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Anastomosing hemangioma: A case report of a benign tumor often misdiagnosed as a malignant epithelioid angiosarcoma

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A B S T R A C T

Anastomosing hemangioma (AH), a rare benign genitourinary tract hemangioma is subject to frequent misdiagnosis due to its rarity and clinical, histological, and immunohistochemical similarities it shares with several diagnoses, including well-differentiated angiosarcoma (AS). This is particularly true of angiosarcoma, nearly identical to AH when presented in tissue samples of limited size. Lack of specific clinical and radiologic manifestations on initial preoperative assessment, coupled with limited diagnostic experience or awareness, can lead to misinterpretation of this entity, potentially leading to unnecessary clinical management. We present an initial misdiagnosis of AS which, upon review of the entire lesion, was identified as AH.

1. Introduction

Anastomosing hemangioma (AH), a rare benign vascular lesion, has remarkably similar histology paralleling angiosarcoma (AS), a malignant vascular neoplasm warranting comparatively intensive clinical management. Over 120 AH cases were reported so far, with approximately 60 reports demonstrating renal localization, while remainder cases exhibited non-renal localization throughout urogenital and gastrointestinal systems, liver, and soft tissue.[1] Despite AH increased prevalence, clinical awareness has straggled behind due to innate rarity, atypia, and lack of specific clinical or radiological manifestations, often presenting as diagnostic confounders.[1] The main challenge therein lies within its identification.

Special attention is paramount for recognizing landmark AH characteristics prior to embarking on differential diagnosis paths such as AS. We report an AH case necessitating diagnostic re-evaluation, for a patient who presented with initially misdiagnosed and mismanaged AS.

2. Case presentation

A 66-year-old male patient with history of irritable bowel syndrome presented with intermittent abdominal pain and was referred to gastroenterology for symptom review. Unremitting symptoms and severe exacerbation of epigastric pain prompted transfer to the emergency department. CT-scan revealed a retroperitoneal soft-tissue density, along with a left ureter mass measuring 2.4 × 2.3 cm. Biopsy findings suggested a diagnosis of AS, prompting stent placement via cystoscopy retrograde pyelogram and robotic-assisted periureteral mass excision.

Pathology analyses reported an incompletely excised epithelioid AS present at the inked margin with typical findings for malignant neoplasm containing epithelioid-appearing cells and irregular vascular channels.

Immunohistochemistry analyses revealed positivity for CD31, CD34 (Fig. 1), and ERG and KI-67 (Fig. 2A and B respectively), though proved negative for cytokeratin AE1/AE3 and HHV8. Ki-67 demonstrated a proliferation index limited to 50%.

PET-scan followed excision, showed a new perinephric stranding. Staging imaging did not reveal additional disease-sites. Multiple additional nodular lesions and stranding were found on repeat abdominal CT.

The patient was referred for further management recommendations two months post-surgery. Further internal pathology analyses confirmed

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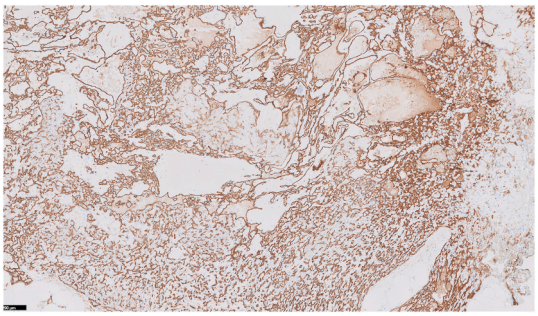

Fig. 1. Immunohistochemical staining. Tumor cells demonstrate immunoreactivity with antibodies for CD34 (Original magnification ×100).

a diagnosis of AH. (Fig. 3). Due to unremitting mass-effect symptoms, complete lesion-excision seemed mandatory.

Subsequent exploratory laparotomy revealed abnormal-appearing tissue, 2 cm of which involved a firm mass bordering the left iliac vessels and ureter. Mass was excised along the left ureter and iliac vessels, together with ureterolysis. The patient had no post-operative complications on 2-years follow-up.

3. Discussion

AH is rare, though can manifest across patients spanning 2-85 years-old.[2] Renal AH disproportionately presents in males, with 49 years overall-incidence median-age across genders.[2] Most AH cases are asymptomatic, though hematuria and back pain were recorded in renal AH, typically linked to end-stage renal disease, while mass-effect-driven local pain was reported in extrarenal AH.[2]

AH is typically non-discernible from differentiated AS when analyzed through CT-/MRI-imaging, leading to misdiagnosis for such a benign condition that is cured through simple excision.[2,3] Clinically, AS can be associated with pain across lesion area. However, AS lesions grow gradually, conversely to AH.

Although localized primarily to the kidney, AH lesions have been identified across almost all parenchymal organs.[2] Contrastingly, ASs are localized throughout the body. Both AS and AH have positive immunohistochemical staining for CD31, CD34, and ERG, though AH demonstrates additional diagnosis-driving positivity for FVIII, apart from being negative for CD8, D2-40, and HHV8, indicating a respective lack of splenic sinusoidal involvement, lymphatic origin, and Kaposi sarcoma.

AH-histopathology includes non-lobular architecture, single-endothelial-cell layer, hobnailed endothelial cell morphology, nonexistent/minimal presence of nuclear atypia or mitosis, nonexistent/minimal border infiltration, intravascular fibrin thrombi, extravasated erythrocytes (common), and extra-medullary hematopoiesis (50%-prevalence). Conversely, AS demonstrates significant cytologic atypia, multiple endothelial cell layers, highly infiltrative architecture, and broad infiltration.

Extra-medullary hematopoiesis in AH is more frequently seen within end-stage renal disease.[2] Although high Ki-67 proliferative index predicts malignant soft tissue sarcoma,[4] an increased Ki-67 proliferation index within the context of AH, as seen in our report, can instead be revelatory for a focus of extramedullary hematopoiesis, sometimes seen in this condition.

ASs confirm closest resemblance to AH, particularly regarding histology for well-differentiated AS containing anastomosing sinusoidal-like vascular patterns/hobnail endothelial cells with little nuclear atypia and rare mitosis.[2] Additionally, histologic characteristics often observed in AH can themselves draw concern for malignancy, despite benign-lesion categorization.[2,3,5] However, endothelial cells in AH typically have a pericytic layer, a characteristic finding that is not present in angiosarcoma. Multilayering of endothelial cells, a characteristic finding in AS, is not found in AH.[2]

In examining the entirety of the lesion, regardless of location, observation of a homogenous pattern throughout the area is a quintessential AH-finding. Contrastingly, deep-seated AS is heterogeneously composed of well and poorly differentiated areas. Molecular analysis for GNAQ mutations, present (though not pathognomonic) in AH, can serve additional utility in distinguishing these entities, as GNAQ mutations have not been identified in angiosarcoma.[2]

Although, both lesions present as a growing mass, with obstructive symptoms or UTI at presentation, the outcome is different since AH is a

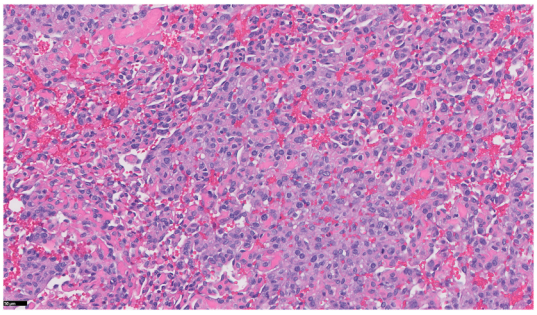

Fig. 3. Hematoxylin and Eosin staining. Tumor cells demonstrate proliferation of capillary sized vessels within a framework of nonendothelial supporting cells.

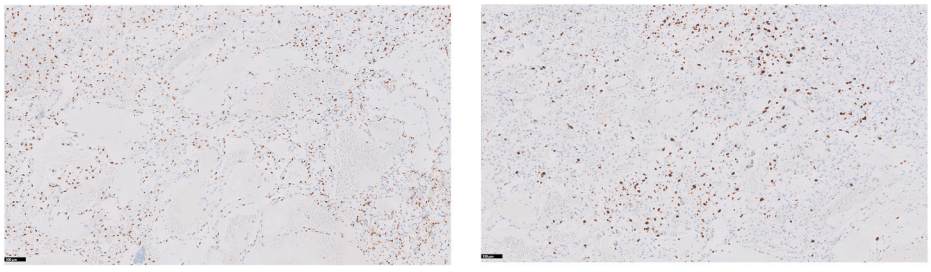

Fig. 2. (A, B). Immunohistochemical staining. Tumor cells demonstrate immunoreactivity with antibodies for ERG and KI67. (Original magnification ×100).

benign tumor, completely resolved after complete resection. The prognosis of epithelioid angiosarcoma is poor with high probability of early metastasis. Surgical resection is the main treatment strategy, in addition to chemotherapy and radiotherapy.

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