Giant Adrenal Myelolipoma and Congenital Adrenal Hyperplasia: A Case Report and Review of the Literature

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Abstract

Purpose: Adrenal myelolipomas (AMs) are rare, benign tumors without endocrine activity comprised of mature adipose and hematopoietic tissue. Surgical excision may be required for lesions which have associated symptoms, those that are growing, or have features concerning for malignancy. Congenital adrenal hyperplasia (CAH) is often associated with adrenal masses such as AM. The majority of literature regarding AMs consists of case reports and case series with few describing giant AMs in the context of CAH.

Case Report: We present the case of a 50-year-old woman with CAH and surgical history relevant for left adrenalectomy who presented to the emergency department with abdominal pain. Computed tomography (CT) imaging led to a diagnosis of diverticulitis which was treated non-operatively. Their scan also revealed a 20x13x23-cm right retroperitoneal mass causing mass effect on the duodenum, pancreas, right kidney, and inferior vena cava. CT-guided biopsy demonstrated adrenal and adipose tissue with hemolymphoid aggregates possibly representing myelolipoma but unable to rule out malignancy. Due to concern for retroperitoneal liposarcoma, the patient underwent an exploratory laparotomy, resection of >40-cm right retroperitoneal mass, right nephrectomy, right adrenalectomy, and cholecystectomy. Final pathology demonstrated a myelolipoma with intra-tumoral ossification and hemorrhage as well as diffuse cortical hyperplasia with lymphoid aggregates. Due to acquired complete adrenal insufficiency, the patient required stress-dose steroids and steroid taper post-operatively.

Conclusion: Key points from this report include the occurrence of a giant AM in the context of CAH and special considerations in the diagnosis and operative approach of a giant retroperitoneal mass.

Introduction

Adrenal myelolipomas are benign, endocrinologically inactive tumors composed of mature adipose tissue and hematopoietic elements [1, 2] with an estimated incidence rate of 0.08-2.0% [2]. While most adrenal myelolipomas are diagnosed at autopsy, they have been increasingly detected as incidental lesions on cross-sectional imaging [1, 3] and are the second most common type of adrenal incidentaloma after adrenocortical adenomas [4]. First described in 1905, adrenal myelolipomas have been mainly described through case reports and case series [2, 5, 6]. Management is usually with observation, although surgery may be indicated for large or increasing size, diagnostic ambiguity, or symptoms such as abdominal pain, constipation, or emesis. Congenital adrenal hyperplasia (CAH) has been reported to be associated with adrenal myelolipomas to varying rates [7–9], and few case reports describe giant adrenal myelolipomas (>10-cm) in the context of CAH [4, 10–12]. In this case report, we describe a giant adrenal myelolipoma incidentally diagnosed in a woman with CAH who had previously undergone contralateral adrenalectomy.

Case Presentation

A 50-year-old woman with CAH presented to an outside hospital emergency department with abdominal pain. Computed tomography (CT) scan demonstrated uncomplicated left-sided diverticulitis and was also notable for a retroperitoneal mass measuring 23-cm in maximum diameter causing inferior-medial displacement of the duodenum, pancreas, and right kidney, and attenuation of the vena cava, however, without invasion. Following non-operative management of diverticulitis, the patient was referred to our surgical oncology clinic for evaluation.

The patient had a medical history significant for CAH for which they had been previously prescribed prednisone and spironolactone but stopped taking 10 years prior due to changes in health insurance. Pertinent surgical history consisted of vaginal reconstruction at a young age, open appendectomy, ventral hernia repair with mesh, and open left adrenalectomy 18 years prior for a reportedly benign adrenal lesion.

The patient reported increasing abdominal girth for 3 months associated with a 15-lb weight loss, early satiety, and occasional abdominal pain managed with non-opioid analgesia. The patient denied headaches, respiratory symptoms, nausea, emesis, or changes in bowel function. On physical exam the patient was normotensive, well appearing, and without hirsutism or Cushingoid features. Notable exam findings were faded abdominal surgical scars consistent with the patient's prior surgical history and distension and firmness in the upper abdomen slightly tender to palpation.

Laboratory studies were remarkable for elevated adrenocorticotrophic hormone (ACTH) 137 pg/mL, free testosterone 29.3 pg/mL, total testosterone 177 ng/mL, and renin activity 14.64 ng/mL/hr. Fractionated plasma metanephrines, luteinizing hormone, follicle-stimulating hormone, estradiol, morning cortisol level, hemoglobin A1C, and thyroid function tests were normal. Tumor markers were also notably normal with lactate dehydrogenase 129 U/L, alpha-fetoprotein <6.0 ng/mL, and beta-human chorionic gonadotropin <4 mIU/mL.

CT-scan demonstrated a surgically absent left adrenal gland and a large fat containing mass within the right retroperitoneum measuring at least 20 x 13.4 x 23-cm in diameter with mass effect on the liver, duodenum, and pancreas and displacement of the right kidney (Fig. 1). The right adrenal gland was unable to be visualized. CT chest was negative for metastatic disease.

Pathology from a CT-guided biopsy showed adrenal gland and adipose tissue with hematolymphoid aggregates possibly representing myelolipoma but unable to rule out malignancy. After multi-disciplinary discussions and evaluation by endocrinology and radiation oncology, it was determined that due to the large size of the mass and diagnostic uncertainty with concern for a retroperitoneal liposarcoma, the patient would benefit from surgical resection. The patient underwent an exploratory laparotomy, resection of right retroperitoneal mass, right nephrectomy, right adrenalectomy, cholecystectomy, lysis of adhesions, and complex abdominal closure (Fig. 2). Due to mass size, mass proximity to the inferior vena cava, and concern for malignancy, the patient was prepared for possible veno-venous bypass intra-operatively; however, bypass was not required. During the dissection, the superior aspect of the mass was noted to be adherent to the inferior vena cava and duodenum but without invasion and thus easily

separated. Intra-operative frozen specimen pathology showed a mixed inflammatory cell population. The patient was treated with stress-dose steroids of intravenous hydrocortisone prior to the case and continued every 6 hours.

The final surgical pathology was a myelolipoma. The specimen that was sent in two segments measured 5.5-cm and at least 40-cm in dimension. The mass was described grossly as encapsulated, well circumscribed, tan-yellow and red-brown, and made of fibro-adipose tissue containing hemorrhage and focal calcified necrosis (Fig. 3A). On microscopic pathology, the specimen was noted to have retroperitoneal extension, focal intra-tumoral ossification, hemorrhage, and diffuse cortical hyperplasia with pigment deposition and lymphoid aggregates (Fig. 3B-D). Margins were negative for tumor with no evidence of extension into adjacent structures. Cytogenetic studies were not performed due to lack of any dividing cells in the specimen. At surgical follow-up 4 weeks post-operatively, the patient was doing well on a steroid taper and had no evidence of post-operative complications.

Discussion

Adrenal myelolipomas are diagnosed at an average age of 51 years and occur equally between male and female patients [3, 4]. The etiology of adrenal myelolipomas remains unclear, although several hypotheses exist: 1) metaplastic changes of mesenchymal cortical cells in response to stress, infection, and/or necrosis, 2) metaplasia or hyperplasia of myeloid cells that migrated during embryogenesis *in utero*, 3) degeneration of adenomas or hyperplastic nodes within the adrenal cortex, 4) metaplasia of undifferentiated stromal cells, or 5) altered mesenchymal stem cell functions in the setting of abnormal hormonal stimuli [2, 4, 5, 7]. In the context of CAH, it has been theorized that myelolipomas develop as a result of chronic stimulation of the adrenal glands by ACTH [6, 11].

On CT, an adrenal myelolipoma appears as a round, well-defined, heterogeneous mass containing low-density, high-attenuation fat less than -30 Hounsfield units and may be associated with a pseudo-capsule, hemorrhage, or calcifications [3, 13, 14]. Ultrasound will demonstrate well-defined, hyperechoic fatty tissue mixed with hypoechoic myeloid tissue [3]. Magnetic resonance imaging may provide value in surgical planning [3] and differentiating myelolipomas from adrenal adenomas using fat suppression imaging protocols [15]. Extra-adrenal myelolipomas are even more rare than adrenal myelolipomas and occur in various locations including but not limited to the pre-sacral space, retroperitoneum, pelvis, and thorax [16]. Radiologic features of extra-adrenal myelolipomas may resemble adrenal tissues but also liposarcomas, thus presenting a diagnostic challenge [14].

Depending on the differential diagnosis and level of concern for possible malignancy, additional work-up for adrenal myelolipomas may include biopsy by fine needle aspiration [3]. Biopsy demonstrating mixed adipose and normal hematopoietic tissue are suggestive of adrenal myelolipoma [14, 17]. Gross surgical pathology will consist of a capsule or pseudocapsule of compressed zona glomerulosa and zona fasciculata with yellow and red or brown cut surfaces representing fat and hematopoietic tissue with varying levels of hemorrhage [4]. Microscopic pathology will show adipose tissue and hematopoietic

tissue containing erythrocytes, granulocytes, lymphoid cells, and megakaryocytes [2, 4]. Additionally, it is not uncommon to find other adrenal anomalies such as hyperplasia, calcifications, and adrenocortical adenomas within the same surgical specimen [4].

The majority of adrenal myelolipomas can be safely managed with observation [3, 16, 18]. A retrospective review of patients with adrenal myelolipomas by Han et al. reported that 13 of 15 patients who did not undergo resection remained asymptomatic over a 3-year observation period suggesting that patients may be safely observed [3, 18]. Additionally, Han et al. found that although over half of the tumors grew in size on serial imaging, growth did not appear to correlate with the development of symptoms [18]. The frequency of imaging studies in observing adrenal myelolipomas remains to be clarified. While Patel et al. recommend ultrasound or CT periodically over 1-2 years of observation [16], Gershuni et al. recommend one additional imaging study at 6-12 months after which if the lesion is stable in size, no further imaging is recommended [19]. Contrastingly, the European Society of Endocrinology recommends against serial imaging for lesions measuring less than 4-cm diameter with homogenous appearance and benign imaging [4].

Operative indications for adrenal myelolipomas include size, growth, symptoms, hormonal activity, and diagnostic ambiguity. Case studies have described a rare complication of spontaneous rupture and hemorrhage that is more likely to occur in myelolipomas >10-cm diameter. For this reason, current literature suggests that large myelolipomas should be considered for resection [12, 13, 16, 17]. Symptoms from larger lesions such as abdominal pain, constipation, and emesis are also relative indications for resection [1]. Sanders et al. performed a retrospective review of 7 patients with adrenal myelolipomas: of the 5 patients who underwent resection, 4 patients were symptomatic and had complete resolution of symptoms following resection. Meanwhile, asymptomatic patients remained asymptomatic without resections, thus supporting symptomatology as an indication for surgical intervention [2]. In our patient, it is unclear if their abdominal pain on presentation was solely attributed to diverticulitis; however, they did report several months of mild abdominal pain associated with early satiety and unintentional weight loss that were likely attributed to by the mass. Furthermore, the large retroperitoneal mass had radiologic features concerning for myelolipoma versus malignancy as well as indeterminate pathology after biopsy, thus warranting excision.

Although adrenal myelolipomas are endocrinologically inactive, they are commonly associated with endocrine disorders such as CAH [3, 8]. Nermoen et al. performed a population-based study of 101 adult Norwegian patients with 21-hydroxylase deficiency, of whom 6% were diagnosed with adrenal myelolipomas ranging from 33-55-mm in diameter [15]. Similarly, Decmann et al. reviewed 420 histologically verified cases of adrenal myelolipomas over a time period of nearly 50 years and found that CAH was associated with 10% of all reviewed cases [4]. Lastly, in a literature review of case series and case reports through PubMed and Cochrane Library databases, Shenoy et al. found that nearly half of cases of adrenal myelolipomas associated with endocrine dysfunction occurred in the context of CAH [9].

The need for endocrine evaluation of suspected adrenal myelolipomas remains unclear with conflicting recommendations and guidelines. The American Association of Clinical Endocrinologists recommends endocrine screening of all adrenal incidentalomas and regular endocrine surveillance if they do not meet surgical resection criteria, with the exception of adrenal myelolipomas [20]. Contrastingly, the European Society of Endocrinology recommends at least overnight dexamethasone suppression testing in all patients with adrenal incidentalomas, without the exclusion of myelolipomas [21]. Varying approaches to endocrine testing have been described. Shenoy et al. suggest endocrine screening for patients at high risk of associated endocrine dysfunction (hypertension, diabetes, pre-diabetes, young age, bilateral adrenal myelolipomas) [9], while Maas et al. recommend hormonal screening of all incidentalomas with plasma free metanephrines, urinary fractionated metanephrines, and 1 mg dexamethasone suppression test [22]. Gershuni et al. make similar recommendations in addition to considering evaluating for cortisol dysfunction and suggest excluding small adrenal myelolipomas from endocrine testing [19]. Lastly, because adrenal myelolipomas may be associated with hormonal hyper-secretion secondary to concurrent adenomas or adrenal hyperplasia, endocrine evaluation should be considered in patients with clinical features or suspected co-existing adenomas [6]. Given our patient's history of untreated CAH, we elected to pursue a full hormonal work-up. While guidelines remain unclear, patients should be evaluated on a case-by-case basis with low threshold for evaluation for hormone production abnormalities, especially in patients with predisposing conditions.

Our case report is one of several describing a giant myelolipoma in the context of CAH. Similar to our patient, German-Mena et al. described a patient with untreated CAH with a symptomatic 24-cm giant adrenal myelolipoma that was resected [11]. The patient described by German-Mena et al. also had a contralateral adrenal myelolipoma that was managed with observation due to its small size <10 cm [11]. Additionally, Ioannidis et al. described a young woman with CAH with symptomatic, bilateral giant adrenal myelolipomas that were both resected: much like our patient, their patient also required post-operative steroids for iatrogenic adrenal insufficiency [12]. Our patient had bilateral adrenal masses occurring over 10 years apart, suggesting that CAH patients may remain at long-term risk of developing adrenal masses.

In conclusion, we describe the successful management of a complex patient with untreated CAH and prior adrenalectomy who underwent resection of a giant adrenal myelolipoma with resultant iatrogenic complete adrenal insufficiency. Key considerations in the evaluation and management of a suspected giant adrenal myelolipoma include vigilance for the inability to rule-out malignancy, staging, biopsy, endocrine function screening, and safe operative interventions that allow complete tumor resection, especially when malignancy remains part of the differential diagnosis. Lastly, we recommend early collaboration with endocrine specialists in guiding steroid therapies intra- and post-operatively for patients at risk of adrenal insufficiency.

Declarations

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Author Contributions:

Stephanie Chen prepared the manuscript and figures 1-2. Monica Justo contributed to the manuscript text and obtained informed patient consent. Kenekchukwu Ojukwu and Bonnie Balzer analyzed the pathology specimens and prepared figure 3. Ashley Russo performed the operation and managed care of the patient. Allan Silberman performed the operation and contributed to the manuscript. Alexandra Gangi was the lead surgeon who performed the operation and dictated all work-up and care of the patient. All authors read and reviewed the manuscript.

Ethics Approval:

This is a case report and does not require ethical approval, per the Cedars-Sinai Medical Center Office of Research Compliance and Quality Improvement as documented in form HRP-171.

Consent to Participate:

No procedures were performed solely for research purposes.

Consent to Publish:

The authors affirm that written informed consent was obtained from the patient for publication of this case report and accompanying figures. A copy of the consent form is available for review by the Editor of this journal.

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Figures

Figure 1

A large right retroperitoneal mass incidentally detected on CT scan caused inferior displacement of the right kidney and attenuation of the inferior vena cava

Figure 2

Surgical field (left) and gross specimen (right) after resection

Figure 3

Gross and microscopic specimens of the resected adrenal myelolipoma demonstrating the following: (A) yellow-tan cut surface with red-gray areas; (B) thinned adrenal cortex and presence of intra-tumoral hemorrhage; (C) clear demarcation between the underlying lesion (*) and the adrenal cortex which is typically thinned, although this patient has adrenocortical hyperplasia; (D) mature adipocytes (**) and three distinct hematopoietic cell lines (erythroid, myeloid, and megakaryocytic)