this manuscript.

REFERENCES

1. McAdam JA, Stewart F, Reid R. Vaginal epithelioid angiosarcoma. J Clin Pathol. 1998;51(12):928-930. doi:10.1136/jcp.51.12.928
2. Weishaupt J, Miller J, Oehler MK. Vaginal epithelioid angiosarcoma: A literature review of a rare entity in an unusual site. Gynecol Oncol Rep. 2021;36:100706. Published 2021 Jan 21. doi:10.1016/j.gore.2021.100706
3. Avancini J, Sanches JA, Cherubim AP, et al. Angiosarcoma in HIV-negative patients is not associated with HHV-8. An Bras Dermatol. 2016;91(6):738-741. doi:10.1590/abd1806-4841.20164730
4. Wu J, Li X, Liu X. Epithelioid angiosarcoma: a clinicopathological study of 16 Chinese cases. Int J Clin Exp Pathol. 2015;8(4):3901-3909. Published 2015 Apr 1.
5. Weiss SW, Ishak KG, Dail DH, Sweet DE, Enzinger FM. Epithelioid hemangioendothelioma and related lesions. Semin Diagn Pathol. 1986 Nov;3(4):259-87. PMID: 3303234.
6. Li C, Chen Y, Zhang H, Zheng X, Wang J. Epithelioid angiosarcoma arising in schwannoma: report of three Chinese cases with review of the literature. Pathol Int. 2012;62(7):500-505. doi:10.1111/j.1440-1827.2012.02827.x
7. Wenger DE, Wold LE. Malignant vascular lesions of bone: radiologic and pathologic features. Skeletal Radiol. 2000;29(11):619-631. doi:10.1007/s002560000261
8. Branch, K Drake MD; Smith, M Timothy MD Epithelioid Angiosarcoma, Pathology Case Reviews: November 2008 - Volume 13 - Issue 6 - p 264-268 doi: 10.1097/PCR.0b013e31818bb9b9
9. Suchak R, Thway K, Zelger B, Fisher C, Calonje E. Primary cutaneous epithelioid angiosarcoma: a clinicopathologic study of 13 cases of a rare neoplasm occurring outside the setting of conventional angiosarcomas and with predilection for the limbs [published correction appears in Am J Surg Pathol. 2011 Apr;35(4):619]. Am J Surg Pathol. 2011;35(1):60-69. doi:10.1097/PAS.0b013e3181fee87
10. Meis-Kindblom JM, Kindblom LG. Angiosarcoma of soft tissue: a study of 80 cases. Am J Surg Pathol. 1998;22(6):683-697. doi:10.1097/00000478-199806000-00005

11. Young RJ, Brown NJ, Reed MW, Hughes D, Woll PJ. Angiosarcoma. Lancet Oncol. 2010;11(10):983-991. doi:10.1016/S1470-2045(10)70023-1

12. Gaballah AH, Jensen CT, Palmquist S, et al. Angiosarcoma: clinical and imaging features from head to toe. Br J Radiol. 2017;90(1075):20170039. doi:10.1259/bjr.20170039

13. Razek AA, Huang BY. Soft tissue tumors of the head and neck: imaging-based review of the WHO classification. Radiographics. 2011;31(7):1923-1954. doi:10.1148/rg.317115095

14. Walker EA, Salesky JS, Fenton ME, Murphey MD. Magnetic resonance imaging of malignant soft tissue neoplasms in the adult. Radiol Clin North Am. 2011;49(6):1219-vi. doi:10.1016/j.rcl.2011.07.006

15. Chang JH, Kim JH, Hong SH, et al. Angiosarcoma presenting with spontaneous hydropneumothorax: report of a case and review of the literature. Open Respir Med J. 2014;8:48-54. Published 2014 Dec 26. doi:10.2174/1874306401408010048.

16. Almogy G, Lieberman S, Gips M, et al. Clinical outcomes of surgical resections for primary liver sarcoma in adults: results from a single centre. Eur J Surg Oncol. 2004;30(4):421-427. doi:10.1016/j.ejso.2004.01.004

17. Murinello A, Mendonça P, Abreu A, et al. Cardiac angiosarcoma--a review. Rev Port Cardiol. 2007;26(5):577-584.

18. Allison KH, Yoder BJ, Bronner MP, Goldblum JR, Rubin BP. Angiosarcoma involving the gastrointestinal tract: a series of primary and metastatic cases. Am J Surg Pathol. 2004;28(3):298-307. doi:10.1097/00000478-200403000-00002

19. Scott MT, Portnow LH, Morris CG, et al. Radiation therapy for angiosarcoma: the 35-year University of Florida experience. Am J Clin Oncol. 2013;36(2):174-180. doi:10.1097/COC.0b013e3182436ea3

20. Penel N, Marréaud S, Robin YM, Hohenberger P. Angiosarcoma: state of the art and perspectives. Crit Rev Oncol Hematol. 2011;80(2):257-263. doi:10.1016/j.critrevonc.2010.10.007

21. Okada E M.D, Matsumoto M M.D, Nishida M, et al. Epithelioid Hemangioma of the Thoracic Spine: A Case Report and Review of the Literature. J Spinal Cord Med. 2019;42(6):800-805. doi:10.1080/10790268.2017.1390032

22. Sundaram M, Vetrichevvel TP, Subramanyam S, Subramaniam A. Primary multicentric cutaneous epithelioid angiosarcoma. Indian J Dermatol Venereol Leprol. 2011;77(1):111. doi:10.4103/0378-6323.74990

23. Hart J, Mandavilli S. Epithelioid angiosarcoma: a brief diagnostic review and differential diagnosis. Arch Pathol Lab Med. 2011;135(2):268-272. doi:10.5858/135.2.268

24. Fata F, O'Reilly E, Ilson D, et al. Paclitaxel in the treatment of patients with angiosarcoma of the scalp or face. Cancer. 1999;86(10):2034-2037.

25. Koontz BF, Miles EF, Rubio MA, et al. Preoperative radiotherapy and bevacizumab for angiosarcoma of the head and neck: two case studies. Head Neck. 2008;30(2):262-266. doi:10.1002/hed.20674

26. Breiteneder-Geleff S, Soleiman A, Kowalski H, et al. Angiosarcomas express mixed endothelial phenotypes of blood and lymphatic capillaries: podoplanin as a specific marker for lymphatic endothelium. Am J Pathol. 1999;154(2):385-394. doi:10.1016/S0002-9440(10)65285-6

27. Gao Y, Warshaw H, Singtong B, Polan-Couillard L, Aziz M, et al. (2021). Proximal-Type Epithelioid Sarcoma. A case Report of a Rare Tumor with Challenging Diagnosis and Review of the Literature. SM J Sarcoma Res 5: 4.