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Primary adrenal angiosarcoma: A case report and review of the literature

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ABSTRACT

Primary adrenal angiosarcoma is an extremely rare malignant tumor with challenging diagnosis. A 66-year-old woman had a 4.3 cm right adrenal mass suspicious for adrenal cortical carcinoma. Pathological examination demonstrated a hemorrhagic adrenal cyst with numerous irregularly shaped anastomosing vascular channels lined by atypical endothelial cells that had frequent atypical mitotic figures (12/10 HPF, Ki67 10%). The tumor cells were positive for CD31, ERG, and FLI-1, but negative for adrenal and other tumor lineage markers by immunohistochemistry. NGS fusion gene testing ruled out epithelioid hemangioendothelioma. Accurate diagnosis and differential inclusion are important for appropriate treatment of this rare tumor.

1. Introduction

Angiosarcoma is an aggressive and rare endothelial cell tumor, accounting for 2–4% of all sarcomas, and it is exceedingly rare in the adrenal gland. This presentation varies from incidentally found lesions to symptomatic metastatic disease. Diagnosis of angiosarcoma is challenging due to its rarity, and it is typically not included in the initial differential diagnosis of an adrenal mass. Biopsy diagnosis can be more difficult due to tumor necrosis, hemorrhage, and cystic degeneration. A panel of immunohistochemical stains may be helpful in establishing the diagnosis.[1] Herein, we report a case of primary adrenal angiosarcoma of a 66-year-old woman.

2. Case presentation

A 66-year-old woman presented with abdominal discomfort and was found a 2.6 × 2.0 × 2.1 cm right adrenal mass on computed tomography (CT). A year later, follow-up imaging with magnetic resonance imaging (MRI) with and without contrast showed significant enlargement of the non-hormonally active mass to 4.3× 3.1 × 3.4 cm (Fig. 1). The patient denied any prior oncologic or endocrinological disorders (Table 1). Colonoscopy and CT of the chest, abdomen, and pelvis, with and without contrast showed no evidence of metastatic disease, supporting a primary adrenal lesion. Due to the rapid growth kinetics, heterogenous and enhancing features on imaging, the leading differential diagnosis was adrenal cortical carcinoma. The patient underwent a right-sided robotic-assisted laparoscopic adrenalectomy.

Grossly, the adrenalectomy specimen weighed 58 g and consisted of a 9 × 5 × 3 cm adrenal gland with a 4 × 3 × 2.5 cm tan-brown hemorrhagic-cystic mass arising from the cortex. The residual medulla was unremarkable with a gray narrow band (Fig. 2). Microscopic examination of the tumor revealed numerous irregularly shaped anastomosing vascular channels lined by atypical endothelial cells with intraluminal erythrocytes and hemorrhage. The high grade atypical endothelial cells are enlarged, hyperchromatic and pleomorphic, with frequent atypical mitotic figures (12/10 high power fields), but no tumor necrosis was present (Fig. 3A–D). Immunohistochemical staining of the tumor cells showed positive expression for multiple endothelial markers CD31, ERG, and FLI-1 (Fig. 3E–G), but negative for various markers including cytokeratin AE1/AE3, SMA, Desmin, HHV8, STAT6, S100,

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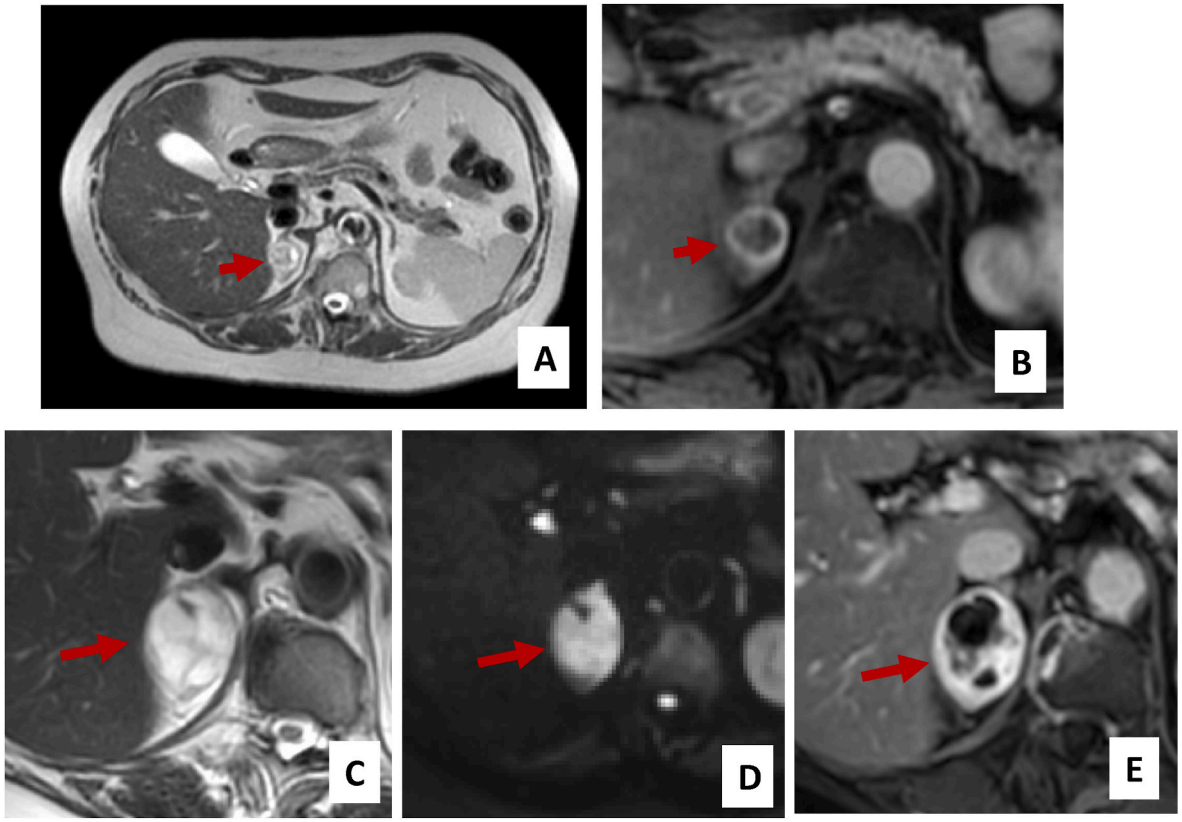

Fig. 1. MRI Axial T2 (A) imaging shows a 1.9 cm right adrenal ovoid mass with heterogenous T2 signal. Post-contrast axial region of interest images shows rim enhancement (B). Follow-up MRI Axial T2 (C) imaging obtained 9 months later show significant increase in size of the right adrenal mass compared to prior study, now measuring 4.3 cm consisting of predominantly T2 hyperintense signal with hypointense septations. Diffusion weighted imaging (D) shows diffusion restriction. Dynamic post-contrast T1 image obtained at 6 minutes (C) shows progressive enhancement of the mass with non-enhancing internal component. In and out of phase images (not pictured) showed no significant signal drop-out comparing out of phase to in phase, confirming a lack of intralesional fat.

Table 1
Endocrinology work-up and preoperative laboratory results.

Laboratory component	Results and units
Serum sodium	144 mmol/L
Serum potassium	4.1 mmol/L
Serum creatinine	0.8 mg/dL
Serum bicarbonate	25 mmol/L
24-h urinary metanephrines	54 mcg/24 hour (L)
24-h urinary normetanephrines	236 mcg/24 hour
Thyroid-stimulating hormone	1.76 μIU/mL
Serum aldosterone	6 ng/dL
Plasma renin activity (PRA)	0.71 ng/mL/hour
Aldosterone/PRA ratio	8.5
24-h urinary free cortisol	3.9 mcg/24 hour (L)
Urinary free cortisol	11.2 mcg/g creatinine
Dehydroepiandrosterone (DHEA) Sulfate	19 mcg/dL (L)
Serum testosterone, total	9 ng/dL
Serum testosterone, free	1.1 pg/mL
Serum estradiol	<5 pg/mL
Sex hormone binding globulin	35 nmol/L

Synaptophysin, Chromogranin, Calretinin, and HMB45. The Ki-67 proliferative index was 10% (Fig. 3H). Next gene sequencing (NGS) for sarcoma and solid tumor fusion genes, especially those seen in epithelioid hemangioendothelioma, was negative.

Following the surgery, the patient has an uneventful recovery and was discharged on post-operative day 1 with a prescription of 5 mg of prednisone per day. Due to the limited available data on the efficacy of adjuvant chemotherapy, no such treatment was initiated. The patient is currently under close monitoring by medical oncology and reported to be doing well.

3. Discussion

Angiosarcoma is a rare malignant vascular tumor typically with a highly aggressive clinical course and high mortality rate. Local recurrences rate and distant metastases are frequent.[2]

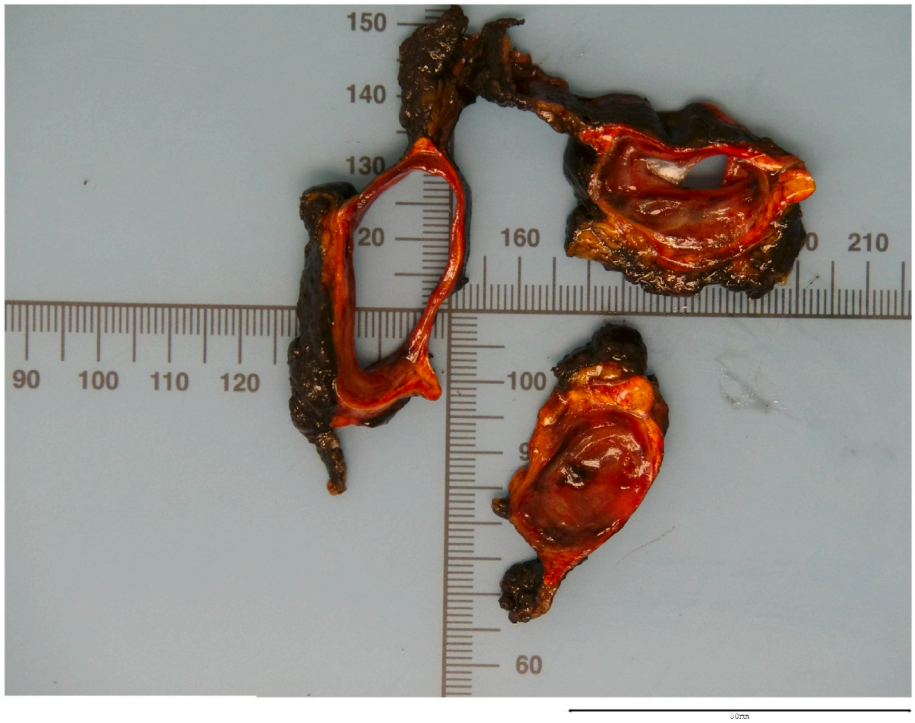

Fig. 2. Gross examination of the adrenal gland shows a 4 cm tan-brown and hemorrhagic and cystic lesion. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

It primarily affects males, with peak incidence in the seventh decade of life, and its etiology is largely unknown. Cutaneous angiosarcoma is the most common form (>50% of cases), which can arise post-radiation or longstanding lymphoedema. Deep soft tissue and visceral organ angiosarcomas may be spontaneous or secondary to chemical exposure. Poor prognostic indicators include patient age over 60, retroperitoneal location, large tumor size, and high Ki-67 proliferation rate.[2–4]

While primary adrenal angiosarcoma is extremely rare, it is important to exclude other original sites in the diagnosis of adrenal primary, as most adrenal sarcomas represent metastases from another primary tumor site. Most primary adrenal angiosarcomas are of the epithelioid type. Given its rarity and morphologic overlap, it can be misdiagnosed as adrenal cortical carcinoma, epitheloid sarcoma-like hemangioendothelioma (EHE), or melanoma.

Histopathologically, angiosarcomas have a wide morphological spectrum ranging from well-formed, anastomosing vascular channels to solid sheets of high grade epithelioid or spindled cells lacking prominent vasoformation. Mixed morphologic features often occur within a single tumor. The tumor cells have minimal resemblance to normal vascular endothelium to variable nuclear atypia (marked pleomorphism is rare), increased mitotic activity and coagulative necrosis. Angiosarcoma may be associated with blood lakes, extensive hemorrhage, and organizing hematoma, making recognition difficult for diagnosis. Generous sampling is critical for the diagnosis. Immunostaining is typically positive for vascular markers CD31, ERG, Fli-1, CD34, D2-40 and factor VIII, but negative for SMA (pericytes) and HHV8. Due to differences in sensitivity and specificity, a panel of immunostains should be performed.

Angiosarcoma of the endocrine or visceral organs carries a poor prognosis, making diagnosis crucial for optimal clinical management. In our case, clinical, imaging and studies did not reveal other tumor outside adrenal gland. The sarcoma-like epithelioid hemangioendothelioma (EHE) was on the top differential diagnosis, which contains *WWTR1::CAMTA1* or *YAP1::TFE3* fusion gene. However, morphological features and NGS result did not support the diagnosis of EHE.

The correlation between histological grade and prognosis of angiosarcoma is not always linked.[5] Treatment guidelines incorporating mutation panel results for angiosarcoma are not well developed. However, given its aggressive nature, close surveillance with interval imaging is necessary. Follow-up plans for our patient include a close whole-body positron emission tomography (PET) scan and MRI abdomen with contrast for at least 10 years. To date, our patient is stable.

4. Conclusion

The patient's adrenal tumor highlights the importance of multimodal testing, including immunohistochemical phenotyping and molecular analysis, in the accurate diagnosis and classification of adrenal tumors.

A multidisciplinary evaluation of adrenal tumors is also crucial for determining the most appropriate therapeutic approach for each patient. Complete tumor resection and close follow-up are essential for achieving a favorable prognosis. Further case studies are needed to improve our understanding of the biological characteristics, pathogenetic mechanism, and clinical outcomes of this rare entity.

Author contributions

ZN, AM, JYL, ES, PAM made contributions to writing the manuscript. AH contributed to the specimen grossing. AG contributed to imaging study. JYL and MM performed the surgery. LL contributed to the design and revision of the manuscript. All authors read and approved the final manuscript.

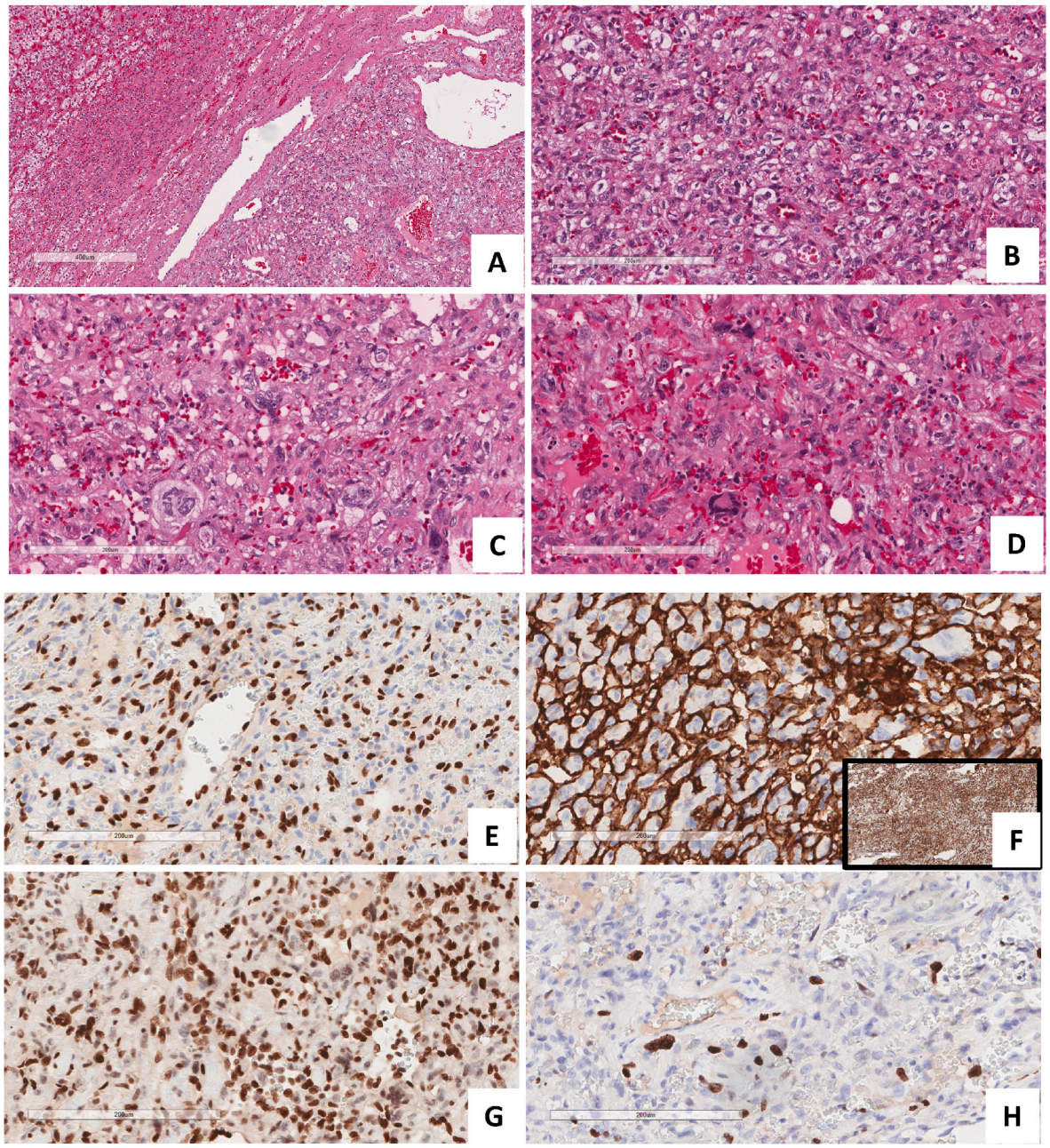

Fig. 3. Adjacent to adrenal cortex, there is hemorrhagic and cystic lesion (A, magnification, 54×) with irregularly shaped anastomosing vascular channels lined by mild to severe atypical endothelial cells showing multinucleated, hyperchromatic and pleomorphic features (B–D) with atypical mitosis (D). (B-D, magnification, 200×). Immunohistochemical stain shows that the tumor cells are positive for endothelial cell markers ERG (E), CD31 (F, lower magnification, inset.), and FLi-1 (G) (magnification, 44×). Ki-67 shows approximately 10% proliferative activity (magnification, 200×).

Declaration of competing interest

The authors declare that they have no competing interests.

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Availability of data and materials

The data of the present study are available from the corresponding author upon reasonable request.

Ethics approval and consent to participate

Written informed consent of the patient has been obtained.

Patient consent for publication

The patient has consented to the submission of the case report to the journal.

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