Angiomyolipoma of the adrenal gland: clinical experience and literature review

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Abstract: Angiomyolipomas, a type of benign mesenchymal tumor originating from perivascular epithelioid cells, are composed of mature adipose tissue, smooth muscle, and thick-walled vessels. With fewer than 20 cases reported in English literature, adrenal angiomyolipoma is extremely rare. In these cases, the patient is usually asymptomatic and the tumor is found incidentally. Adrenal angiomyolipoma has never been reported in association with lung cancer. A 62-year-old man presented with an enlarged mass in the left adrenal gland. The mass had persisted for two years previously and was first discovered during a routine follow-up CT examination after lung cancer resection in 2016. Subsequently, partial left adrenal resection was performed. Postoperative histopathology confirmed a benign angiomyolipoma comprising adipose tissue, blood vessels, and smooth muscle cells. At three months follow-up, the patient was alive and had experienced no recurrence after the operation. Eighteen cases were identified on literature review, among which no patients had a history of lung cancer. These cases occurred more often in females and lesions mostly located on the right side. All of the reported cases were nonfunctional, ranging in size from 0.2 to 16 cm (95% of the masses exceeding 4 cm). In this case report, we consider a rare case of a patient with an adrenal angiomyolipoma with a history of lung cancer. Adrenal angiomyolipoma should be considered as one of the differential diagnoses of adrenal metastasis for patients with a history of primary tumors.

Keywords: Case report; angiomyolipoma; adrenal metastasis; imaging; computed tomography (CT)

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Introduction

Angiomyolipoma, a benign form of tumor of mesenchymal origin, is characterized by smooth muscle cells, thick-walled blood vessels, and adipose tissue. Angiomyolipoma is most commonly found in the kidney and in the extra-renal area in the liver. It is rarely reported that angiomyolipoma is found in the retroperitoneum, spleen, bone, lung, ovary and so on (1). Adrenal angiomyolipomas are extremely rare and usually asymptomatic. Patients with adrenal angiomyolipoma may present with nonspecific symptoms, such as abdominal pain. The detection of adrenal angiomyolipoma is usually incidental, arising from a physical examination or routine ultrasound (US) and computed tomography (CT) examination for another unrelated disease (2). Little is known about the disease, and in cases of primary malignancies with adrenal spread, such as lung cancer, distinguishing adrenal incidentalomas from metastasis presents a considerable diagnostic challenge (3,4). Herein, we describe the case of a patient with adrenal angiomyolipoma who had previously undergone lung cancer

resection, with the aim of sharing the clinical experience and CT imaging distinctions between adrenal angiolipoma and tumor metastasis. Finally, we carried out a review of the relevant literature, and the information is summarized in *Table 1*. We present the following case in accordance with the CARE reporting checklist (available at http://dx.doi.org/10.21037/atm-20-3147).

Case presentation

A 62-year-old man presented at our hospital with a small oval-bounded mass in the left adrenal gland. The mass was first discovered during a routine follow-up CT examination after the patient received lung cancer resection in 2016. During a two-year follow-up period, the mass increased from 1 to 3.5 cm (the maximum cross section) (*Figures 1*,*2*). Consequently, the patient was referred to our hospital for more complete evaluation and management.

The patient exhibited no symptoms, and a physical examination of the patient's abdomen proved unremarkable. A history of lung cancer resection was recorded. The laboratory tests revealed that the patient's epinephrine, 24-hour urinary catecholamine, aldosterone and plasma cortisol levels were all within the normal range.

On dual-phase enhanced CT scan, the mass displayed ring enhancement surrounded by unenhanced flocculent exudate (*Figure 2*). A diagnosis of adrenal metastases was made based on the CT imaging findings and the patient's history of lung cancer.

Subsequently, the patient underwent retroperitoneal laparoscopic partial resection of the left adrenal gland under general anesthesia. Postoperative pathology indicated left adrenal adipose tissue and hemangiomatous hyperplasia (*Figure 3*); thus, the diagnosis of adrenal angiomyolipoma was reached. After seven days, the patient recovered with no surgery-related complications and was discharged. At three months follow-up, the patient was alive and had experienced no recurrence after the operation.

Literature review

The PubMed, Medline, Web of Science, and Ovid databases were searched for English-language case reports and case series of adrenal angiomyolipoma published between January 1, 1990 and March 31, 2019. The following key words were used: (Adrenal Glands or Adrenal Gland or Gland Adrenal or Glands Adrenal) and (Angiomyolipoma or Angiomyolipomas). The flow chart of the literature screening process is set out in *Figure S1*. A total of 15 full-text articles involving 18 cases were included for analysis. For each case, the first author, publication year, and country were documented, along with the patient's age, sex, size, weight, affected side, symptoms, imaging characteristics, complications, and follow-up results (*Table 1*).

According to the literature, angiomyolipomas are most commonly found in the kidneys and are rare in the adrenal gland. Prior to our case, only 18 cases of adrenal angiomyolipoma had been documented, among which none of the patients were reported to have a history of cancer.

The 19 reported cases (including of our case) of adrenal angiomyolipoma comprise 13 women and 6 men, with a female to male ratio of 2.2 to 1. Remarkably, as shown in *Figure S2*, the age distribution of the female patients was mainly between 30 and 50 years old, and these patients predominantly suffered from abdominal back pain, with lesions mostly located on the right side. However, the ages of the male patients were more scattered and most of the lesions were located on the left side. All of the adrenal angiomyolipomas reported in the literature were nonfunctional (5), and ranged in size from 0.2 to 16 cm, with 95% of the masses exceeding 4 cm.

Discussion

In this case report, we reported a case of a 62-year-old man who developed an enlarged mass in the left adrenal gland after lung cancer resection. Due to the patient's history of lung cancer, clinicians were highly concerned about whether the adrenal mass was a metastasis. As mentioned in the literature, adrenal metastasis is the second most common tumor after adrenal adenoma, especially in people with a history of primary tumors, and solitary adrenal metastasis is common in patients with lung cancer with adrenal spread (6). The diagnosis of adrenal metastases was supported by the imaging features and the patient's clinical history of lung cancer. Consequently, we provided a diagnosis of adrenal metastasis; however, the pathological results after the operation confirmed that the mass was in fact an adrenal angiomyolipoma.

Angiomyolipoma, a benign mesenchymal tumor originating from perivascular epithelioid cells, is composed of mature adipose tissue, smooth muscle, and thick-walled vessels (3). Angiomyolipoma is commonly found in the kidneys and liver but rarely appears in other places. Adrenal angiomyolipoma is typically asymptomatic and found incidentally during physical examination or routine

Table 1 Clinical features of the cases of adrenal angiomyolipoma from the literature review

Case No.	Author/year/country	Sex/age	Size (cm)/weight (g)	Side	Presentation	Imaging	CT		MRI		Complication	Follow-up (year)
							Non-enhanced (density/calcification)	Contrast-enhanced	Non-enhanced (T1WI/T2WI)	Contrast-enhanced		
1	Lam/2001/China	F/46	8.0 (CT)/115	L	Asym	CT	Heterogeneous/–	Heterogenous contrast enhancement	–	–	Ovarian cystic teratoma	1
2	Lam/2001/China	M/20	0.2 (on specimen)/3	L	Asym	–	–	–	–	–	Tuberous sclerosis	8
3	Elsayes/2005/USA	F/49	12.2×9.8×6.8 (MRI)/–	R	Asym	CT/MRI	–	–	Bright fat signal/hyperintensity	Mild enhancement	–	–
4	Sutter/2007/Switzerland	F/32	6.0 (CT)/–	R	AP	CT/MRI	–	Partially enhancing	–	Mild enhancement	Lymphangioleiomyomatosis	–
5	Godara/2007/India	F/45	15.0×12.0 (US)/–	L	EP	CT	Nonhomogeneous/–	_	–	–	–	1.5
6	D'Antonio/2009/Italy	M/42	6.0×4.5 (CT)/100	L	FP and BP,	CT/MRI	Heterogeneous/–	Heterogeneous contrast enhancement	–/hyperintensity	–	Hypertension, hypercholesterolemia anemia	1
7	Yener/2011/Turkey	F/45	5.0×6.0 (CT)/–	R	EP	CT/US	Low-attenuation/–	–	–	–	–	0.3
8	Hu/2012/China	F/55	15.0×16.0 (CT)/–	R	AP	CT/US	–	–	–	–	–	0.5
9	Goswami/2014/India	F/43	9.5×8.0×2.0 (MRI)/–	R	GP	MRI	–	–	Hyperintensity/hyperintensity	–	–	–
10	Zhao/2014/China	F/47	6.0 (MRI)/45	L	Asym	CT/MRI	–	–	Hyperintensity/hyperintensity	–	–	6.2
11	Zhao/2014/China	M/70	8.0 (MRI)/121	L	Asym	CT/MRI	–	–	hyperintensity/hyperintensity	–	–	5.4
12	Li/2015/China	M/53	9.0×6.0 (US)/–	L	AP	CT/MRI/US	–	–	–/hyperintensity	–	–	0.7
13	Antar/2016/USA	F/48	10.0 (CT)/290	R	FP	CT	–	–	–	–	–	0.6
14	Kwazneski/2016/USA	F/65	11.3×9.4 (CT)/626	R	AP	CT/US	Heterogeneous/scattered calcification	–	_	_	Hypothyroidism, coronary artery disease	3
15	Ghimire/2017/China	M/36	5.2×4.2×3.1 (CT)/–	R	Asym	CT/MRI	–	–	–	–	–	–
16	Ghimire/2017/China	F/61	8.6×9.5×8.1 (CT)/–	R	Asym	CT/MRI	–	–	–	–	–	–
17	Duralska/2018/Poland	F/35	7.0×6.0×9.0 (MR)/–	L	AP	CT/MRI/US	–	–	–	–	–	2
18	Kord/2019/USA	F/33	7.3×6.9 (CT)/–	L	AP	CT	Heterogeneous/–	Enhanced soft-tissue Density mass	–	–	TS	–
19	PC	M/64	3.6×4.0 (CT)/–	L	Asym	CT	Low-attenuation/–	Ring enhancement	–	–	Lung cancer	0.3

PC, present case; F, female; M, male; L, left; R, right; US, ultrasound; CT, computed tomography; MRI, magnetic resonance imaging; AP, abdominal pain; IF, Incidental finding; FP, flank pain; Asym, asymptomatic; BP, back pain; GP, groin pain; EP, epigastric pain; –, not recorded

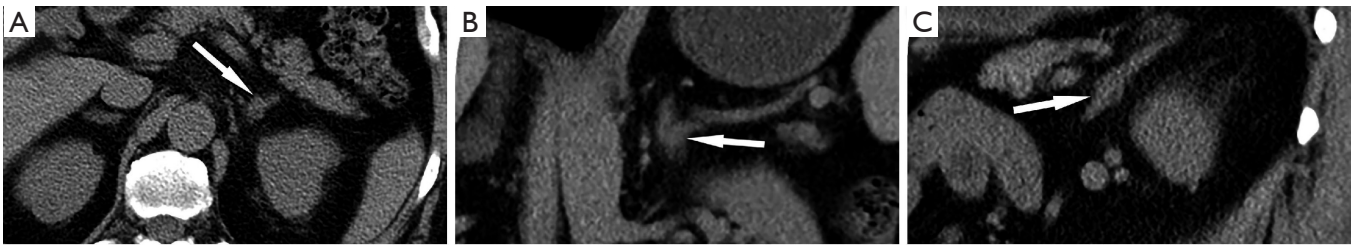

Figure 1 A 62-year-old male patient who had previously undergone lung cancer resection in 2016 underwent routine follow-up CT examination, which found a small oval-bounded nodule (white arrows) in the left adrenal gland. (A) Axial unenhanced CT image; (B) coronal unenhanced CT image; (C) sagittal CT image.

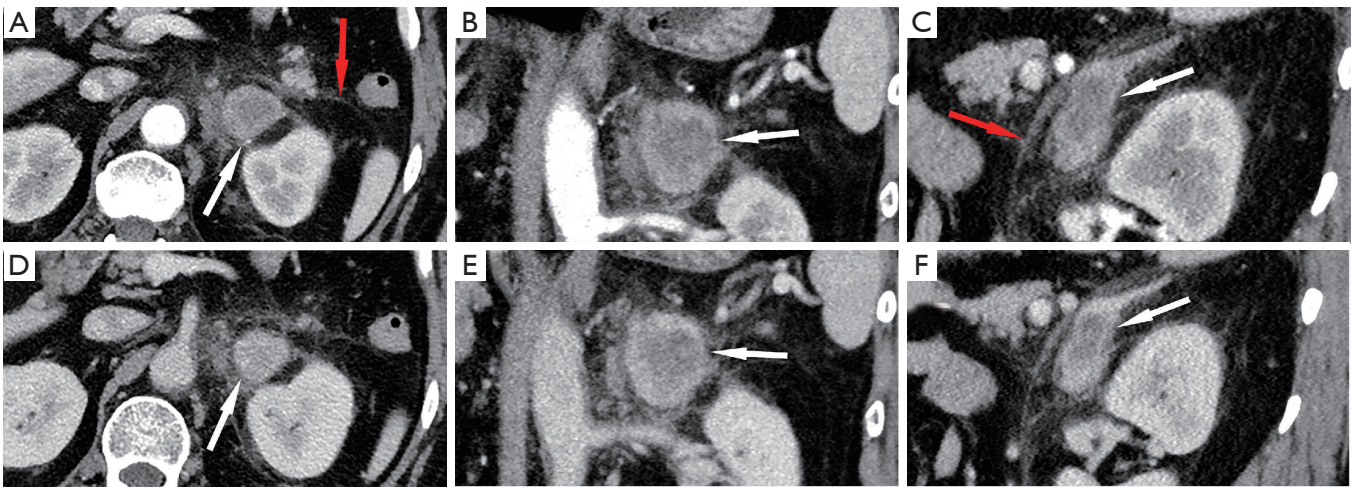

Figure 2 The mass (white arrows) on enhanced CT was significantly larger in 2018 than in 2016 and displayed ring enhancement with unenhanced flocculent exudate around it, accompanied by thickened renal peritoneal fascia (red arrows). The mass showed obvious ring enhancement on the dual-phase enhanced CT scan. (A) Axial enhanced CT image in the arterial stage; (B) coronal enhanced CT image in the arterial stage; (C) sagittal CT image in the arterial stage; (D) axial enhanced CT image in the venous phase; (E) coronal enhanced CT image in the venous phase; (F) sagittal enhanced CT image in the venous phase.

US and CT examinations for another unrelated disease. Imaging examinations, such as US, CT, and magnetic resonance imaging (MRI), serve an important role in the diagnosis of adrenal angiomyolipoma, and the findings vary depending on the proportion of the components. Adrenal angiomyolipoma usually appears on imaging as round or ovoid with clear borders, low density, and no or mild enhancement. If the tumor is large (>4 cm) and inhomogeneous or has scattered calcifications, it is often misdiagnosed as a malignant tumor (7-10). One reported case of adrenal angiomyolipoma presented on US as a hyperechoic mass (11). Originating from perivascular epithelial cells, angiomyolipoma has a unique immunohistochemical and morphological structure (1). The immunohistochemical characteristics of the tumor are the positive expression of melanocyte markers (HMB-45, Melan-A, and Desmin) and smooth muscle actin (SMA) with negative expression of cytokeratin. The positive expression of HBM-45 in epithelioid or fusiform tumor cells is a diagnostic clue and is helpful in distinguishing this tumor from other similar lesions (4).

Based on large autopsy studies, the percentage of malignant tumors that progress to metastases in the adrenal glands is approximately 58% for breast cancer, 42% for lung cancer, 10.3% for esophageal cancer, 16% for gastric cancer, 50% for malignant melanoma, and 14% for colorectal cancer.

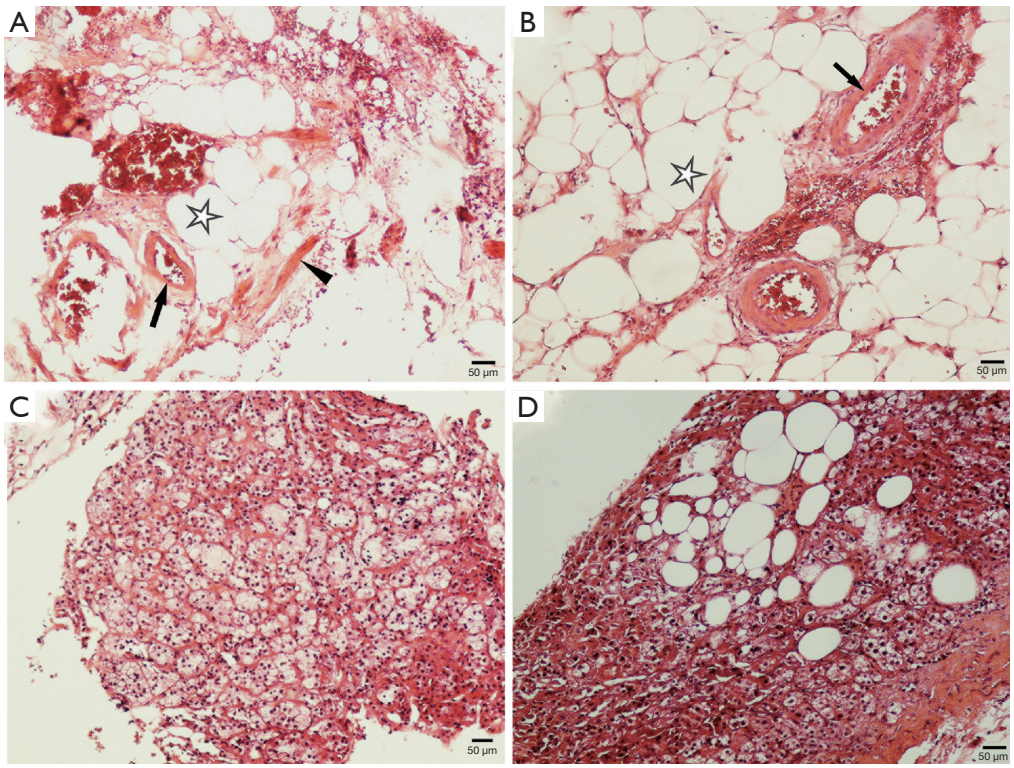

Figure 3 Hematoxylin and eosin staining (×100) showing large vascular spaces lined by endothelial cells and separated by thick fibrous septa and adjacent normal adrenal tissues (black arrow). Under the microscope, the tumor is composed of thick-walled blood vessels (black arrows), fat (star) and smooth muscles (triangle). The fat cells are mature, Smooth muscle fibers are distributed around the blood vessels (A and B). (C) and (D) show the surrounding normal adrenal tissues.

Despite their small size, the adrenal glands are considered as the most common location for the metastatic spread of multiple malignant tumors (12). In the majority of cases, patients are asymptomatic, and the metastases are discovered incidentally during the follow-up of antecedent malignant disease. CT and MRI, as well as the evaluation of tumor characteristics, play a key role in the diagnosis of adrenal angiomyolipoma. In contrast to lipid-poor metastatic tumors, benign adrenal lesions contain abundant intracytoplasmic fat (an attenuation value of <10 Hounsfield units suggests a lipid-containing benign lesions). Small metastases are often homogeneous analogues of benign tumors, whereas large metastases frequently represent heterogeneous metastases as a result of hemorrhages and necroses within the lesions. Meanwhile, calcifications in metastases are rare (13). It should be emphasized that the CT features of adrenal metastases are nonspecific, and metastasis cannot be discriminated from benign lesions based on size alone (12). On MRI, the T2 signal of metastasis is higher than that of hormonally inactive and benign lesions. According to several authors, dynamic gadolinium-enhanced MRI and chemical-shift MRI may be helpful for distinguishing between metastatic tumors and benign lesions (13).

Angiomyolipomas are mainly composed of mature adipocytes, which facilitate an easy, accurate diagnosis based on the imaging and pathology results and distinction from metastasis. However, some angiomyolipomas mainly comprise epithelial smooth muscle, which makes it difficult to make a true diagnosis based on the imaging or pathology findings known to pathologists. At this time, the differential diagnoses of adrenal metastatic carcinoma, adrenal carcinoma, and renal cell carcinoma are challenging because of their epithelial morphology, especially in people with a history of cancer (3). Careful examination of the adipocytes and abnormal blood vessels is helpful for diagnosis (14). Two of the reported cases of adrenal angiomyolipoma were misdiagnosed as malignant tumors, one of which

was diagnosed as an adrenal malignant tumor because of scattered calcifications in the adrenal mass (9). The other cases featured adrenal masses that were diagnosed as adrenal metastases because of the high uptake in the adrenal masses during systemic 18F-FDG PET/CT (15).

In the case we reported, the patient was misdiagnosed with adrenal metastasis based on his history of lung cancer and the findings for imaging examination (the mass significantly increased in size during the 2-year follow-up and showed obvious ring enhancement in the enhanced CT scan). The patient was asymptomatic, and the adrenal mass also showed unenhanced exudation-like changes on contrast-enhanced CT, which we suspect was caused by vascular rupture and bleeding caused by a lack of elastic fibers in the vascular wall of the angiomyolipoma. However, the appearance of adrenal metastases varies on CT, and they are usually asymptomatic. Metastasis can also manifest as bleeding and peripheral invasion (16). In addition, some adrenal metastases, such as renal clear cell carcinoma and hepatocellular carcinoma, contain lipids (17), and in these cases, it is difficult to distinguish adrenal metastases from angiomyolipoma. In summary, adrenal metastases usually have a high unenhanced density (>10 HU) and delayed contrast medium washout compared to adrenal angiomyolipoma (precontrast HU less than 10, no enhancement or mild enhancement). Local invasion, central necrosis, and irregular borders are predictors of adrenal metastasis. However, if the main component of the angiomyolipoma is epithelial smooth muscle, there is a lack of adipose tissue (as in our case), which makes it difficult to correctly distinguish from metastasis. Therefore, despite its rarity, adrenal angiomyolipoma should be considered in the differential diagnosis when an adrenal mass is incidentally found in a patient with a history of primary tumors.

Finally, if the tumor is smaller than 4 cm and the patient has no symptoms, routine US or CT examination should be recommended every 3–6 months (18). Surgical treatment or selective arterial embolization should be performed if the tumor is symptomatic or measures more than 4 cm (19), as large angiomyolipomas have a tendency to rupture spontaneously and there is a risk of local recurrence (14) and increased spontaneous bleeding (20). All of the patients reported with adrenal angiomyolipoma underwent surgery. In recent years, laparoscopic adrenalectomies have been primarily considered over open surgery because laparoscopic surgery is less invasive, has fewer complications and a lower mortality rate than open surgery (12,15).

Conclusions

In conclusion, metastatic tumors are the second most common adrenal tumor after adrenal adenoma, especially in patients with a history of primary tumors. Because of the rapid progression and highly invasive nature of metastatic tumors, an accurate diagnosis is of great significance for the follow-up treatment and prognosis of these patients. Although adrenal angiomyolipoma is uncommon, it should be considered as one of the differential diagnoses of adrenal metastasis.

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Footnote

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/atm-20-3147). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was approved by the ethics committee of The Affiliated Hospital of Zunyi Medical University, and written informed consent was obtained from the parents of the participant for the publication of this manuscript and any potentially-identifying images/information.

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Supplementary

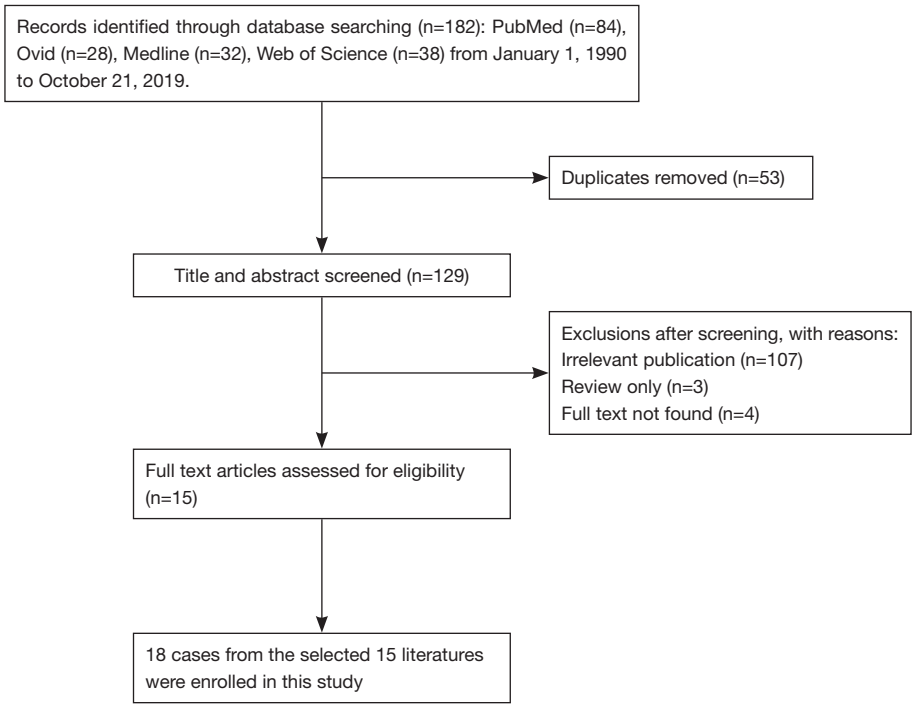

Figure S1 Flow chart of the literature screening process for adrenal angiomyolipoma.

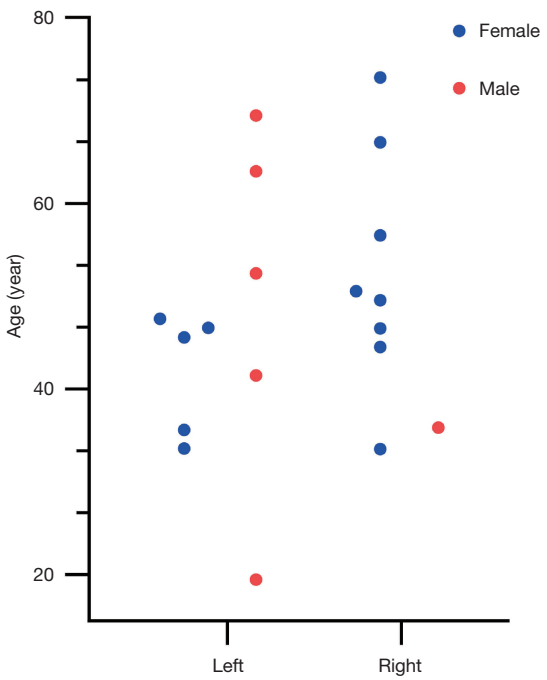

Figure S2 Clinical distribution of adrenal angiomyolipomas. There was no difference between the left and right sides, and the age distribution was mainly between 30 and 50 years old. Women were more likely to develop adrenal angiomyolipomas than men (the ratio of males to females was 3:7). There was no significant difference in the distribution on the left and right sides in female patients; however, male patients were more likely to develop adrenal angiomyolipomas on the left side.