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Case report

Adrenal angiosarcoma with metastasis: Imaging and histopathology of a rare adrenal cancer

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ABSTRACT

Adrenal angiosarcoma is an extremely rare malignancy with few reported cases in the literature. Patients may be asymptomatic or have nonspecific complaints at presentation. There are no pathognomonic imaging findings, while histopathology can be confounding due to overlap with other disease processes. We present a case of a 38-year-old woman with a long history of cocaine abuse who had metastatic adrenal angiosarcoma at the time of presentation. The adrenal tumor was an incidental finding on imaging. CT demonstrated a heterogeneous mass in the right adrenal gland with central calcification, and MRI identified central necrosis in the mass. Histopathology demonstrated sheets of epithelioid cells, dilated anastomatic vascular spaces, and abundant necrosis, and immunohistochemistry was positive for various vascular markers. The findings were consistent with adrenal angiosarcoma. The patient underwent adrenalectomy and is now receiving adjuvant chemotherapy. Due to the aggressive nature of adrenal angiosarcoma, timely diagnosis and treatment is critical. This case adds to the sparse literature surrounding this disease by highlighting crucial imaging and histopathologic findings that will aid in more efficient diagnosis. Although rare, the disease should be considered in the context of suspicious adrenal lesions. In the future, structured review of all reported cases of adrenal angiosarcoma can help inform diagnosis and therapy for this rare disease.

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Introduction

Angiosarcoma of the adrenal gland is a rare malignancy that is sparsely reported in the literature. To date, approximately 40 cases have been documented, with a median age of 60. Due to its extremely rare nature, the most effective treatment for this

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Fig. 1 – Contrast enhanced CT of the chest demonstrates bilateral consolidations with surrounding ground glass halo appearance (arrows) consistent with pulmonary hemorrhage.

disease is not well understood [1]. We present a case of adrenal angiosarcoma with metastasis in a 38-year-old female who initially came to medical attention due to cocaine-induced diffuse alveolar hemorrhage and was found to have several bony metastases at presentation.

Case report

A 38-year-old female with a history of cocaine abuse initially presented to our institution with a 6-month history of hemoptysis, resulting in severe anemia. The hemoptysis was attributed to cocaine-induced pulmonary hemorrhage. She was stabilized and discharged. Over the next 2 months, she had 2 more admissions for similar presentations. Bronchoalveolar lavage demonstrated diffuse alveolar hemorrhage and no malignancy. A CT to assess for pulmonary emboli demonstrated a new left-sided lateral seventh rib fracture with several lytic lesions in the ribs. Two days later, a CT angiogram of the chest to evaluate for possible bronchial artery embolization

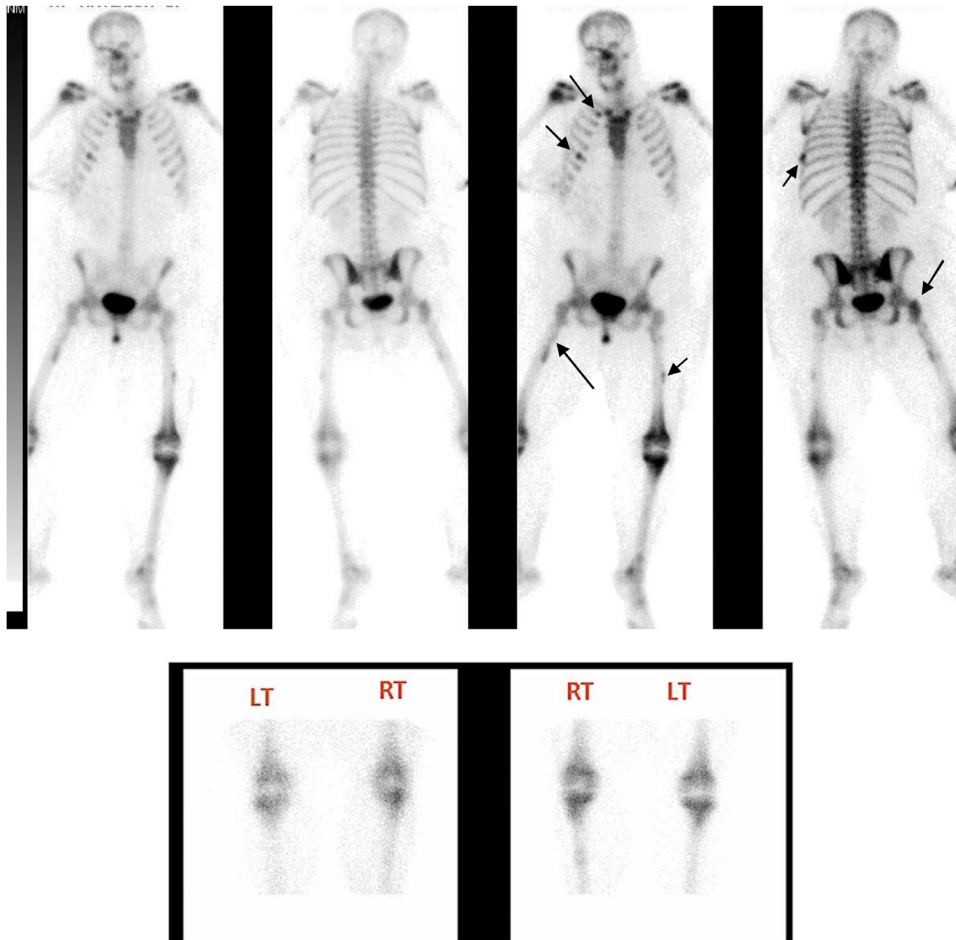


Fig. 2 – (a) Tc-99m MDP bone scan demonstrates multifocal MDP avid osseous lesions in the ribs (arrows), consistent with osseous metastatic disease. (b) Tc-99m MDP bone scan posterior and anterior views of the knees show symmetrical uptake in the knees. No focal lesions were appreciated during that admission.

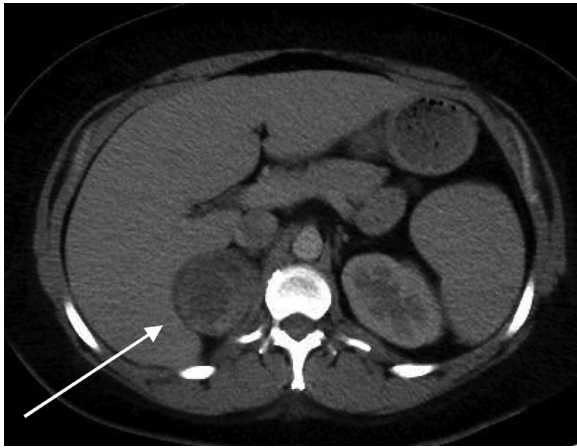


Fig. 3 – Axial contrast enhanced CT of the abdomen demonstrates a heterogeneous mass in the right adrenal (arrow).

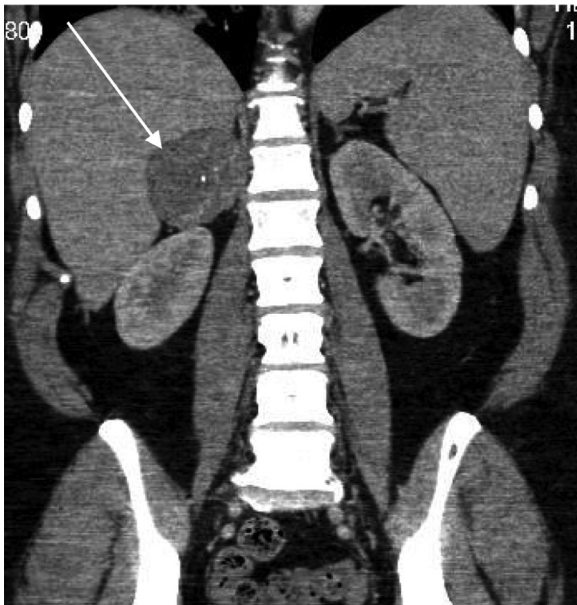


Fig. 4 – Coronal contrast enhanced CT demonstrates the heterogeneous mass in the right adrenal with central calcification (arrow).

demonstrated bilateral lobar and segmental pulmonary emboli, which were likely subacute. Bilateral basilar consolidative and ground glass opacities were also noted which were felt to represent areas of pulmonary hemorrhage (Fig. 1). The CT angiogram incidentally showed a heterogeneously enhancing mass in the right upper quadrant with large internal vessels, prompting a differential diagnosis including adrenal cortical carcinoma. A bone scan was obtained that showed multifocal uptake in the calvarium, ribs, and proximal femurs with high suspicion for malignancy (Fig. 2a and b). A CT examination of the abdomen and pelvis was completed for staging and failed to demonstrate metastases in the abdomen or pelvis (Figs. 3 and 4). MRI was obtained to further characterize the mass,

demonstrating a 5.6 cm mass in the right adrenal with central necrosis and possible hemorrhage (Fig. 5a, b, –c). Also noted was a fifth rib fracture that was concerning for metastatic disease and a pathologic fracture in the seventh rib. A rib biopsy during this admission was initially interpreted as negative for malignancy. The patient was medically stabilized and discharged with close outpatient follow-up and plan for adrenal biopsy.

Three weeks later, the patient returned for severe bilateral lower extremity pain. Imaging at that time showed pathologic fractures through the right fibula with multiple lytic lesions in the lower extremities, concerning for metastatic disease. Prior to discharge, the patient was found to have elevated urine and serum metanephrines, so further endocrine evaluation was pending prior to adrenal biopsy.

One week later, the patient was readmitted for right lower extremity pain and edema concerning for cellulitis. Further imaging of the right tibia and fibula at that time demonstrated a cortical lytic lesion in the right fibula with associated pathologic fracture in addition to several other cortical lytic lesions (Fig. 6a, and b). A right tibial biopsy was suggestive of a neoplasm showing biphasic differentiation such as sweat gland, salivary, and certain pulmonary neoplasms and chordoma. An adrenal neoplasm was lower on the list of differential diagnoses.

After multidisciplinary assessment, a decision was made to proceed with adrenalectomy. Gross examination demonstrated a 135 g, 8.5 × 6.4 × 5.5 cm enlarged right adrenal gland with smooth external surface. Sectioning through the tissue revealed a bright yellow and thickened adrenal cortex measuring 1.2 cm in thickness. At the center of the gland, an 8 × 3.6 × 3.5 cm tan-red, predominantly solid, and irregular lesion was identified associated with focal areas of necrosis, hemorrhage and invasion into the surrounding adrenal cortex (Fig. 7). Histology showed sheets or nests of epithelioid cells scattered between dilated anastomotic vascular spaces, lined by similar cells forming papillations or intraluminal buds (Fig. 8A). Occasionally, tumor cells had intracytoplasmic vacuoles containing red blood cells (Fig. 8B). Tumor cells were invading into the adrenal cortex (Fig. 8C), lymphatic channels and blood vessels. Abundant necrosis (more than 50% of the tumor), nuclear atypia, and brisk mitoses were also noticed. The findings were consistent with a high-grade angiosarcoma. Resection margins were free from tumor. The diagnosis was supported by positive immunohistochemical staining for vascular markers including CD31, CD34, and factor 8. CAM5.2 and vimentin were also positive. Tumor cells were negative for inhibin, calretinin, and neuroendocrine markers. Review of the patient's previous biopsies of the anterior rib and right tibia lytic bone lesions revealed similar histology to the adrenal lesion in a few cells, which was suggestive of metastatic disease. Postoperatively, the patient developed adrenal insufficiency managed with steroids. She subsequently left against medical advice but returned to the hospital shortly thereafter and was admitted for acute leg pain and rehabilitation placement. During the admission, the decision was made to proceed with chemotherapy with Paclitaxel to treat the metastatic adrenal angiosarcoma. The patient is currently undergoing an 8-cycle course of chemotherapy. Her response to treatment will be evaluated at a later time.



Fig. 5 – (a) Axial pre- and postcontrast fat saturated T1 weighted MR image demonstrates a central nonenhancing portion of the right adrenal mass suggesting necrosis (arrow). (b) Axial diffusion weighted imaging demonstrates mild restricted diffusion with a few foci of moderate restricted diffusion. (c) Axial T2 weighted fat saturated images show a heterogeneous T2 hyperintense mass with internal hypointense regions suggesting hemorrhage.

Discussion

Adrenal angiosarcoma is a rare malignancy with approximately 40 cases documented in the literature since 1988. The median age at presentation is 60 years, with the youngest at 34 [1]. Our patient thus represents one of the youngest individuals affected by this malignancy. Males appear to be affected more often than females [1,2]. Presentations are diverse and can include an asymptomatic adrenal mass or nonspecific complaints such as abdominal pain, weight loss, and fevers [1–3].

The exact cause of the malignancy is unknown. Exposure to arsenic-containing pesticides has been documented in some case reports [2]. Extra-adrenal angiosarcomas have

been associated with factors like chronic lymphedema, anabolic steroids, thorotrast, familial angiodysplasia, vinyl chloride, arsenic, and copper [4].

Adrenal angiosarcoma poses a diagnostic challenge in part due to its rarity. It can be difficult to find the primary focus of malignancy because of concomitant necrosis and hemorrhage. Pathologically, tissue is often characterized by epithelioid structure as opposed to the vasoformative structure that is typically identified in angiosarcomas. Tissue is often positive for cytokeratins, which can prompt a misdiagnosis of metastatic epithelial cancer [5]. Cells are large and round with prominent nucleoli, while nuclei may appear vesicular [3,6,7]. The tumor may be predominantly cystic [7]. This can be problematic due to similar appearance with other tumors such as pheochromocytomas. The cystic component may represent a



Fig. 6 – (a) Coronal CT of the fibula demonstrates a lytic lesion in the proximal fibular metadiaphysis and pathologic fracture. (b) Sagittal CT of the tibia demonstrates a cortical based lytic lesion.

bulk of the tumor yet produce no viable tumor cells, while the solid component will demonstrate the neoplastic process [5]. Accurate diagnosis relies on strong immunohistochemistry utilizing an extensive set of stains, including CD31, CD34,

FLI1, and factor VIII, while entertaining the strong possibility of positive keratin staining [5,6,8].

Accurate diagnosis on imaging is challenging, as there are no pathognomonic findings [2,5]. However, imaging can often serve as the first indication that the mass exists, as it did in our case. It can demonstrate local and distant spread of the malignancy, which helps with surgical and medical treatment planning [9]. Typically, imaging reveals a heterogeneous mass with solid and cystic components [5]. Unenhanced CT images demonstrate heterogeneous low attenuation. Hyperattenuation suggests hemorrhage or calcification, while hypointensity suggests necrosis. Unenhanced MRI may reveal heterogeneous intensity, with T1 hyperintensity and T2 hypointensity correlating with various foci of hemorrhage. Post-contrast images may reveal dilated vessels with heterogeneous enhancement and areas of necrosis [9]. In our case, CT demonstrated tumor heterogeneity with large internal vessels and postcontrast MRI showed a nonenhancing portion of likely necrosis, findings consistent with previously reported cases.

Generally, adrenal masses greater than 4 cm appear to be associated with higher risk of malignancy, although an angiosarcoma as small as 3 cm has been identified [5]. The tumor may be nonenhancing and have well-defined borders, thus appearing misleadingly benign [2]. Other tumors can be confused with adrenal angiosarcoma, including cortical carcinoma, pheochromocytoma, and metastatic diseases among others. [4]. On imaging, adrenocortical carcinomas are consistently located in a suprarenal position and are often associated with renal vein or IVC thrombosis. On MRI, they may have low T1 signal and areas of high T2 signal [10]. They may have necrotic, hemorrhagic, or calcified foci with heterogeneous appearances pre- and postcontrast [9,11]. A subtle distinguishing feature is that calcifications within angiosarcomas tend to be more regularly shaped compared to their counterparts in adrenocortical carcinomas. This is because they are the product of vascular thrombi that underwent cal-

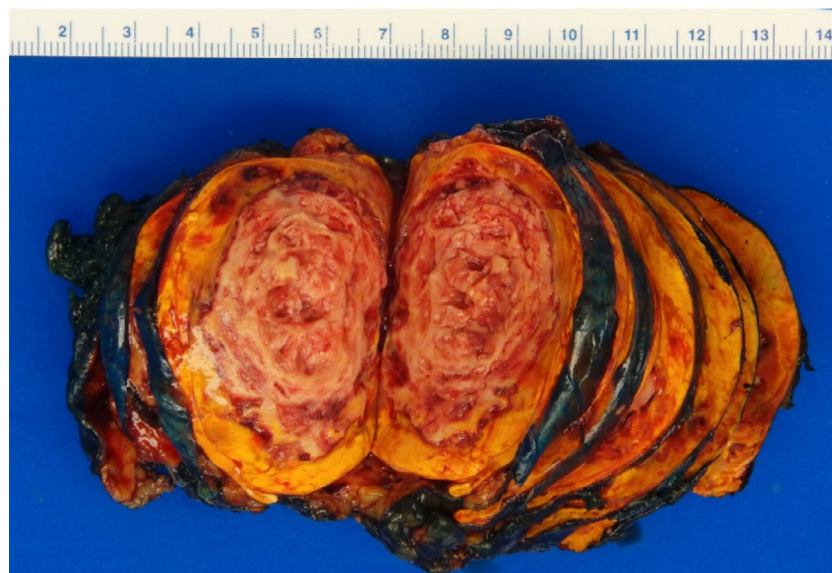


Fig. 7 – Gross photo of adrenal gland. At the periphery of the gland is the adrenal cortex which is thickened. In the middle of the gland is a necrotic, focally hemorrhagic mass that invades into the adrenal cortex.

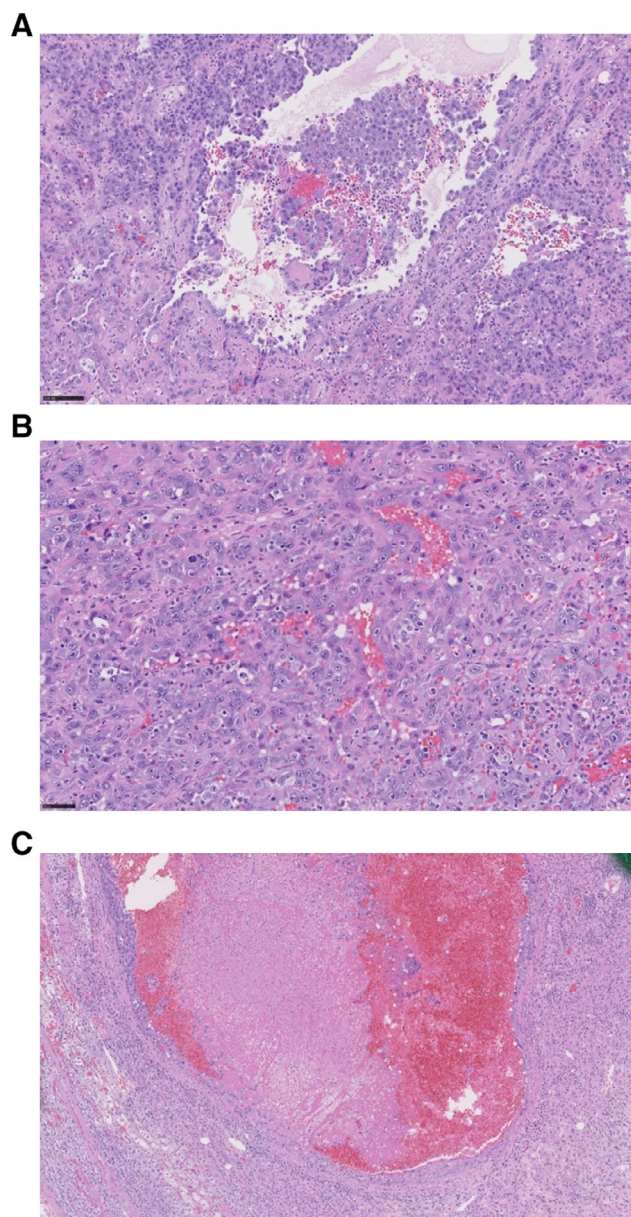


Fig. 8 – Histopathologic examination (A, C: H&E; original magnification: 200 \times ; B: H&E; original magnification: 400 \times). (A) Tumor cells have a nested pattern of growth and in some areas they form vascular spaces that are lined by similar cells forming intraluminal tufting or hobnailing. (B) Tumor cells show solid growth pattern with small vascular spaces in between. (C) Invasion into the adrenal cortex and it also shows anastomosing vascular spaces formed by tumor cells.

cification. The appearance of pheochromocytomas overlaps with adrenal angiosarcomas based on size and presence of cysts and calcifications [9]. Generally, pheochromocytomas can be identified as round lesions that attenuate like nearby structures on unenhanced imaging. However, because of significant variation in appearance, with either homogeneity or heterogeneity and sometimes with calcifications and necrosis [10,11], they can appear similar to angiosarcomas.

Importantly, both pheochromocytomas and adrenocortical carcinomas can sometimes be distinguished from adrenal angiosarcoma because of functional secretions leading to symptoms [11]. Meanwhile, metastatic disease to the adrenal glands can have a variety of appearances but is frequently remarkable for bilaterality [9,10]. Furthermore, metastases should be suspected in patients with known malignancy, particularly when lesions are greater than 3 cm in size [10].

Due to the rare nature of adrenal angiosarcoma, the treatment regimen is not adequately defined [1]. Resection is typically the treatment of choice. Laparoscopic approaches are feasible, but there may be some hesitation in the setting of potential malignancy [9]. Various cases have been documented in which adrenalectomy alone had no evidence of recurrence at 6 months, 9 months, 18 months, 1 year, 2 years, 11 years, 12 years, and 13 years [1]. Still, a number of cases with adrenalectomy alone have had poor outcomes, with some resulting in death due to metastatic disease [1].

Angiosarcoma is generally an aggressive malignancy, so adjuvant therapies may be beneficial when complete surgical resection is not guaranteed. Complete eradication followed by 3–6 month control intervals can help inform the need for adjuvant agents [2]. The literature has shown variable clinical outcomes in patients treated with surgery, adjuvant chemotherapy, and radiation therapy [1,5,12,13], most likely due to the rarity of this disease process. Previous authors have offered the possibility of relaparotomy and radical en bloc resection after diagnosis [14].

Among angiosarcomas of various origins, 5-year survival rates have been reported from 24% to 31% [9,15]. A median overall survival of 2.6 years has been documented for angiosarcomas [15]. Definitive data on survival in angiosarcomas of adrenal origin are not reported, as there are presently no large systematic reviews of this malignancy.

There is no established guideline for imaging surveillance of adrenal angiosarcoma. As mentioned previously, 3–6 month postresection control intervals have been suggested [2]. Whole body CT, abdominopelvic CT, thoracic CT, and FDG PET have been utilized in various case reports with reported follow-up up to 18 or 24 months [3,6,8,9].

Conclusion

We present a case of a 38-year-old female with a long history of cocaine abuse who presented with widespread bony metastases from adrenal angiosarcoma. The adrenal cancer was an incidental finding in this case. Adrenal angiosarcoma is an extremely rare diagnosis. Patients can be asymptomatic or have nonspecific complaints. Accurate tissue diagnosis is challenging due to overlap with other disease processes and requires strong immunohistochemistry. Imaging may demonstrate tumor heterogeneity with large internal vessels and areas of necrosis or hemorrhage. The ideal therapy is poorly defined due to the rarity of the disease, although resection is the current treatment of choice. The role of adjuvant therapies is poorly delineated. In the future, structured study of all reported cases will help alleviate the diagnostic and therapeutic challenges of this rare disease.

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