Rare Adrenal Tumors and Adrenal Metastasis

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KEYWORDS

• Adrenal tumors • Metastatic adrenal disease • Functional adrenal tumors • Adrenal incidentalomas • Adrenal oncology

KEY POINTS

- Rare adrenal tumors encompass a wide variety of neoplasms, each with unique behaviors, appearance, and hormonal activity.
- Accurate diagnosis and management of rare adrenal tumors requires a multidisciplinary approach potentially including advanced imaging techniques, unique therapeutic interventions, and uncommon metabolic workups.
- An understanding of rare adrenal tumor behavior is essential for obtaining maximum oncologic control while balancing the need to preserve endocrine function.

INTRODUCTION/HISTORY/DEFINITIONS/ BACKGROUND

Like most organs, the adrenal glands are known to harbor neoplasms of various types. The list of possible adrenal neoplasms is long, and while adenomas are the most common, several other types of benign and malignant tumors with varying degrees of rarity can occur. Adrenocortical carcinoma (ACC) and pheochromocytomas are covered in depth elsewhere in this *Clinics* issue. This article is dedicated to rare adrenal tumors including functional adenomas, myelolipomas, neuroblastomas and ganglioneuromas, and sex hormone producing tumors. This article will also cover metastasis to the adrenal gland.

Adrenal tumor incidence has increased due, in part, to the increased use of cross-sectional imaging. As a result, the role of the urologist in the workup and surgical management of adrenal tumors is essential. While the management of these lesions has historically been divided among urologists and general surgery subspecialists, the comfort of the urologist in managing these lesions should remain a natural component of their skill set given the close relationship between the adrenal gland and kidney, the urologist's familiarity with the retroperitoneum, and the advanced minimally invasive surgical techniques commonly employed in urologic practice. Therefore, it is vital that the urologist maintains a comprehensive differential in mind when an adrenal mass is encountered as well as up-to-date surgical skills for excision of problematic tumors if such services are required and to avoid over treatment in the vast majority of cases.

CLINICAL PRESENTATION

Adenoma

Adenomas are the most common type of adrenal tumor, representing 90% of all adrenal incidentalomas, with the majority being metabolically inactive. However, 7.1% of benign adenomas can secrete metabolically active substances, including aldosterone (1%) and glucocorticoids (6%), leading to Conn's syndrome and Cushing's syndrome, respectively.[1,2] Exceedingly rare is the ability of these adenomas to secrete sex hormones.[3] The

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Abbreviations	
ACC	adrenocortical carcinoma
HPA	hypothalamic-pituitary-adrenal
MIBG	metaiodobenzylguanidine

physiologic activity of these hormones and their associated medical syndromes are covered elsewhere in this issue, but the evaluation for secretion of metabolically active substances places tumors with such capability under the purview of this rare tumor article. Tumors that do not initially possess the ability to secrete metabolic substances rarely gain the ability to do so.[4] The rate of transformation to metabolically active adenoma has been documented at 1.7% but is exceedingly rare.[4]

The work-up of an incidental adrenal mass should begin with CT imaging targeted to the area of concern when available and clinically indicated. This modality offers the most value and allows for characterization of size, density, and homogeneity. Adrenal adenomas are typically small (<4 cm) with a uniform appearance throughout and smooth borders. A Hounsfield attenuation of less than 10 units is considered strongly suggestive of a benign adrenal adenoma as these tumors are lipid rich.[5] However, some adenomas are uncharacteristically dense because of lower lipid content, and consequently, these neoplasms will have attenuation greater than 10 HU on computed tomography (CT) imaging. In these cases, contrast washout may further inform the clinician about the nature of the neoplasm, as adenomas display washout of 40% to 60% of their initial enhancement on delayed contrast CT imaging.[6–9] The scope and criteria for adrenal-specific imaging for incidentally diagnosed adenomas is beyond the scope of this article. However, additional details can be found within the American College of Radiology Incidental Findings Committee's 2017 White Paper on incidental adrenal masses.[10]

Complementary to the visual characterization of adrenal neoplasms with cross-sectional imaging is the evaluation of metabolic activity. The undifferentiated adrenal neoplasm brings forth a broad spectrum of potentially metabolically active substances, including cortisol or aldosterone in the case of adrenal adenoma, catecholamines in the case of pheochromocytoma, and rarely, sex hormones for sex hormone producing tumors. Therefore, current recommendations suggest additional testing for metabolic activity, and laboratory analysis should include cortisol and catecholamine levels for all adrenal incidentalomas.[1,5] Further evaluation of aldosterone levels should be included for the patient with hypertension.[5]

Aldosteronoma

For aldosterone-secreting adenomas, the resulting hyperaldosteronism is not subject to the normal physiologic regulation of the renin-angiotensin-aldosterone system, and hyperaldosteronism causes increased sodium resorption and potassium excretion in the distal aspect of the renal nephron. Increased sodium resorption causes increased water resorption, and the downstream effect is elevated blood pressure. Conn's syndrome (primary hyperaldosteronism) is differentiated from secondary hyperaldosteronism by plasma renin levels. As aldosterone is the substance secreted in primary hyperaldosteronism, renin levels are suppressed by negative feedback caused by elevated blood pressure. However, in secondary hyperaldosteronism, elevated renin levels are the cause of downstream aldosterone secretion. Adenomas are responsible for about one-third of all cases of Conn syndrome. Other causes include bilateral adrenal hyperplasia (60%), unilateral adrenal hyperplasia (2%), adrenal carcinoma (less than 1%), ectopic aldosteronoma (less than 1%), and familial hyperaldosteronism (less than 1%).[11]

Once primary hyperaldosteronism has been identified, further workup via adrenal venous blood sampling to confirm laterality of hormone secretion may be indicated. Young and colleagues demonstrated the importance of confirmatory venous blood sampling by showing that 21.7% of patients with primary hyperaldosteronism would have been excluded from adrenalectomy based on initial CT findings, and another 24.7% would have undergone surgical intervention when alternative treatment options would have been indicated.[12] The evaluation of laterality is determined using the following formula: $(A_{dominant}/C_{dominant})/(A_{nondominant}/C_{nondominant})$, where A = aldosterone and C = cortisol. The test for laterality is considered positive if the ratio is greater than 2.0 or greater than 4.0 if cosyntropin is used to stimulate the adrenal gland. Adrenal vein sampling is an intricate process, and additional information can be found in Rossi and colleagues's 2014 expert consensus on the use of adrenal vein sampling for the subtyping of primary aldosteronism.[13]

One primary purpose of adrenal vein sampling is to determine eligibility for surgery. If vein sampling does not demonstrate laterality of aldosterone secretion, then medical management with aldosterone receptor antagonists to correct hyperaldosterone-induced hypertension is often the mainstay of treatment. Other indications for medical management include familial hyperaldosterone syndromes or if the patient is not a surgical

candidate.[13] In contrast, surgical indications include lateralization of aldosterone secretion, large tumor size with or without suspicious features, the patient is young (<40 years old), or obvious unilateral adenomas.[13]

Cushing Syndrome

Cushing's syndrome is caused by hypercortisolism which is regulated by the hypothalamic-pituitary-adrenal (HPA) axis. Therefore, the management of this syndrome often involves internists, neurosurgeons, and an urologist or endocrine surgeon.[14] Endogenous hypercortisolism can be caused by HPA-dependent or HPA-independent pathways. HPA-dependent hypercortisolism results from either hypothalamic secretion of adrenocorticotropic hormone or pituitary secretion of corticotropic releasing hormone. HPA-independent hypercortisolism is caused by the secretion of cortisol from adrenal neoplasia. This HPA-independent phenomenon is rare and accounts for approximately 10% of cases of hypercortisolism, typically unilateral in nature but occasionally bilateral in origin.[15–18]

Classic external symptoms of Cushing syndrome include central obesity, abdominal striae, buffalo hump, and moon facies.[19] Laboratory findings may also include dyslipidemia, hyperglycemia, and hypertension.[20,21] Laboratory evaluation for the diagnosis of Cushing syndrome involves either measurement of 24-hour urinary-free cortisol level or low-dose dexamethasone suppression testing. Any abnormal result warrants referral to an endocrine specialist for definitive diagnosis.[22] In evaluation of the origin of Cushing syndrome, the low-dose dexamethasone suppression test can be useful. This test involves evening administration of dexamethasone followed by morning evaluation of cortisol levels. Dexamethasone should suppress adrenocorticotropic hormone levels, and thus cortisol levels should fall. However, autonomous secretion of cortisol by an adenoma is the cause of Cushing syndrome, then dexamethasone will not suppress morning cortisol levels.[19] The most appropriate treatment for Cushing syndrome depends on whether excess cortisol is adrenocorticotropic hormone (ACTH) dependent or independent. However, treatment may involve surgical resection of the culprit lesion, which may include neurosurgical or urologic intervention, or alternatively, medical therapy to block steroid synthesis if surgical intervention is not possible.

Myelolipoma

The adrenal gland may also harbor myelolipomas. These tumors are benign and do not possess the ability to secrete metabolically active substances.[23] They are composed of adipocytes and hematopoietic cells.[24] These tumors are generally asymptomatic unless they become large, at which point symptoms may depend on the affected surrounding structures. Generally, the primary presenting symptom is abdominal or flank pain.[23] On occasion, these tumors can grow to be greater than 10 cm.[23] Rarely, tumors of this size will spontaneously rupture.[25]

As with adenomas, myelolipomas are typically diagnosed with cross-sectional imaging, and CT scan offers excellent value in the characterization of the lesion. Like adenomas, these lesions are well defined with smooth borders. However, myelolipomas contain elements of myeloid tissue among their fatty components, and on CT scan, these areas display greater attenuation. The myeloid tissue will further enhance with contrast. Some myelolipomas display calcification or areas of hemorrhage.[26] MRI can also be used to further characterize myelolipomas. If fat is visualized on MRI, then myelolipoma diagnosis is highly likely, although definitive diagnosis still requires tissue sampling.[27] The proximity of the adrenal gland and kidney may make identification of the primary location of the neoplasm difficult. Indeed, a renal angiomyolipoma may display similar characteristics to adrenal myelolipomas, and although both tumors are benign, the location of such a neoplasm may dictate the diagnostic algorithm the physician chooses to follow. In contrast to the myelolipoma (and angiomyolipoma of renal origin), malignant liposarcoma often infiltrates surrounding tissue and exhibits irregular borders (**Figs. 1** and **2**).

Myelolipomas have also been associated with the occurrences of adenomas and pheochromocytomas. Therefore, if a myelolipoma is discovered, additional workup for metabolically active neoplasms may be warranted.[30,31] However, this opinion is challenged by others who believe that such workup should only take place if clinical suspicion is high for a metabolically active adenoma or pheochromocytoma.[23] As such, National Institute of Health (NIH) recommendations state that, should the physician discover a myelolipoma, compulsory workup for additional metabolically active lesions is not required.[5] In the absence of additional findings, myelolipomas are generally benign lesions and may be treated conservatively. Indications for intervention include large size, rapid growth, atypical features on imaging, or impingement on surrounding structures with or without associated symptoms.[32]

Ganglioneuroma

Ganglioneuromas are exceedingly rare neoplasms that may arise from the adrenal gland in 40% of

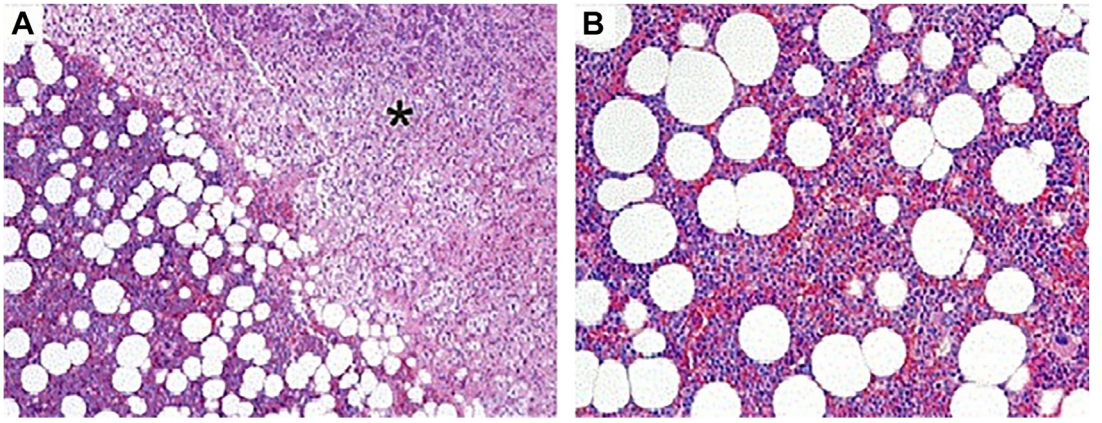

Fig. 1. (*A*) 100x view of adrenal cortex (*asterisk, top right*) and myelolipoma displaying hematopoietic cells (*bottom left*). (*B*) 200x view of hematopoietic component of a myelolipoma. (*Image obtained from* Adapa S, Naramala S, Gayam V, et al. Adrenal incidentaloma: challenges in diagnosing adrenal myelolipoma. J Investig Med High Impact Case Rep 2019;7:2324709619870311. https://doi.org/10.1177/2324709619870311 under Creative Commons Attribution License.[28])

cases.[33] However, they may also develop anywhere along the sympathetic chain, including the cervical (5%), thoracic (15%), abdominal (25%), and pelvic (5%) chain.[33] These tumors are most common in children, but when discovered in adults, it is usually incidentally in the fourth or fifth decade of life.[33] These neoplasms are benign and can grow quite large, but most are asymptomatic.[34] If symptoms exist, diarrhea or hypertension may be the presenting symptom secondary to vasoactive intestinal peptide or catecholamine secretion in a minority of ganglioneuromas.[33] These neoplasms have also been shown to encase vessels without impingement or invasion of the lumen, and such cases pose a challenge to surgical resection[34] (**Fig. 3**).

Ganglioneuromas present with low attenuation on both contrast-enhanced and unenhanced CT.[34,36] Furthermore, calcifications are a typical finding (**Fig. 4**).[33,34] Thus, a metabolically inactive lesion with calcifications and less than 40 HU enhancement may indicate the presence of a ganglioneuroma.[37] If suspicion for ganglioneuroma is high, additional diagnostic workup may

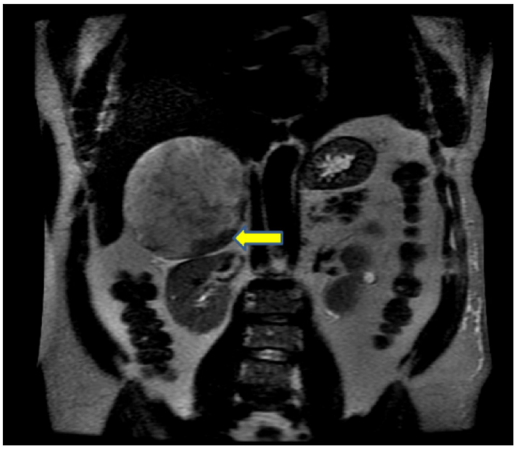

Fig. 2. Coronal section of T2 MRI displaying an adrenal myelolipoma with inferior area of hemorrhage (*yellow arrow*) and mass effect on the right kidney. (*Image obtained from* Zulia YS, Gopireddy D, Kumar S, et al. A rare case of hemorrhagic giant adrenal myelolipoma: radiographic and pathologic correlation. Cureus 13(8):e17353. https://doi.org/10.7759/cureus.17353 under Creative Commons Attribution License.[29])

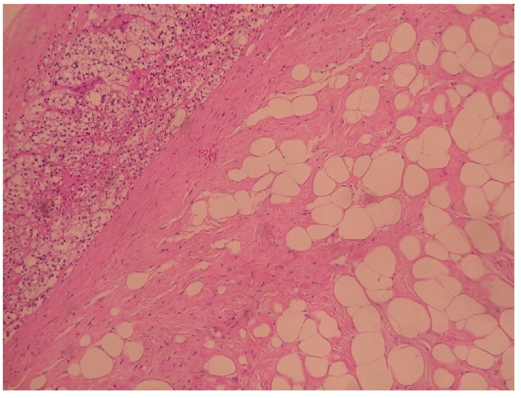

Fig. 3. Histology of a ganglioneuroma demonstrating adrenal cortex abutting Schwann cells and adipose tissue. (Sapalidis K, Mandalovas S, Kesisoglou I. Laparoscopic Excision of an Adrenal Ganglioneuroma Presented as an Incindentaloma of the Retro Peritoneum. Current Health Sciences Journal, 2018; 44(1): 71-75. https://doi.org/10.12865/CHSJ.44.01.12.[35])

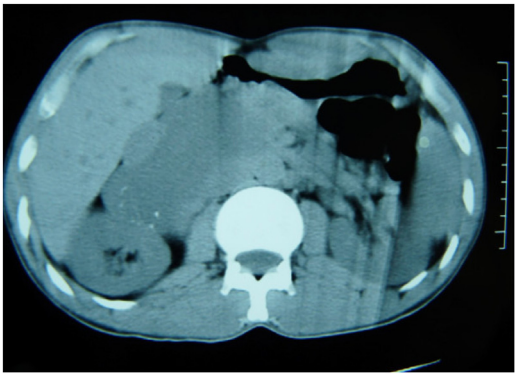

Fig. 4. A noncontrast CT demonstrating a right-sided adrenal mass with calcifications. (*Image obtained from* Majbar AM, Elmouhadi S, Elaloui M, et al. Imaging features of adrenal ganglioneuroma: a case report. BMC Res Notes 2014;7(1):791. https://doi.org/10.1186/1756-0500-7-791 under Creative Commons Attribution License.[43])

be accomplished with a metaiodobenzylguanidine (MIBG) scan. MIBG is a norepinephrine analog tagged to iodine-123 or iodine-131. Its usefulness in diagnosis of ganglioneuromas is based on increased uptake of the MIBG molecule in the ganglioneuroma, which is then associated with increased signal on imaging. MIBG uptake is observed in tumors with increased catecholamine activity.[38] Therefore, MIBG imaging is useful for differentiating ganglioneuromas from other adrenal tumors without catecholamine activity. However, some tumors, such as pheochromocytomas, paragangliomas, and neuroblastomas also exhibit catecholamine activity, and the urologist must consider these other tumors when evaluating a positive MIBG scan.[39] MIBG scans may also be useful to evaluate for recurrence after resection of ganglioneuroma. Operative indications for ganglioneuromas include size greater than 5 cm or rapid increase in size, suspicious features on imaging, compression of surrounding structures, symptoms including pain or discomfort, or hormonal activity.[40] Despite the typical benign course of these tumors, diagnosis is made via histology, and as radiographic findings can be ambiguous, many proceed to surgical resection.[40–42]

Neuroblastoma

Neuroblastomas are tumors that arise from neural crest stem cells. They are most commonly found in the adrenal medulla, but like ganglioneuromas, these tumors may develop anywhere along the sympathetic chain as well.[33] This tumor is the most common extracranial solid tumor in children and the most common malignancy in infants, although very rarely, cases can occur in adults as well.[44,45] About one-third of patients present with metastatic disease. Patients who present at the age of 18 months or less are more likely to have disease that spontaneously regresses or achieve remission with surgical treatment alone, whereas patients greater than age 18 are more likely to require medical therapy to assist with the management of their disease.[45] Patients may not exhibit symptoms, but when symptoms are present, they may be related to mass effect from the tumor, or be nondescript such as fevers, weight loss, and fatigue if disease is advanced.[45]

CT and MRI findings show a lobulated mass with heterogenous consistency, and they may exhibit necrosis or internal hemorrhage. On CT, calcifications are seen in 85% of cases as well as in 30% of cases on plain radiography. Both CT and MRI are useful for assessing invasion of surrounding structures, and special attention should be paid to the neural foramen and spinal canal. MIBG scan may also demonstrate high uptake in neuroblastoma as well.[33] A functional work-up of neuroblastoma should also include a urinary vanillylmandelic acid to homovanillic acid ratio, serum ferritin, and lactate dehydrogenase level, as any elevation of these levels indicates a worse prognosis.[33,45]

Preoperative staging of neuroblastoma is accomplished using the International Neuroblastoma Risk Group Staging System, which is based on image-defined risk factors and does not consider extent of surgical resection.[45,46] Tumor staging is classified as either L1, L2, M, or MS. L1 is defined as localized tumors that do not involve vital structures. L2 tumors are locoregional with one or more image-defined risk factors. M tumors are metastatic unless they are classified as MS, which is for metastatic disease in children under the age of 18 months but confined to skin, liver, and/or bone marrow. Image-defined risk factors include but are not limited to ipsilateral tumor extension in 2 body compartments, tumors that encase or compress vessels or other structures, or tumor invasion into adjacent structures.[46] L1 tumors are potentially resectable at the time of diagnosis, but the presence of an image-defined risk factors, which therefore classifies a tumor as L2, makes resection much more challenging and warrants consideration of antineoplastic medical therapy.[45]

Sex Hormone Producing Tumors

Cortisol and aldosterone are the most common substances secreted from functional adrenal tumors. However, in rare cases, adrenal tumors

may secrete androgens, typically dehydroepiandrosterone, dehydroepiandrosterone sulfate, or androstenedione (A4). Testosterone is directly secreted only in small amounts. In other, more exceedingly rare cases, adrenal tumors may secrete estrogens.[47] These tumors may be benign or malignant, malignant tumors are typically classified as ACC. One series found that 76% of ACCs were functional, and of these functional tumors, 46% co-secreted cortisol and androgens, and 6% secreted only androgens. Estrogen-secreting tumors are assumed malignant in all cases.[48]

Symptoms at presentations are usually manifestations or androgen or estrogen excess. For females with androgen-secreting tumors, virilization, hirsutism, or menstrual irregularity is typical, while males with estrogen-secreting tumors often display gynecomastia and hypogonadism. For males with androgen-secreting tumors, there does not appear to be any major effect from excess androgens. Females with estrogen secreting tumors may experience abnormal uterine bleeding or dense or tender breast tissue.[47]

Suspicion for androgen or estrogen excess that warrants biochemical workup can be challenging as many conditions may result in similar signs and symptoms. For example, only 0.2% of cases of androgen excess are caused by adrenal tumors, and about half of those are malignant. In contrast, polycystic ovarian syndrome is the cause of 95% of hirsutism in females.[47] As a result, the Endocrine Society recommends screening for androgen excess in females only if hirsutism can be qualified as moderate to severe.[49] Screening for androgen excess can be accomplished with a low dose dexamethasone suppression test which has been shown to be 100% sensitive and at least 88% specific for differentiating androgen-secreting adrenal tumors from polycystic ovary syndrome (PCOS) in 2 studies.[50,51]

Classification of an adrenal lesion as benign or malignant is challenging but follows the same methodology that has been discussed elsewhere in this article and issue of *Urologic Clinics of North America*. Namely, suspicion for malignancy should be increased for tumors that are greater than 4 cm and display heterogeneity with or without calcifications on contrast-enhanced CT. Furthermore, as most sex hormone producing tumors fall under the category of ACC, the imaging features of the tumors are also the same. Additional details of ACC imaging features may be found elsewhere in this issue.[47]

Definitive treatment for sex hormone secreting tumors is most safely achieved with en bloc resection. Even still, the recurrence rate is upwards of 80%. Surgical treatment may be combined with radiotherapy to further discourage recurrence, or to aid cases with positive margins or locoregional disease. Medical therapy may include mitotane for unresectable cases, but trials are ongoing with additional newer antineoplastic agents.[47]

Metastasis to the Adrenal Gland

Metastasis to the adrenal glands is a common occurrence. A large variety of malignancies have been shown to exhibit metastasis to the adrenal gland, including basal cell carcinoma, breast cancer, cervical cancer, chronic myelogenous leukemia, cholangiocarcinoma, contralateral ACC, gastrointestinal tumors, medullary thyroid carcinoma, prostate adenocarcinoma, pancreatic malignancies, renal cell carcinoma, seminomas, squamous cell carcinoma, thymomas, and urothelial carcinoma.[52,53] This diversity of primary lesions poses a diagnostic challenge to the physician when an incidental adrenal lesion is identified, and particularly when the patient has a known history of malignancy (**Fig. 5**).

Metastatic lesions are often well circumscribed with consistent internal appearance on radiographic imaging. Additionally, adrenal metastasis often lacks overt central necrosis (Boland and colleagues, 2008). The differentiating factor between metastasis and adrenal adenomas is the lipid content of the neoplasm. Metastatic sites do not have

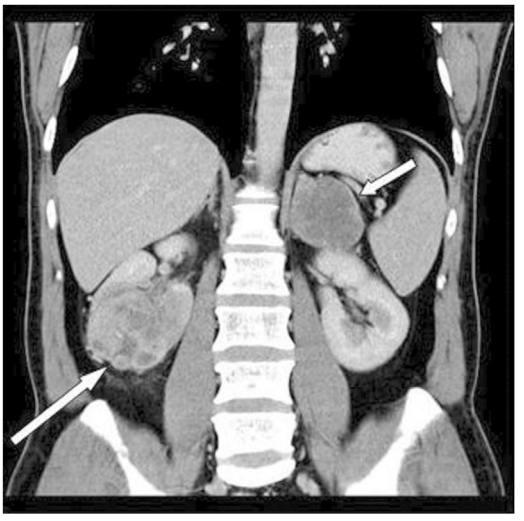

Fig. 5. Coronal CT slice demonstrating a left-sided adrenal metastasis (*short arrow*) from a right-sided renal cell carcinoma (*long arrow*). (*Image obtained from* Öztürk H. Bilateral synchronous adrenal metastases of renal cell carcinoma: a case report and review of the literature. Oncol Lett 2015;9(4):1897–901. https://doi.org/10.3892/ol.2015.2915 under Creative Commons Attribution License.[54])

a significant amount of lipid, and as such, they attenuate to a greater extent than adenomas (usually >10 HU) and washout is insignificant on washout studies.[55] There are some newer studies that suggest a small proportion of adrenal metastatic sites (about 7%) do attenuate less than 10 HU.[56,57] To further complicate matters, certain benign adenomas may have washout characteristics similar to hepatocellular and renal cell carcinoma metastatic sites.[56,57]

When an incidental adrenal lesion is identified, the growth rate of the lesion can be a useful tool for determining the need for additional diagnostic workup and the treatment plan.[58] Tissue sampling via adrenal biopsy remains the gold standard for diagnosis, but metabolic workup is required before any attempt at tissue sampling is undertaken for differentiating metabolically active adrenal nodules from metabolically inactive adrenal lesions.[53,59] Some data show that the rates of metabolic activity do not differ between individuals with and without a known history of malignancy. Therefore, it is important to gather further information about the potential origin of the neoplasm via laboratory workup.[60] Additionally, whereas metastasis in other organ tissue is often a late manifestation with widespread disease, adrenal metastasis can often occur early in the disease course, which informs decision making when considering metastatectomy. However, the therapeutic benefit of adrenal metastatectomy is heavily influenced by the primary disease process, and any surgical decisions must be made in the context of multidisciplinary discussion with the patient's primary oncology team.

While the literature supporting adrenal metastatectomy is sparse, retrospective cohort studies indicate that metastatectomy may offer oncologic benefit. In very select cohorts, surgical resection of isolated adrenal metastasis has been shown to produce survival rates greater than 25%.[61–63] In comparison of metachronous metastasis to the adrenal gland versus an isolated adrenal metastasis at initial diagnosis, a 2008 study found similar rates of 5-year survival for those individuals who undergo resection of the metastatic disease.[61] Additional data support metastatectomy in cases of nonsmall cell lung carcinoma or melanoma origin.[64,65] In the case of melanoma, one study demonstrated that patients treated with both systemic therapy and adrenalectomy had a median overall survival of 29.2 months compared with 9.4 months in the group treated only with systemic therapy.[66] For nonsmall cell lung cancer, data show that patients treated with chemotherapy and metastatectomy had an overall survival of 31 months compared with 8 months in the chemotherapy only group.[67] Renal cell carcinoma (RCC) is a common source of adrenal invasion, either directly via extension of large primary tumors due to the proximity of the adrenal gland and renal parenchyma, or as a site of metastasis.[68,69] However, while ipsilateral adrenal resection was initially described and often performed as part of a traditional radical nephrectomy, in the contemporary era, concurrent adrenal resection should only be undertaken if the adrenal gland shows radiographic abnormality or if the presence of a tumor thrombus is identified at or above the level of the adrenal gland.[70–73]

DISCUSSION

Adrenal incidentalomas are common and present a challenge to the urologist due to the breadth of benign and malignant lesions. Cross-sectional imaging offers great utility in the initial evaluation of adrenal neoplasms, but the patient's clinical presentation can help inform the need for additional diagnostic measures. It is important to consider that adrenal adenomas are more common with age, and so younger individuals presenting to the clinic warrant a higher index of suspicion for dangerous pathology.[1]

In addition to cross-sectional imaging, metabolic work-up can be informative of underlying lesion pathology. About 10% of adrenal lesions are shown to be metabolically active.[5] The American Association of Clinical Endocrinologists and American Association of Endocrine Surgeons recommend metabolic workup of incidental adrenal masses with 1 mg overnight dexamethasone suppression testing, plasma-free metanephrine levels, and, in the setting of hypertension, morning aldosterone, and aldosterone/renin ratio.[74] For lesions that do not show initial metabolic activity, repeat metabolic evaluation at a later time is not indicated unless new a symptom indicative of metabolic activity develops.[56]

Additional evaluation of the adrenal incidentaloma may be accomplished via biopsy in certain specific scenarios. However, adrenal biopsy is not without risk, which includes the potential for bleeding, hemothorax, pneumothorax, and needle tract seeding in the case of ACC. Therefore, if strong suspicion for ACC exists prior to biopsy, the risks of biopsy may not warrant the procedure. Furthermore, in the case of a pheochromocytoma, tumor disruption can lead to potentially dangerous catecholamine spillage. As a result, it is essential to exclude pheochromocytoma from the differential prior to biopsy to avoid intraoperative hypertension.

The utility of adrenal mass biopsy may be highest in patients who present with incidental adrenal neoplasms in the setting of a prior diagnosis of

extra-adrenal malignancy or discovery of a concurrent extra-adrenal mass. For patients with prior malignancy and an incidental adrenal mass suspicious for metastasis, the probability of a positive biopsy approaches 90% for lung cancer and 80% for renal cancer.[75]

SUMMARY

Rare adrenal tumors encompass a wide range of possible neoplasms, from metabolically active adenomas to adrenal metastases. The clinical presentation of these tumors varies, with many asymptomatic tumors discovered incidentally. Advanced imaging techniques and laboratory analysis are the hallmarks of adrenal tumor diagnosis. It is important to undertake a multidisciplinary approach to the management of patients with adrenal neoplasia, especially considering the variety of tumors and associated presentations. Endocrinologists, oncologists, neurosurgeons, radiologists, and urologists must remain up-to-date on medical and surgical diagnosis and management of such lesions in order to elicit superior outcomes.

CLINICS CARE POINTS

- All adrenal neoplasms should undergo metabolic workup to evaluate for hormonal activity.
- Biopsy of adrenal neoplasms can be informative in select cases, but benefits and risks must be carefully evaluated prior to performing the procedure.
- Adrenal adenomas are the most common tumor of the adrenal gland and incidence increases with age; therefore, younger individuals with incidentalomas warrant higher suspicion for dangerous pathology.
- A multidisciplinary approach that involves urologists, endocrinologists, neurosurgeons, radiologists, and oncologists can help ensure the good patient outcomes.
- CT imaging is the most useful modality for evaluation of adrenal incidentalomas, but further evaluation via MRI or metaiodobenzylguanidine scan can provide valuable information for some tumors.

DISCLOSURE

The authors have nothing to disclose.

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