Primary Epithelioid Angiomyolipoma of Adrenal Gland: Case Report and Literature Review

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Abstract: Angiomyolipomas (AMLs) are mesenchymal tumours derived from perivascular epithelioid cells. Although AMLs are generally known as benign and extremely rare epithelioid variants of AML, they may be potentially aggressive. Here we present an adrenal epithelioid AML and the literature review. A 64-year-old female patient was diagnosed with a left adrenal mass detected incidentally on ultrasonography. Preoperative abdominal CT (computed tomography) showed a 95×68 mm heterogeneous contrast enhancement mass lesion in the left adrenal gland. The lesion was hormone inactive in the endocrinological evaluation, and left laparoscopic adrenalectomy was performed. The patient was discharged on the 2nd postoperative day. Pathology was reported as epithelioid subtype AML. The patient has no local recurrence or metastasis in the 18-month follow-up period and imaging. Adrenal epithelioid AML is an extremely rare and potentially aggressive variant. According to the literature, open or laparoscopic adrenalectomy seems to be suitable option for disease management.

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Introduction

Angiomyolipomas (AMLs) are benign mesenchymal tumours which originate from perivascular epithelioid cells with the substance of mature fat cells, blood vessels, and smooth muscle cells. General prevalence is 4–5/1000 and female to male ratio is approximately 1.5. AMLs are most commonly found in the kidney (Aydin et al., 2009; Li et al., 2015). Extrarenally located AMLs are rare in the literature. To our knowledge, 28 cases of adrenal AML have been reported in the literature up to date. With the present report, 5 were reported as epithelioid angiomyolipoma (eAML). While they are usually diagnosed on incidental imaging, larger AMLs may cause bleeding and pain. The growth rate of AMLs is slow, and the probability of morbidity is very low.

Epithelioid subtype AMLs are distinguished from other AMLs by their potential to display malignant character. In this extremely rare variant of AML, immunoreactivity for myelocytic markers such as human melanoma black 45 (HMB-45), predominance of epithelioid cells, and absence of mature adipocytes are characteristic diagnostic features (Konosu-Fukaya et al., 2014). The renal eAML has limited clinical data in the literature. Likewise adrenal localized eAML is very rare. In this manuscript, we report a case with adrenal eAML who was successfully treated with surgical resection and English-language literature reviewed by scanning the publications up to date. This report has been prepared in accordance with the current CARE checklist.

Case report

A 64-year-old female patient was admitted to our clinic due to microscopic hematuria. Patient had no family history of malignancy, no smoking or alcohol addiction. She had a history of hysterectomy due to premalignant cervical lesion and previous subtotal thyroidectomy. The patient was on regular medical therapy due to the diagnosis of hypertension and hypothyroidism and had no other chronic diseases. An incidental left adrenal mass was detected on urinary system ultrasonography. Preoperative contrast-enhanced abdominal CT (computed tomography) showed a 95×68 mm heterogeneous, spherical-shaped mass lesion in the left adrenal gland with smooth borders. The Hounsfield unit (HU) of the lesion was measured as 66 ± 12 to 79 ± 9 on non-contrast and contrast sections respectively (Figure 1). Furthermore, there was a second lesion with a diameter of 14 mm compatible with AML in the right kidney posterior middle zone. During physical examination, there was no finding other than the scar of the hysterectomy in the pelvis. The lesion was hormone inactive in the endocrinological evaluation, and left laparoscopic adrenalectomy was performed. There were no postoperative complications. The patient was discharged on the 2nd postoperative day. Gross examination revealed a grey-orange 8.5 cm diameter solid lesion with hemorrhagic foci reaching 1 cm in some areas and including adipose adrenal tissue with the largest diameter of 2 cm (Figure 2). In the microscopic examination, vimentin, calretinin,

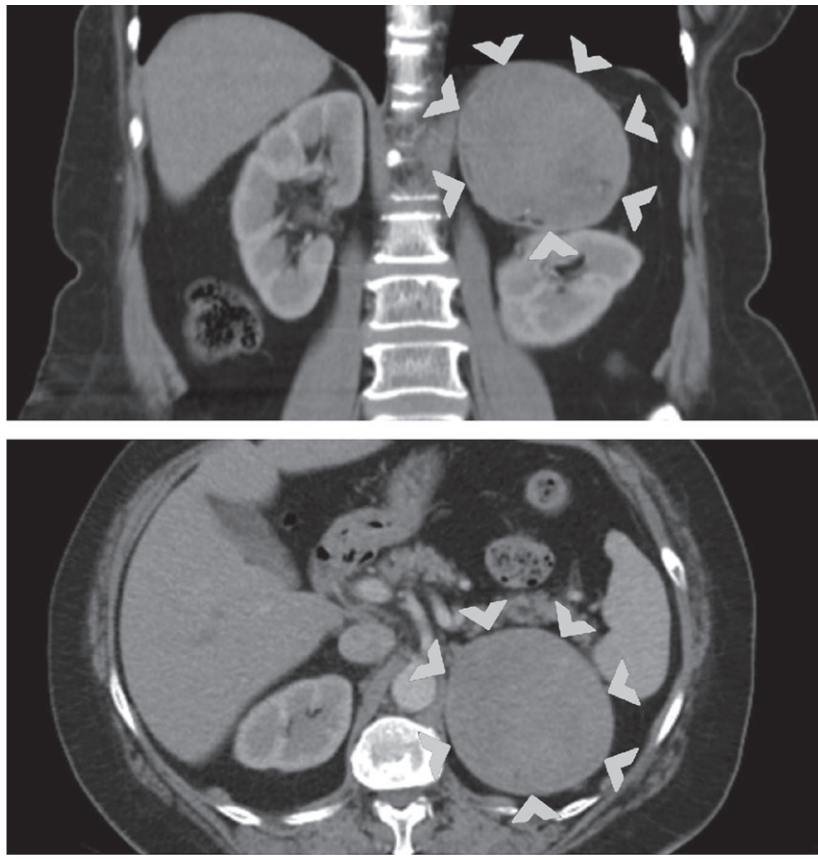

Figure 1 – Axial and sagittal computed tomography section of 95×68 mm heterogeneous, spherical-shaped mass lesion in the left adrenal gland with smooth borders.

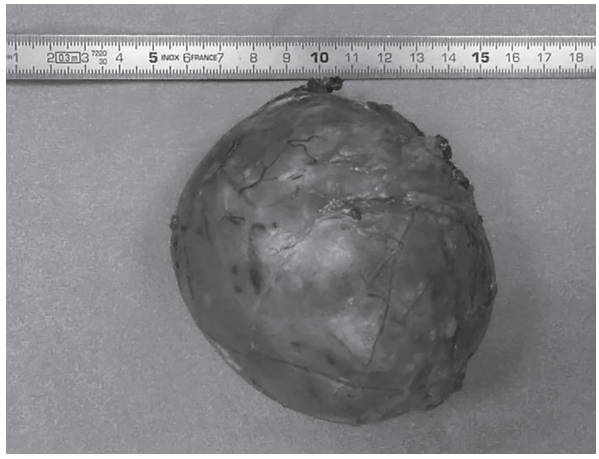

Figure 2 – Macroscopic aspect of the adrenalectomy specimen.

and Melan A were positive, and the findings were evaluated in favour of epithelioid angiomyolipoma. No histomorphological risk factor was observed in favour of an aggressive clinical course, except for the large diameter of the lesion. There was no local recurrence or metastasis in the 18-month follow-up period and imaging. Preoperatively diagnosed 14 mm AML in the right kidney persisted.

Discussion

We reported a rare case of epithelioid AML of adrenal gland. The PubMed, Medline, Web of Science databases were searched for case reports and case series of adrenal angiomyolipoma published in English language between January 1, 1980, and December 31, 2021. The following key words were used: (Adrenal Glands or Adrenal Gland or Gland Adrenal or Glands Adrenal) and (Angiomyolipoma or Angiomyolipomas or epithelioid angiomyolipoma).

The most common extrarenal site for angiomyolipomas is the liver. AML also may be encountered in retroperitoneum, adrenal, breast, genital tract, pancreas, colon, and several other locations (Lam and Lo, 2001; Godara et al., 2007). According to our literature search, 28 cases have been reported for adrenal localized AML with the presented case. Only 5 of these cases are eAML (Table 1). AML is more common in the 5th decade and approximately two times more often diagnosed in women. In this present report the mean age of diagnosis of adrenal AML is 47 and female to male ratio is 4:3. It is known that the frequency of AML increases in hereditary diseases such as tuberous sclerosis (TSC) and lymphangiomyomatosis. Tuberous sclerosis has been reported in approximately 20% of patients in recent AML case series (Aydin et al., 2009). Three of the patients with adrenal AML reported in this review had a history of TSC (11%). Sporadic lymphangioleiomyomatosis was reported in 1 patient. Two of 5 patients with eAML have a history of TSC. Although the limited case number restricts for consequences, history of TSC may be related with increased risk of epithelioid subtype likelihood on adrenal AMLs.

Urgent surgical procedures may be required due to bleeding, which can result in organ loss or mortality (D'Antonio et al., 2009). D'Antonio et al. (2009) reported a case of adrenal eAML with kidney loss resulting in hemorrhagic shock due to spontaneous retroperitoneal hemorrhage. The most important risk factor associated with bleeding is the size of the lesion. Patients who have large AMLs with increased bleeding risk and are not suitable for surgical intervention or unwilling to undergo surgical intervention, selective arterial embolization is an eligible option. Antar et al. (2017) reported an unsuccessful attempt for selective arterial embolization in a case of adrenal AML, with the thought that the lesion might originate from the kidney. Then, they reported that the adrenalectomy procedure was performed. Our literature search revealed that the data related to the successful use of selective arterial embolization in adrenal localized AML does not exist. The use of mTOR (mammalian target of rapamycin) inhibitors in large or symptomatic

Table 1 – Demographic, imaging, and pathological characteristic of epithelioid angiomyolipoma in the literature

Author name (publication date)	Age	Sex	Laterality (left or right)	Largest diameter (cm)	Imaging features	Surgery	Open or laparo-scopic	Histo-pathological features	Follow--up (years)
D'Antonio et al. (2009)	42	M	L	6	Heterogeneous contrast enhancement with a lipidic struma and sign of haemorrhage	Nephrectomy and adrenalectomy	open	Focally seen adipose tissue, HMB-45+, cyto-keratin–, sign of haemorrhage	1
Komarowska et al. (2015)	39	M	R	16	Large retroperitoneal tumour with uncertain origin	Nephrectomy and adrenalectomy	open	HMB-45+, Me-lan A+, SMA+, tumour was infil-trated capsule of right kidney	0.5
Valeshabad et al. (2019)	33	F	L	7.3	Solid and enhancing soft-tissue density mass in the left adrenal gland, which enlarged from 1.5 cm to 7.3×6.9 cm over approximately 21 months	Adrenalectomy and partial nephrectomy (for renal AML)	–	Melan A+ cytoke-ratin and largely PAX8 negative	–
Torres Luna et al. (2020)	32	M	R	20	Areas of necrosis, hemorrhage, and parenchymal calcification	Nephrectomy and adrenalectomy	open	Melan A+, MART-1+, HMB-45+	–
Present case	64	F	L	9.5	Round mass lesion with heterogen contrast enhancement. Additional 14 mm right sided AML	Adrenalectomy	laparo-scopic	Melan A+, vimen-tin+, calretinin+	1.5

M – male; F – female; R – right; L – left; AML – angiomyolipoma; HMB-45 – human melanoma black 45; SMA – smooth muscle actin

AMLs is spreading in recent years especially in patients who have TSC. There is no information in the literature regarding its use in adrenal localized AMLs.

Classical fat-predominant AMLs may be detected by the typical diagnostic features of the fat density on imaging. Negative HU measurement in non-contrast CT imaging gives an important clue for diagnosis. In eAML located in the kidney, the decision to surgery is usually taken with the preliminary diagnosis of RCC (renal cell carcinoma). It seems difficult to diagnose with the typical imaging finding for eAML in preoperative imaging. For the adrenal eAMLs reported in this review, the mean diameter on preoperative imaging was calculated as 11.8 cm (6–20 cm). Only D'Antonio et al. (2009) defined a lesion with significant fat density on preoperative CT. In other eAML cases, the presence of an area of fat density was not reported on imaging. Surgery indications are usually made by the suspicion of adrenocortical carcinoma (D'Antonio et al., 2009; Komarowska et al., 2015; Valeshabad et al., 2019; Torres Luna et al., 2020).

In pathological classification, AMLs are evaluated within the group of perivascular epithelioid cell (PEComa) tumours. Angiomyolipomas, clear cell "sugar" tumour (CCST), pulmonary lymphangioleiomyomatosis, clear cell myomelanocytic tumour of the falciform ligament, and rare clear cell tumours of other anatomical regions are included in this group. In the WHO (World Health Organization) 2002 classification, PEComa was defined as "a mesenchymal tumour composed of histologically and immuno-histochemically distinctive perivascular epithelioid cells". In epithelioid AML, the lesion is microscopically composed of pure or dominant large epithelioid cells. These cells are characterized by large hyperchromatic nuclei with a clear or eosinophilic cytoplasm. Varying degrees of nuclear atypia may be observed. The size of the lesion, growth pattern, nuclear grade determined by microscopic examination, mitotic activity, necrosis and vascular invasion are poor prognostic indicators. In our case, only increased size of lesion existed as a poor prognostic factor. Myelocytic marker positivity in epithelioid cells is one of the characteristic features for diagnosis. Desmin and smooth muscle actin (SMA) positivity were other immunohistochemical markers indicating the presence of smooth muscle components in the tissue.

The data on prognosis and malignancy potential in eAML are controversial in the literature due to limited number of the cases. In general, an aggressive course has been reported in approximately one third of the cases. However, Aydin et al. (2009) reported no recurrence or metastasis in a large case series of 15 patients with renal eAML and an overall follow-up time of 5.1 years. Since the literature data usually consists of case reports of a single or several patients, the authors' tendency to report tumours with an aggressive course may overestimate the potential for an aggressive course (Aydin et al., 2009). Aggressive course and local recurrence were reported in 1 of 5 eAML cases reviewed in this report. However, except for our case, the postoperative follow-up period was not longer than 1 year in any of the 4 cases presented.

In conclusion, adrenal epithelioid AML is an extremely rare and potentially aggressive variant. According to the literature, open or laparoscopic adrenalectomy seems to be suitable options for disease management. There is insufficient data on arterial embolization and the use of mTOR inhibitors in case of adrenal AML.

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