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Adrenal cavernous hemangioma: A rare tumor that mimics adrenal cortical carcinoma☆

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ABSTRACT

Background: Adrenal cavernous hemangioma is a rare tumor with only 60 cases previously reported. The aim of this study was to determine the frequency and clinical significance of adrenal cavernous hemangioma at our institution.

Methods: A retrospective review of consecutive patients undergoing adrenalectomy from 1994 to 2018 was completed to determine the frequency of cavernous hemangioma, characterize the clinical presentation, imaging and pathologic features and review the operative management and outcome.

Results: Of 144 consecutive patients who underwent adrenalectomy by a single surgeon, 5 (3.5%) had an adrenal cavernous hemangioma. All were incidentally discovered, nonfunctional adrenal masses varying in size from 7 to 12 cm with imaging features that were indeterminate in differentiating a benign adenoma from an adrenal cortical carcinoma. Attenuation values for the adrenal masses on noncontrast computed tomography varied from 28 to 34 Hounsfield units. All adrenal cavernous hemangiomas were large, heterogeneous, complex masses with a variable presence of calcification, hemorrhage, and necrosis. These features, along with tumor enlargement were concerning for adrenal cortical carcinoma. During the operation, there was no local invasion and all adrenal tumors were successfully removed laparoscopically without tumor rupture or bleeding. All patients had an uneventful postoperative course without complications.

Conclusion: Adrenal cavernous hemangioma is a rare tumor that can grow to a very large size without causing symptoms, making it difficult to differentiate from adrenal cortical carcinoma clinically or radiographically. Despite its large size, adrenal cavernous hemangioma can be safely resected laparoscopically.

INTRODUCTION

Incidental adrenal masses are being diagnosed more frequently due to the widespread use of abdominal cross sectional imaging. Imaging characteristics as well as laboratory findings are utilized to further define these incidentalomas and distinguish functional and nonfunctional as well as benign and malignant tumors. Certain imaging features raise suspicion for malignancy including large size (diameter >4 cm), lack of evidence for microscopic fat, delayed contrast washout, increased FDG PET activity, heterogeneity, calcification, and necrosis; however, these features may also be present in benign cavernous hemangiomas of the adrenal gland, making it difficult to distinguish a cavernous hemangioma from primary adrenal cortical carcinoma [1]. The lack of diagnostic specificity is further complicated by reports of the coexistence of cavernous adrenal hemangioma and malignant hemangioendothelioma [2].

To our knowledge, only 60 cases of adrenal cavernous hemangiomas have been reported, frequently presenting as a large, incidentally discovered retroperitoneal mass or as a result of hemorrhage with findings on imaging that are indistinguishable from malignancy [2–4]. All of these cases have required operative management due to diagnostic uncertainty and rarely hemodynamic instability from rupture. The primary purpose of this study was to determine the frequency of cavernous hemangioma of the adrenal gland in patients who underwent adrenalectomy at our institution. The secondary aims of the study were to evaluate the imaging features, functional status, and the pathologic characteristics of the cavernous hemangiomas and review the patients' clinical manifestations and operative management.

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Table 1
CT attenuation values measured for the adrenal cavernous hemangiomas

Patient	Hounsfield units, precontrast (unenhanced)	Hounsfield units, early postcontrast (enhanced phase)	Hounsfield units, delayed postcontrast
1*			50
2†	29	29	34
3		53	50
4†	34	39	41
5‡	28		

* The patient had CT images before and after intravenous contrast at an outside hospital and the mass was reported to have a "maximum" attenuation value of 50 HU.
† CT adrenal protocol.
‡ No contrast given due to renal impairment.

METHODS

We performed a single-institution, single-surgeon retrospective cohort study of patients who underwent adrenalectomy during the period from 1994 to 2018. Patients with a final pathologic diagnosis of benign cavernous hemangioma of the adrenal gland were identified from a prospectively maintained adrenal surgery database. Data were then collected from the adrenal surgery database and the electronic health record for patients with a final pathologic diagnosis of benign cavernous hemangioma of the adrenal gland. The data that were collected included demographics, presenting clinical manifestations, laboratory results, adrenal imaging characteristics, outcome of surgical management, and pathologic features. All of the data is descriptive.

The adrenal protocol for computed tomography (CT) at our institution consists of initial imaging without contrast and measurement of the attenuation value of the adrenal mass. If the Hounsfield units (HU) are less than 10, no contrast is administered as this is diagnostic for adenoma. For an adrenal mass with greater than 10 HU, contrast is administered and imaging is repeated at 45 seconds to evaluate the uptake of contrast and at 15 minutes to evaluate the washout of contrast. Absolute washout is then calculated using regions of interest within the lesion (Absolute washout = {[early enhanced CT (HU) – delayed CT (HU)]/[enhanced CT (HU) – unenhanced CT (HU)]} × 100%). Absolute washout greater than 60% is considered diagnostic for an adenoma. All of the imaging studies were re-reviewed by a senior fellowship trained abdominal radiologist.

The results of the pathologic evaluation were re-reviewed by a senior pathologist. The size, dimensions and gross and microscopic features of the tumor were determined, and associated pathologic findings were identified. The study was approved by the Institutional Review Board at MetroHealth Medical Center in Cleveland, Ohio.

RESULTS

During a period from 1994 to 2018, 144 consecutive patients underwent adrenalectomy by a single surgeon, and 5 (3.5%) had a final pathologic diagnosis of benign cavernous hemangioma of the adrenal gland. All benign cavernous hemangiomas were discovered incidentally. All patients underwent a functional evaluation, and all of their tumors were determined to be nonfunctioning. The tumors varied in size from 7 to 12 cm, and all had imaging features that were indeterminate in terms of differentiating a benign adenoma from an adrenal cortical carcinoma (Table 1). Only 2 patients had a CT adrenal protocol and there was no washout of contrast on delayed imaging; 2 patients had a CT with intravenous contrast and 1 patient with renal insufficiency had a CT without contrast. Attenuation values for the adrenal masses on computed tomography varied from 28 to 34 HU on unenhanced images and from 29 to 53 HU on enhanced images with wash out (Table 1).

All of the tumors were large heterogeneous, complex masses with a variable presence of calcification, hemorrhage, and necrosis. These features along with tumor enlargement raised concern for adrenal cortical carcinoma. However, there was no definite imaging evidence of local invasion. As a result, it was elected to begin with laparoscopic exposure with the intent of converting to an open approach if local invasion was present. At operation, there was no evidence for local invasion, and all the adrenal tumors were successfully removed laparoscopically without tumor rupture or bleeding. All patients had an uneventful postoperative course without complications. All patients were seen 2–4 weeks following surgery and no further follow-up was necessary.

Grossly, the tumors were large and well circumscribed; their weights varied from 77 to 450 g, and a thin rim of compressed adrenal tissue surrounded them (Table 2). Associated adrenal cortical hyperplasia was noted in 2 patients. Microscopically, the excised cavernous hemangiomas were noninfiltrative tumors that consisted of aggregates of blood vessels larger than capillaries that were surrounded by a pseudocapsule that abutted the adrenal parenchyma. The walls of the vessels were thickened by fibrosis, sclerosis, and hyalinization. The endothelium was bland and atrophic, and endothelial proliferation was only present when there was organization and recanalization of clot. The blood vessels were expanded by clot and hemorrhage. There was associated dystrophic calcification and hemosiderin deposition (Fig 1).

Case #1. A 71-year-old man with a history of treated prostate and colon carcinoma underwent a follow-up surveillance CT of the chest, abdomen, and pelvis with pre- and post-intravenous contrast imaging, which revealed an incidental right adrenal mass that measured 4.7 cm × 3.9 cm with a maximum attenuation value of 50 HU. There were no other suspicious lesions. He denied headache, palpitations, abdominal pain, diaphoresis, glucose intolerance, or easy bruising. His blood pressure was 142/72 and heart rate 76 beat/min. He had a normal physical examination.

Laboratory evaluation revealed a morning cortisol level of 2.4 μg/dL (<5 μg/dL) after a 1 mg overnight dexamethasone suppression test. A plasma metanephrine level was 43 pg/mL (12–60 pg/mL) and a plasma normetaneprhine level was 105 pg/mL (18–111 pg/mL). Serum aldosterone was 11 ng/dL (4.5–35.4 ng/dL), and plasma renin activity was 0.57 ng/mL per hour. (0.15–2.33 ng/mL per hour).

Table 2
Histopathologic findings

Case number	Size (cm)*	Weight (g)*	Gross and microscopic features	Associated findings
1.	7.0 × 5.0 × 4.0	77	Well circumscribed, trabeculated with central hemorrhage and hyalinization	• Compressed rim of adrenal cortex • Cortical hyperplasia
2.	11 × 10 × 8.5	194	Well circumscribed, central stellate center, fibrosis, hyalinization, fibrin thrombi, and hemosiderin deposition	• Compressed rim of adrenal cortex • Cortical hyperplasia
3.	11.5 × 6.5 × 9.1	450	Multiloculated and variegated with calcification, hemorrhage, fibrosis, extensive thrombosis and ossification	• Compressed rim of adrenal cortex
4.	7.2 × 5.5 × 4.0	96	Well circumscribed and replacing the adrenal medulla with extensive necrosis and hemorrhage	• Compressed rim of adrenal cortex
5.	12.0 × 7.0 × 6.5	220	Well circumscribed with cavitation, hemorrhage, extensive thrombosis and calcification almost completely replacing the normal adrenal	• Thin rim of compressed adrenal

* Size and weight were either determined at operation or by the pathologist.

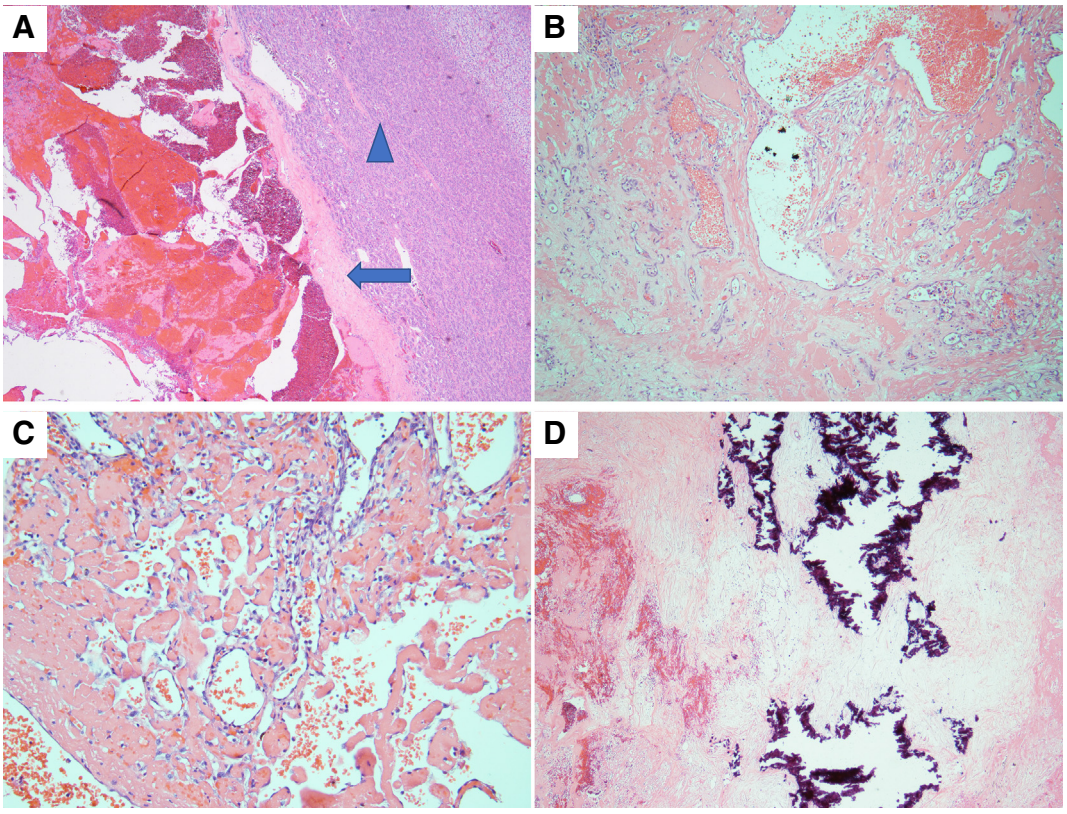

Fig 1. A: Tightly packed vessels filled with clot, abutting adrenal parenchyma (triangle) with a pseudo-capsule (arrow). B: Thin and thick-walled vessels, with fibrosis/sclerosis. C: Recanalization of clot, with minimal endothelial proliferation. D: Dystrophic calcification and hyalinization. (Original magnification for A, B, and D: 40×; for C: 100×).

The patient underwent a laparoscopic right adrenalectomy and a tumor measuring 7.0 × 5.0 × 4.0 cm and weighing 77 g was resected. Pathology revealed a benign cavernous hemangioma with hemorrhage and hyalinization.

Case #2. A 61-year-old white woman with a past medical history significant for Crohn's disease, hypertension, chronic obstructive pulmonary disease, and obstructive sleep apnea was admitted to an outside hospital with Crohn's colitis. CT imaging of the abdomen revealed an incidental 7 cm left adrenal mass without evidence of invasion. The right adrenal gland was normal. Prior to our evaluation, a fine needle aspiration biopsy of the mass was performed at the outside institution and microscopic examination revealed findings consistent with an adrenal cortical neoplasm. The mass was present on a CT scan from 3 years earlier and at that time it measured 2 cm.

She was referred to our institution 4 months after hospitalization for colitis, for evaluation of the adrenal mass. She endorsed decreased appetite with a 70-lb weight loss in the last 3 months, thinning hair, headache, blurry vision, and knee and shoulder pain. The patient had no personal history of malignancy and no personal or family history of endocrinopathies.

On physical exam, she had a body mass index of 37.7 kg/m^2. Her blood pressure was 210/119, and heart rate, 83 beat/min. She had prominent supraclavicular fat pads and a cervicodorsal hump, violaceous striae, bruising of her skin, poor skin turgor, and bilateral brawny induration, and varicose veins of her lower extremities. Repeat CT imaging of the abdomen at our institution demonstrated interval increase in size of the left adrenal mass, now measuring 8 cm in the greatest dimension and abutting the posterior wall of the stomach and the hilum of the spleen. A full biochemical workup was completed, and there was no evidence for a functional tumor. The patient's Cushingoid appearance was attributed to the steroids that she was receiving for treatment of her Crohn's disease.

The patient was lost to follow-up for 6 months, at which point she represented with abdominal pain. A repeat CT scan using an adrenal protocol showed a solid left adrenal mass, now measuring 10 × 9 × 6 cm, with an attenuation value of 29 HU on the noncontrast images (Fig 2, *A*). There was no washout of contrast with attenuation values of 29 HU and 34 HU on the early postcontrast and delayed images, respectively. Retrospective review of the imaging study revealed peripheral nodular discontinuous enhancement seen on the portal venous phase (Fig 2, *B*) that was best seen on the narrow window view (Fig 2, *C*). Delayed imaging demonstrated contrast filling the mass from the periphery (Fig 2, *D*).

A laparoscopic left adrenalectomy was performed and a 11 × 10 × 8.5 cm adrenal mass weighing 194 g was resected (Fig 3). The final pathology revealed a benign cavernous hemangioma with cortical hyperplasia, hyalinization, fibrosis, recently organized fibrin thrombi and hemosiderin deposition.

Case #3. A 60-year-old African-American woman with medically refractory hypertension on 6 antihypertensive agents, type II diabetes mellitus, chronic obstructive pulmonary disease, diastolic heart failure, and obstructive sleep apnea had an incidental right adrenal mass discovered on CT imaging of the chest obtained for evaluation of emphysema. She endorsed headache, diaphoresis, and easy bruising. She had no history of abdominal pain or palpitations. On physical exam, her blood pressure was 165/89 and heart rate 76 beat/min. The remainder of her exam was normal. A full biochemical workup was completed, and there was no evidence for a functional tumor.

A repeat CT scan of the abdomen with intravenous contrast demonstrated a complex heterogeneous right adrenal mass with calcifications and interval enlargement that measured 10.8 × 6.8 × 10 cm with early and delayed post contrast attenuation values of 53 and 50 HU, respectively. The mass was displacing the right kidney inferiorly and an abnormal-appearing, right-sided retrocrural lymph node was also identified.

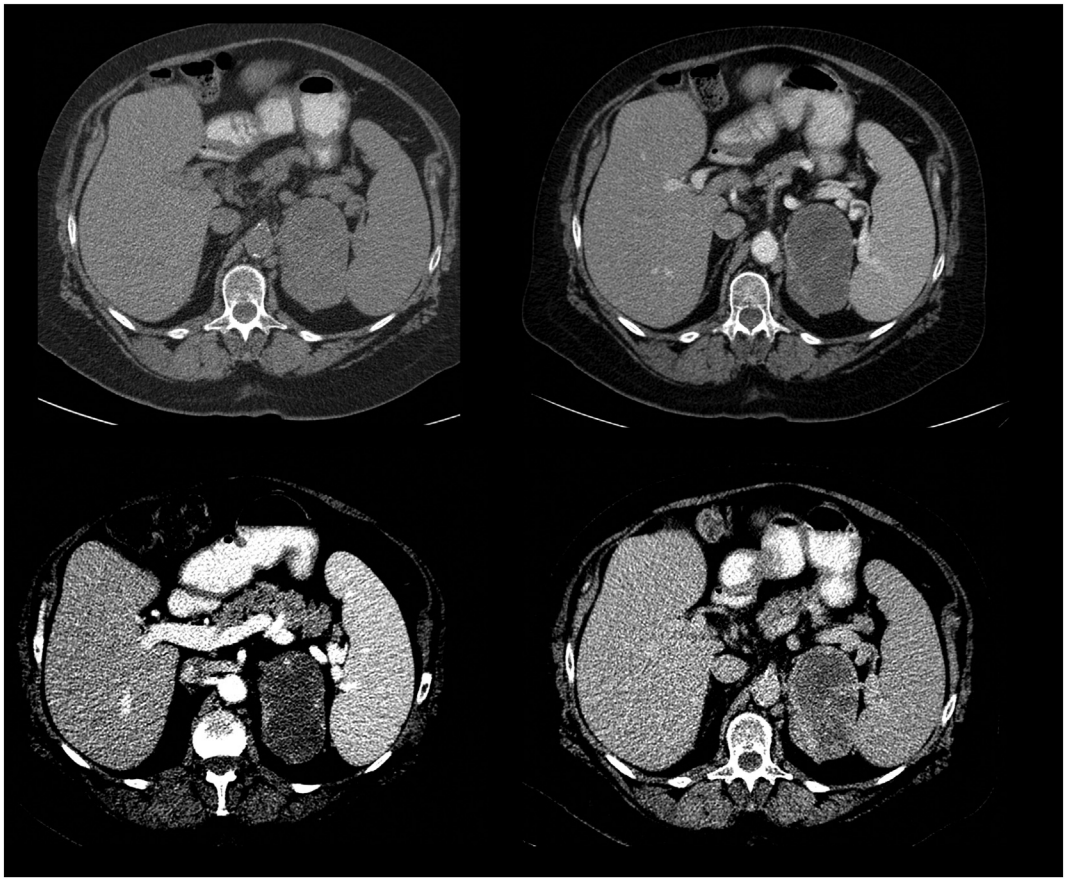

Fig 2. CT imaging of left adrenal mass using an adrenal protocol demonstrating a solid left adrenal mass measuring 10 cm × 9 cm × 6 cm, with an attenuation value of 29 HU on the noncontrast view (A). Peripheral nodular discontinuous enhancement is seen on the portal venous phase (B) and on the narrow window view (C). Delayed imaging demonstrated contrast filling the mass from the periphery (D).

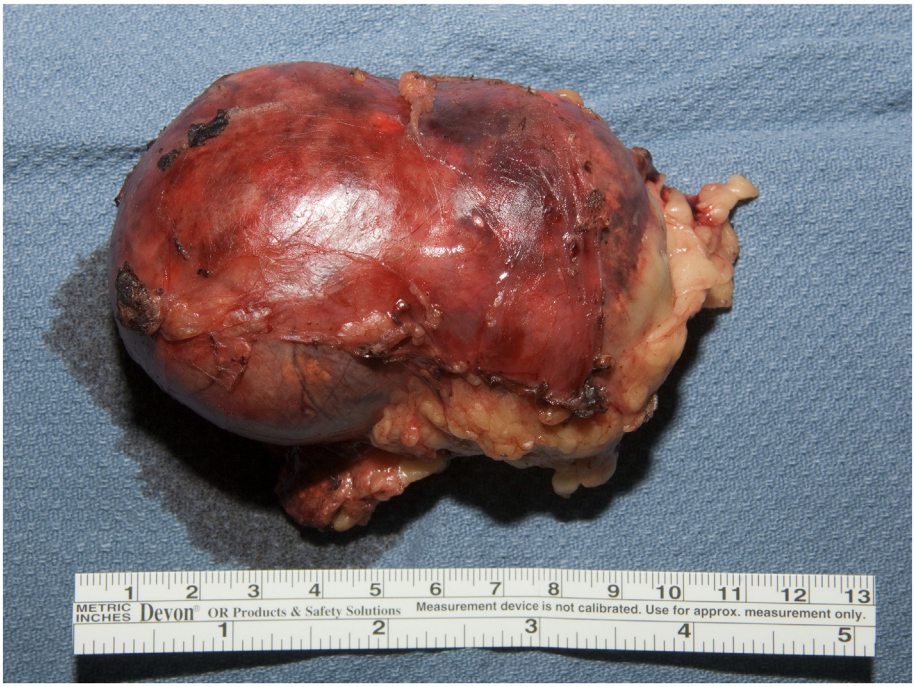

Fig 3. Gross specimen of adrenal cavernous hemangioma.

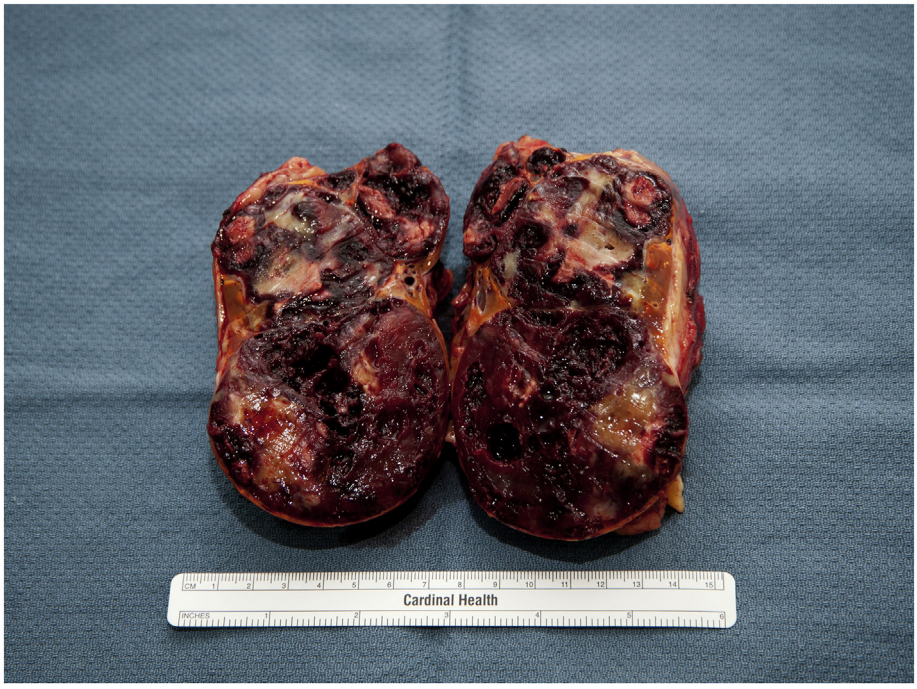

Fig 4. Cross-section of adrenal cavernous hemangioma showing extensive thrombosis, fibrosis, calcification, and ossification.

A laparoscopic right adrenalectomy was performed and a right adrenal mass measuring 11.5 × 6.5 × 9.1 cm and weighing 450 g was excised. The final pathology revealed a benign cavernous hemangioma with extensive thrombosis, fibrosis, calcification, and ossification (Fig 4).

Case #4. A 57-year-old African-American woman with hypertension and kidney stones was referred for evaluation of an incidental left adrenal mass discovered on CT imaging that was obtained for evaluation of right flank pain and hematuria. She denied headache, diaphoresis, palpitations, glucose intolerance, or easy bruisability. The patient had a body mass index of 33.7 kg/m^2. Her blood pressure was 138/60 mm Hg, and heart rate, 77 beat/min. The remainder of her physical exam was unremarkable.

A full biochemical workup was completed and there was no evidence for a functional tumor. A CT scan using an adrenal protocol showed a left adrenal mass measuring 6.3 × 5.1 cm with an attenuation value of 34 HU on unenhanced images, 39 HU on enhanced images, and 41 HU on delayed images with no washout of contrast on delayed images. Central necrosis was present (Fig 5). On retrospective review of the CT images, peripheral nodular enhancement was also noted.

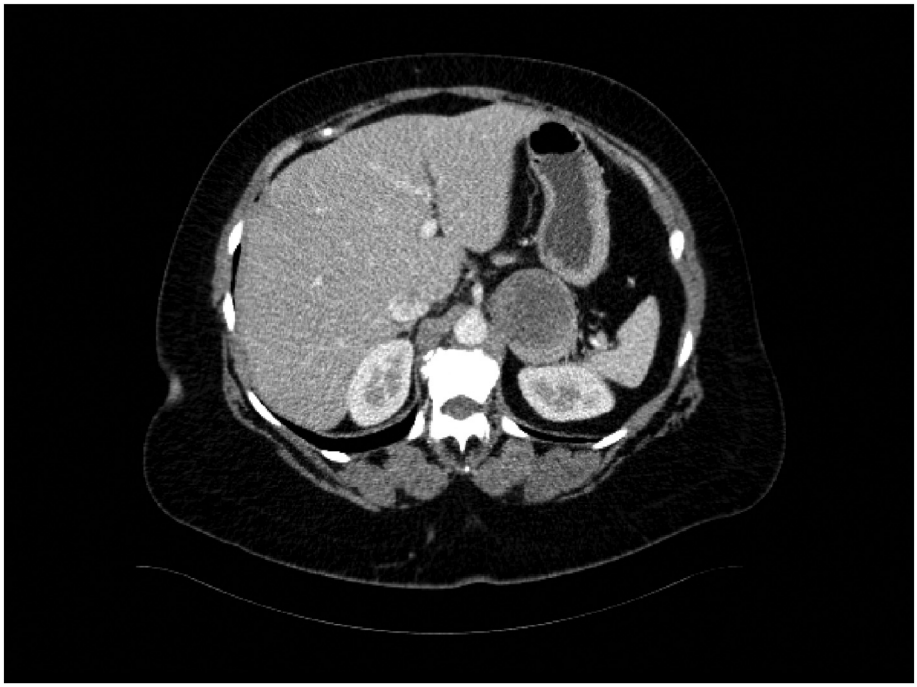

Fig 5. CT image showing a left adrenal mass with peripheral enhancement and central necrosis.

The patient underwent a laparoscopic left adrenalectomy and an adrenal mass measuring 7.2 × 5.5 × 4.0 cm and weighing 96 g was resected. Pathologic evaluation revealed a benign cavernous hemangioma that replaced the adrenal medulla with extensive necrosis, hemorrhage, and cortical hyperplasia.

Case #5. A 70-year-old man with a history of hypertension on 3 antihypertensive agents, chronic obstructive pulmonary disease, stage 3 kidney disease, and peripheral vascular disease was referred for evaluation of an enlarging right adrenal mass that was incidentally discovered on CT imaging of his abdomen prior to a ventral hernia repair. At that time, the mass measured 3.2 × 2.6 cm in size and was thought to be an adrenal adenoma. Seven years after the mass was discovered, the patient presented to the emergency department with abdominal pain. The patient denied headache, palpitations, diaphoresis, tremor, glucose intolerance, or easy bruising. He had no family history of endocrinopathies. A CT scan of his abdomen (Fig 6) was obtained in the emergency department, which revealed that the right adrenal mass had markedly increased in size and now measured 7.2 × 6.2 cm with an attenuation value of 32 HU on a CT without contrast. The mass was heterogeneous with peripheral calcifications. The left adrenal gland appeared normal. Intravenous contrast was not administered due to underlying renal dysfunction (baseline serum creatinine was 2.17 mg/dL).

On physical exam, the patient had a body mass index of 36.44. kg/m^2. His blood pressure was 141/47 mmHg, and heart rate, 65 beat/min. He had a cervicodorsal hump. He had diminished breath sounds bilaterally. He had a grade 3/6 systolic ejection murmur best heard in the right second intercostal space. He had a long midline abdominal scar from a prior aortobifemoral bypass and incisional hernia repair. He had no palpable masses, tenderness, or organomegaly. He had no violaceous striae or bruises. He had normal skin turgor.

Plasma-free normetanephrine and metanephrine levels were 1.59 nmol/L (0.00–0.89 nmol/L) and 0.13 nmol/L (0.00–0.49 nmol/L), respectively. A 24-hour urine normetanephrine and metanephrine were 526 μg/24 h (125–510 μg/24 h) and 105 μg (62–207 μg/24 h), respectively. The remainder of the biochemical workup was normal.

The patient underwent a laparoscopic right adrenalectomy. A 220-g right adrenal mass measuring 12 × 7 × 6.5 cm was resected. Surgical pathology of the mass revealed a benign cavernous hemangioma surrounded by a thin rim of compressed adrenal gland with extensive thrombosis, cavitation, and calcifications.

DISCUSSION

Cavernous hemangiomas are most commonly found in liver, skin, and spine [5]. Adrenal cavernous hemangiomas are rare, most of them found incidentally on imaging studies. To date, there have only been 60 cases reported in the literature since the first surgical case was described in 1955 by Johnson and Jeppeson [6–8]. The clinical significance of cavernous hemangiomas of the adrenal gland is that they are difficult to differentiate from adrenal cortical cancer. Both can exhibit similar clinical and imaging features, including: large size, rapid growth, irregular shape, heterogeneity, tumor calcifications, necrosis, and high attenuation values on CT imaging with minimal or no contrast washout [5]. Most of the reported cases of cavernous hemangioma were asymptomatic and discovered incidentally or found at autopsy. A rare case of cavernous hemangioma of the adrenal gland has been reported to rupture and cause severe retroperitoneal hemorrhage and hypovolemic shock [4].

All 5 of our patients presented with a large incidentally discovered adrenal mass found on CT imaging of the chest or abdomen, which is consistent with what has been previously reported. A functional evaluation was completed in all of our patients, which consisted of a morning serum cortisol level after a 1 mg overnight dexamethasone suppression test, serum aldosterone, plasma renin activity, plasma metanephrines, and 24-hour urine metanephrines when plasma metanephrines were abnormal. This confirmed that all of the tumors were nonfunctional.

All of the adrenal masses had high attenuation values ranging from 28 to 34 HU on noncontrast imaging. Most benign nonfunctioning adrenal adenomas have an attenuation value less than 10 HU. An attenuation value of <10 HU for an adrenal mass has a sensitivity of 71% and specificity of 98% [9]. An adrenal mass with an attenuation value >10 HU is classified as indeterminate and can benefit from additional CT imaging with intravenous contrast to evaluate perfusion and contrast washout from the adrenal mass. It is well recognized that up to 30% of adrenal adenomas are lipid-poor and may be hard to differentiate

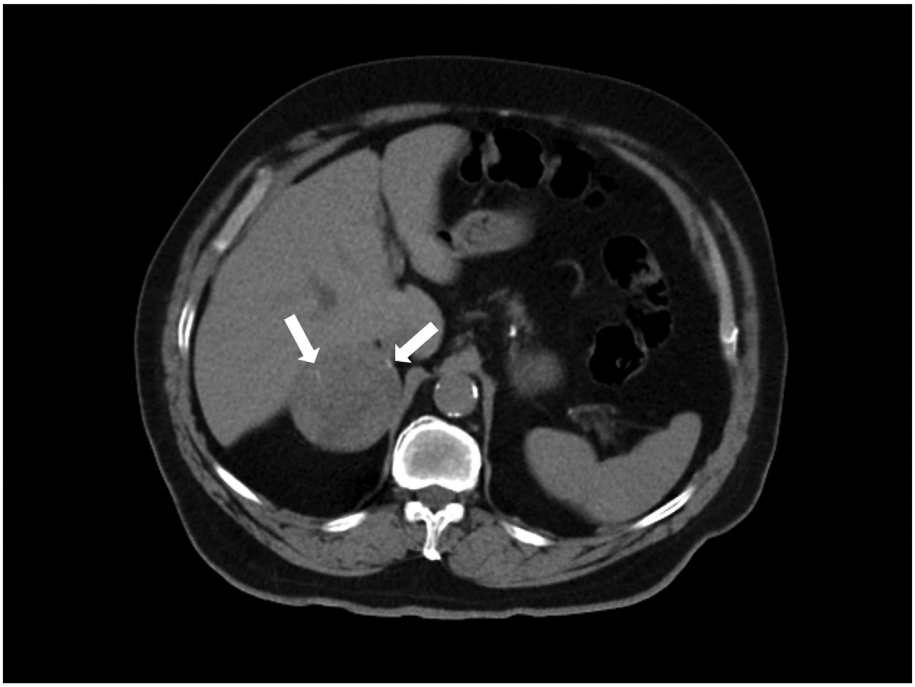

Fig 6. CT image showing heterogeneous right adrenal mass with calcifications (arrows).

from a primary malignancy or a metastasis on an unenhanced CT exam or magnetic resonance imaging with chemical shift imaging. Contrast washout is more rapid for benign adrenal tumors than for malignant adrenal tumors. Only 3 of the 5 patients in our series underwent contrast enhanced CT imaging following unenhanced CT imaging and the results were documented in only 2 patients who had almost no washout of contrast. In one patient, underlying renal insufficiency precluded the patient from receiving intravenous contrast material.

Our series emphasized that adrenal cavernous hemangiomas are large tumors varying in weight from 77 to 450 g and they are difficult to distinguish from adrenal cortical cancer. However, retrospective review of the CT images in case 2 and 4 revealed peripheral nodular discontinuous enhancement on early CT images followed by centripetal filling in of the mass on delayed imaging, features typical of hemangiomas in the liver. Recognizing that hemangiomas may occur in the adrenal gland, the CT imaging features may be the key to making a preoperative diagnosis.

Cavernous hemangioma should be considered in the differential diagnosis of a nonfunctioning adrenal mass along with a lipid rich or lipid poor adenoma, a ganglioneuroma, adrenal cortical cancer, and a metastasis. All of these tumors may increase in size over time. In general, adrenalectomy is recommended for a nonfunctioning adrenal mass >4 cm because of concern for adrenal cortical cancer and for an isolated adrenal metastasis. A myelolipoma and a cyst of the adrenal gland are also considered in the differential diagnosis; however, they can be diagnosed definitively on CT and do not need to be removed. In the future, if a definitive preoperative diagnosis of hemangioma could be made, it is conceivable that these tumors could be observed in an asymptomatic patient. Interval CT evaluation would be reasonable to ensure the accuracy of diagnosis or if patients become symptomatic to exclude the rare possibility of rupture; but similar to hepatic hemangiomas, regular imaging follow-up may not be necessary for all patients with an adrenal hemangioma.

It is worthwhile to emphasize that the needle biopsy that was performed in case #2 was ill-advised and unnecessary. Needle biopsy is rarely indicated for evaluation of an incidentally-discovered adrenal mass and should never be performed prior to excluding the diagnosis of pheochromocytoma because of the risk of precipitating hypertensive crisis and its potential sequelae including stroke and myocardial infarction. The results of needle biopsy do not differentiate benign cortical or medullary tumors from malignant ones. The role of needle biopsy is limited to patients with known underlying malignancy to make a diagnosis of metastatic disease.

Our surgical approach in a patient with a large adrenal mass is to start the operation laparoscopically when preoperative imaging demonstrates no local invasion. Visualization and exposure of the adrenal veins and inferior vena cava is better and ligation of the adrenal veins is easier using a laparoscopic approach. In the event that the mass is found to be invading local structures, immediate conversion to an open approach and an en bloc resection is completed.

Our study has several limitations. Although most of the data was collected prospectively, the specific clinical presentation and the imaging features were obtained retrospectively from the electronic health record and may be affected by the completeness of documentation. A second limitation was that not all patients had multiphasic CT and, in the 3 patients who did, the results were clearly documented in only 2 patients who had no washout of contrast material. Furthermore, two of our patients underwent laboratory evaluation at outside hospitals, creating inherent variance in testing results.

In conclusion, surgeons and radiologists should be aware of a cavernous hemangioma of the adrenal gland and it should be considered in the differential diagnosis for a nonfunctioning adrenal mass. They are typically large tumors that can progressively increase in size and can be difficult to distinguish from adrenal cortical carcinoma. At operation, however, they are noninfiltrative and can be resected laparoscopically.

Author contribution

MN contributed data collection, literature review, and manuscript preparation. DC contributed data collection and manuscript preparation. WB contributed data collection and manuscript preparation. CM contributed data collection, literature review, and manuscript preparation.

Conflict of interest

We confirm that there are no known conflicts of interest associated with this publication.

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