Case Report

A large bi-lobed classic renal angiomyolipoma with vena caval extension

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\begin{abstract}
Renal angiomyolipomas (AMLs) are the most common benign renal tumors encountered, and composed of 3 components: mature adipose tissues, smooth muscles, and blood vessels. Mostly asymptomatic and discovered incidentally, the classic type of AMLs rarely extend to involve great vessels. Radiological confirmation of such lesions is paramount for diagnosis and planned intervention. Management of AMLs is based on clinical presentation and varies from active surveillance to invasive surgical interventions. A case of sizeable classic AML with extension to inferior vena cava is presented here, with successful tumor resection performed after complete liver mobilization. A literature review and a summary of similar cases are also presented. A multidisciplinary approach is required for proper and precise radiological diagnosis to achieve an adequate surgical resection, which might sometimes be complicated and complex, as in this current case.
\end{abstract}

\section{Introduction}

Angiomyolipoma (AML) is the most common mesenchymal tumors of the kidney and is mostly a benign disease [1]. This entity, first reported in 1900, Fisher described its histopathologic characteristics, in the year 1911, encompassing 3 components: mature adipose tissues, dysmorphic blood vessels, and smooth muscle fibers [2]. AML is characterized into 2 main subtypes: the classical subtype, which is almost always benign, and the epithelioid variant, which tends to behave more aggressively [3]. AML can be multicentric or solitary; they are frequently associated with tuberous

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sclerosis or lymphangioleiomyomatosis and more commonly found in middle-aged females. They are usually asymptomatic but may present with gross hematuria or flank pain [4].

It is uncommon for an AML to invade into the renal vessels and extend up to the inferior vena cava (IVC), given its benign nature, especially if it is of the classic subtype. We hereby present a case of an incidental finding of a large classic AML that has extended into the renal vein, to the infrahepatic IVC, requiring a radical nephrectomy with caval thrombectomy, after complete liver mobilization.

**Case presentation**

A 40-year-old lady presented to the urology clinic after an enhanced computed tomography (CT) scan of the abdomen and pelvis was done for abdominal distention and right upper quadrant discomfort of several weeks duration. She denied any flank pain, hematuria, lower urinary tract symptoms, fever, chills, or even lower extremity edema. The patient denied any family history of kidney diseases.

The CT scan reported a predominantly fat-containing mass arising from the medial interlobar region of the right kidney, measuring about 13 cm × 19 cm in size, abutting the inferior border of the liver, gallbladder, duodenum, hepatic flexure of the colon, and the medial aspect of the right psoas muscle. The mass involved the renal vein, with a fat thrombus extending up to the infrahepatic portion of the vena cava, just below the confluence of the hepatic veins (Fig. 1). The tumor within the IVC is partially occlusive. Our differential at this stage was either an aggressive renal AML or a retroperitoneal liposarcoma, given the extent of the disease. Although low in our differential, we also suspected Tuberous Sclerosis, but genetic testing came out negative.

For further characterization of this considerable mass and to accurately identify vital surrounding structures, vessels, and surgical planes for intraoperative planning, we performed an enhanced magnetic resonance imaging (MRI) imaging of the abdomen and pelvis with both arterial and venous phases. A predominately fat-containing renal mass, mostly of the classic type, was again noted, measuring 13 cm × 9.7 cm × 19 cm, with a fat thrombus extending 2.5 cm below the confluence of the hepatic veins. The right renal artery was seen crossing the middle of the lesion. Several thin enhancing septations were seen within the mass, along with an aneurysmal dilatation (Fig. 2).

Given the extension of the mass along with the fear for extension of thrombus and possible embolus, a multidisciplinary decision was made to proceed with a transabdominal exploration of the retroperitoneal mass, through a Mercedes Benz modification of an extended subcostal incision. Intraoperatively and after colonic mobilization, the large fat-predominant mass was seen arising from the right renal hilum and abutting superiorly the liver bed, and laterally deviating the great vessels. A right radical nephrectomy, adrenalectomy, para-caval lymphadenectomy was performed, along with a complete caval thrombectomy, successfully performed after complete liver mobilization, with suprarenal vena caval and contralateral left renal vein clamping to diminish back bleeding for proper sewing of the venotomy line (Fig. 3). No intraoperative complications were encountered, and blood loss was around 400 cc. The patient was discharged home 6 days later with a smooth postoperative course.

The final histopathology was consistent with a classic AML with no epitheloid features. The mass measured 13 cm × 10 cm × 19 cm in size and was arising from the renal hilum. The mass had a homogenous cut surface with few visible blood vessels. The fat thrombus extracted from the venotomy was also consistent with a classical AML (Fig. 4). All excised

Fig. 1 – (A) Enhanced computed tomography (CT) scan of the abdomen and pelvis with intravenous contrast, axial view, revealing a large renal mass composed solely of fat arising from the interpolar region of the right kidney (arrow), constituting an angiomyolipoma (AML). The mass measured around 13 × 19 cm. Noted as well in this axial cross-section is the bifurcation of the right renal artery (arrowhead), with 2 branches, one supplying the anterior portion and the other, the posterior portion of the right kidney. (B) Another axial cross-section of the enhanced CT scan, showing the extension of the right renal AML; cephalad abutting the liver bed, with presence of tumor fat thrombus within the infrahepatic inferior vena cava (arrow). Also noted is a small aneurysm (arrowhead) within the AML. (C) Another axial cross-section showing the extension of the renal AML with deviation of the great vessels medially, along with the presence of a minute left renal angiomyolipoma, posteriorly (arrow), measuring around 5 mm.
lymph nodes were benign and not involved with neither malignant nor metastatic cells.

Discussion

Renal AMLs are typically composed of adipose tissues, blood vessels, and smooth vessels [5], and has been characterized as part of the PEComas family (perivascular epithelioid cell differentiation) [6]. PEComas are a group of mesenchymal neoplasms that are strongly associated with tuberous sclerosis and tumor suppressor genes, TSC1 and TSC2 [7].

Renal AML are the most frequently encountered benign renal tumors, originating from renal parenchyma rather than the capsule or perinephric tissue, with an estimated prevalence between 0.2% and 0.6%, and female predilection of 2:1 [8]. Hereditary lesions affect both genders equally and usually manifest at a younger age, and are usually large, bilateral, and tend to be more aggressive [9].

With the increased use of various radiological modalities, more than 80% of renal AMLs are nowadays discovered incidentally, with hemorrhage at clinical presentation seen in 15% of cases, that is, so-called "Wunderlich syndrome." In contrast, others may present with hemorrhagic shock in less than 10% of those cases [10]. Using an ultrasound, classic AMLs are almost always hyperechoic compared to the renal parenchyma due to the presence of macroscopic fat [6]. However, ultrasounds are never accurately and solely used in diagnosing AML but can be used as a follow-up tool instead [11].

Alternatively, CT scans have excellent sensitivity, specificity, positive, and negative predictive values in distinguishing AMLs [6]. The most hypodense area within a classic AML would have an attenuation value of −15 HU or less,
suggestive of a macroscopic fat content. Nevertheless, in a small portion of AMLs, around 4%-5%, intralobal fat cannot be detected due to its minute amount in these rare lesions, the so-called fat-poor or fat-invisible renal AMLs. Those lesions, in particular, represent a diagnostic challenge to both radiographers and urologists, as they closely mimic renal cell carcinomas (RCC) [12]. Renal AMLs rarely contain calcifications, a diagnostic finding that could differentiate it from RCCs [13]. Unenhanced CT scans will not differentiate fat-poor from fat-invisible AMLs, and as such, a chemical shift imaging (CSI) technique using MRI would be better utilized [14].

MRI is another tool that is equivalent to CT in diagnosing AMLs, and even more potent in diagnosing fat-poor AMLs [12]. An unenhanced MRI is just needed to diagnose AML, which is of particular significance in patients with compromised renal function [6]. Comparing T1-weighted images with and without frequency, selective fat suppression allows for the detection of macroscopic fat within an AML lesion. Renal masses that are hyperintense before fat suppression and hypointense after frequency selective fat suppression are usually consistent with AML [15]. Another MRI sequence, useful in differentiating fat-poor AML from RCC especially that typical T1 sequence findings may not be straightforward, is in phase vs opposed phase chemical shift sequencing. CSI results in a sharp black boundary, the so-called “India-ink artifact” at the interface of macroscopic fat, found in AMLs, and water, contained in the renal parenchyma [15]. On CSI-MRI, a fat-poor AML would exhibit a tumor-to-spleen ratio less than 0.71 or a signal intensity index of more than 16.5%. On the contrary, the too little fat seen in fat-invisible AMLs would exhibit a tumor-to-spleen ratio ratio of more than 0.71 and a signal intensity index less than 16.5% [14].

The role and data on positron emission tomography scans utilizing fluorine-18 fluoro-2-deoxy-d-glucose for differentiating renal AMLs vs other forms of RCCs, is still scarce and controversial. The true positive rate for detecting RCC using positron emission tomography/CT fluorine-18 fluoro-2-deoxyd-glucose scan is around 77%, and that for detecting recurrent or metastatic RCC is around 85% [16]. RCC lesions generally exhibit a much higher SUVmax, than AMLs [17].

Histologically, renal AMLs are broadly classified as typical or atypical AMLs. The former classification is otherwise referred to as triphasic or classic type, where all 3 components are present in the lesion. The detection of adipose tissue on imaging is a crucial criterion for any classic AML, as previously highlighted [6]. On the contrary, atypical AMLs are referred to as monophasic, that is, consisting almost exclusively of one component while other elements are present in very small portions, or the epithelioid variant, consisting of numerous epithelioid muscle cells with abundant eosinophilic and granular cytoplasm and few if no fat cells [5]. Risk factors for malignant AML include size greater than 7 cm, tumor necrosis, and epithelioid carcinoma-like pattern [18].

Grossly, renal AMLs are generally well circumscribed with a tan-white to yellow cut surface, depending on the lipid content. Hemorrhage can be seen, but necrosis is rare. Adipocytes are usually intermingled with the spindle cells and are mature without any cytologic atypia [6].
There have been infrequently reported cases of AML, especially of the classic type, that has extended into the IVC. The current thinking behind this extension is based on multifocal tumorigenesis, rather than metastasis [19]. To our knowledge, 65 cases have been reported so far for classic renal AMLs with vascular extension, either to the renal vein, IVC, or even cephalad toward the right atrium (Table 1). Analysis of those cases reveals the following: a female predilection, 79% (52/66) were right-sided kidney tumors, and most patients (around 62%) had presenting symptoms, mainly flank or abdominal pain.

It has been postulated that surgical treatment is required, whenever renal AML extend into great vessels, even if they are asymptomatic, due to the risk of fatal embolism to the heart or pulmonary veins [20]. Multiple attempts at minimally invasive approaches have been attempted, including selective arterial embolization (SAE) with or without radiofrequency ablation, and have been relatively effective [21]; yet, surgical excision has been the most durable and oncologically safe approach.

Indeed, before any surgical planning, a proper diagnosis of AML is a must. Most AMLs can be diagnosed by imaging, as stated above. In case of difficulty, especially for fat-poor or fat-invisible AMLs vs small-sized RCCs and inconclusive imaging, whether CT and/or MRI, a percutaneous biopsy is recommended in this situation [22].

The optimal surgical treatment would be a nephron-sparing surgery (NSS), since the disease is primarily benign, and this would yield superior renal functional outcomes, and carries a lower mortality compared to radical nephrectomy. These conclusions mimic those extrapolated from series on partial nephrectomy cases for RCC [23]. Given that renal AMLs with extension to renal vessels and IVC tend to be huge compared to isolated lesions within the kidney, and in proximity to major organs and/or vessels, nephrectomy is a safer operative decision, such as the case presented above. Caval thrombectomy follows similar surgical principles as that for RCC and careful dissection of preoperative images is imperative, for the optimal planning of cross clamping of the vena cava.

The literature highlights several options for the management of renal AMLs in general. Initially, advocates for interventions are those for symptomatic lesions larger than...
Table 1 – List of all renal classic angiomyolipoma cases with extra-renal/vascular extension.

| Case | Authors, year | Age/sex | Laterality | Tumor size | Thrombus level | Therapy |
|------|---------------|---------|------------|------------|----------------|---------|
| 1    | Kutcher et al, 1982 | 16/F | Right | Large | IVC | Nephrectomy |
| 2    | Brantly et al, 1985 | 45/F | Right | 9 cm | IVC | Nephrectomy |
| 3    | Rothenberg et al, 1986 | 62/F | Left | 4.5 cm | Right atrium | Nephrectomy |
| 4    | Camuzeau et al, 1987 | 22/F | Right | Small | IVC | Follow-up |
| 5    | Arenson et al, 1988 | 22/F | Right | 8.5 cm | IVC | Nephrectomy |
| 6    | Byrne et al, 1988 | 56/F | Right | 13.5 cm | IVC | Nephrectomy |
| 7    | Umeyama et al, 1992 | 75/F | Bilateral | 16 cm | IVC and renal vein | Partial nephrectomy |
| 8    | Reiff et al, 1993 | 58/F | Right | 10 cm | IVC | Nephrectomy |
| 9    | Honda et al, 1993 | 58/F | Right | Not mentioned | IVC | Nephrectomy |
| 10   | Moulin et al, 1994 | 36/F | Right | Large | IVC | Nephrectomy |
| 11   | Matsuura et al, 1995 | 34/F | Right | Large | IVC | Nephrectomy |
| 12   | Baert et al, 1995 | 53/F | Right | 6.5 cm | IVC | Nephrectomy |
| 13   | Hibi et al, 1995 | 31/F | Right | 10 cm | IVC | Nephrectomy |
| 14   | Leder et al, 1995 | 30/F | Right | Not mentioned | IVC | Nephrectomy |
| 15   | Briosi et al, 1996 | 64/M | Right | 6.5 cm | IVC | Nephrectomy |
| 16   | Citadini et al, 1996 | 65/F | Left | 6 cm | IVC | Follow-up |
| 17   | Citadini et al, 1996 | 67/M | Right | 6 cm | IVC | Nephrectomy |
| 18   | Citadini et al, 1996 | 54/F | Right | 4 cm | Renal vein | Follow-up |
| 19   | Citadini et al, 1996 | 19/F | Left | 8 cm | Renal vein | Nephrectomy |
| 20   | Rubio-Briosi et al, 1997 | 64/M | Right | 6.5 × 4 cm | IVC | Nephrectomy, cavitotomy |
| 21   | Bernstein et al, 1997 | 45/M | Right | 6 × 11 cm | IVC | Pre-op kidney embolization, nephrectomy, thrombectomy |
|      |                |        |        |          |                | extraction |
| 22   | Martignoni et al, 1998 | 60/M | Left | 6 cm | IVC | Nephrectomy |
| 23   | Gotoh et al, 1998 | 52/F | Right | 3.5 cm | IVC | Nephrectomy |
| 24   | Christiano et al, 1999 | 42/M | Right | 20.5 cm | IVC | Nephrectomy |
| 25   | Ito et al, 1999 | 40/F | Right | Not mentioned | Right atrium | Nephrectomy, thrombectomy |
|      |                |        |        |          |                | using extracorporeal circulation |
| 26   | Toda et al, 1999 | 41/F | Right | 18-cm tumor | IVC + right atrium | Nephrectomy |
|      |                |        |        | 13-cm thrombus |          |         |
| 27   | Davydov et al, 2001 | 46/F | Right | 6 cm | IVC and right atrium | Nephrectomy |
| 28   | Kawaguchi et al, 2002 | 40/F | Bilateral | 20 cm | IVC | Died during nephrectomy |
| 29   | Shangra et al, 2002 | 69/F | Right | 10 cm | IVC | Nephrectomy |
| 30   | Wilson et al, 2002 | 69/F | Right | 10 cm | IVC | Nephrectomy |
| 31   | Hatakeyama et al, 2002 | 31/F | Right | 11 cm | IVC | Nephrectomy |
| 32   | Islam et al, 2003 | 40/F | Right | 11 cm | IVC | Nephrectomy |
| 33   | Chandrasoma et al, 2004 | 61/M | Left | 4 cm | IVC | Partial nephrectomy |
| 34   | Chandrasoma et al, 2004 | 20/M | Right | 17.5 cm | IVC | Nephrectomy |
| 35   | Islam et al, 2004 | 40/F | Right | 11 cm | IVC | Nephrectomy |
| 36   | Bibier et al, 2005 | 36/M | Right | Not mentioned | Right atrium | Nephrectomy, thrombectomy |
| 37   | Haritharan et al, 2006 | 48/F | Right | 15 cm | IVC | Nephrectomy |
| 38   | Park et al, 2007 | 69/M | Bilateral | 13 cm | IVC | Nephrectomy |
| 39   | Ban et al, 2008 | 70/F | Right | 14 cm | IVC | Nephrectomy |
| 40   | Shigeo Takebayashi et al, 2008 | 47/F | Left | 7 cm | Renal vein | Nephrectomy |
| 41   | Quiciseda et al, 2008 | 41/F | Left | Not mentioned | IVC and right atrium | Nephrectomy |
| 42   | Dinis da Gama et al, 2008 | 39/F | Right | Not mentioned | IVC | Nephrectomy |
| 43   | Sandstrom et al, 2009 | 81/M | Left | 6 cm | IVC with fat embolus in Rt Pulm. artery | Nephrectomy + embolectomy |
| 44   | Luo et al, 2010 | 27/F | Right | 4 cm | IVC | Nephrectomy |
| 45   | Tan YS et al, 2010 | 44/M | Right | 9.7 × 6.6 × 14.7 cm | IVC | Nephrectomy + IVC; venous clamp 12 min |
| 46   | Jonathan Lopater et al, 2011 | 34/F | Right | 4 cm | IVC | Nephrectomy |
| 47   | Mittal et al, 2011 | 46/F | Right | 7 cm | IVC | Nephrectomy |
| 48   | Luo et al, 2011 | 27/F | Right | 4 cm | IVC | Nephrectomy |
| 49   | Bakshi et al, 2011 | 40/F | Right | Not mentioned | IVC | Nephrectomy + Thrombectomy |
| 50   | Li H et al, 2012 | 43/F | Right | 5.5 × 4.0 × 4.2 cm | IVC | Nephrectomy + venous thrombectomy |
| 51   | Xiaoman Li et al, 2013 | 52/F | Right | 12.5 cm | IVC and right atrium | Nephrectomy |

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4 cm, lesions with suspected malignancy, and lesions found in women with childbearing age [24]. Other indications would be the presence of aneurysms larger than 5 mm [25], concomitant Tuberous sclerosis complex (TSC) syndrome, as lesions in this situation tend to have faster growth rate (1.25 cm vs 0.19 cm yearly for sporadic AMLs) [26], and poor access to emergency care as considerations to proceed with intervention in case of bleeding. The absence of these indications mandates that active surveillance is a valid option [6]. Unfortunately, no current prospective randomized clinical trials have compared active surveillance vs treatment for AMLs and no strict criteria on the frequency of follow-up of such cases.

Partial nephrectomy for renal AMLs has been reported in few case series, the largest being reported by Boorjian et al in 2007, including 58 patients who underwent open NSS for sporadic AML, having a mean size of 3.9 cm (0.8-12.5 cm). Seven (12%) complications were noted, with 2 (3.4%) recurrence rate in this series, with a mean follow-up of 8 years [27].

For patients in whom NSS is not feasible due to size, extension to vessels, and tumor location, another alternative would be to proceed to radical nephrectomy or SAE. The latter is an attractive option in case of acute hemorrhage and hemodynamic instability [6]. Numerous agents have been used for embolization with no superiority of one agent over another [6]. The recurrence rate post-SAE is highly variable and ranges between 11% and 40% [28].

Percutaneous ablation is also another minimal invasive modality but restricted to small AMLs and asymptomatic lesions. Unfortunately, no long-term data are available for this modality [29].

Finally, mammalian Target of Rapamycin pathway inhibitors such as Sirolimus or Everolimus, aims to halt tumor progression and regression of size in existing tumors in hereditary AML and LAM syndrome. Several phase II trials using Sirolimus for AML included a total of 94 patients with a 46.8% response rate after 12 months, but no complete response was shown [30].

### Conclusion

Renal AML of classic subtype remains to be a benign entity, although few cases of its outspread to renal vessels and beyond are reported. Proper use of various imaging modalities is crucial to obtain adequate diagnosis and to base our future management on. Optimal treatment options are still not well defined and versatile. Surgery seems to be inevitable in cases similar to ours, with extension to IVC, for fear of embolus. Sur-
geons performing such complex procedures must be trained to do so, especially that complete liver mobilization may be necessary for proper venotomy and thrombectomy.

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Authors’ contributions

Degheili JA and Abou Heidar NF carried out the literature review and wrote the manuscript, including the case presentation. Abi Saad G and Khalui R performed proofreading of the manuscript. Abou Heidar NF and Degheili JA contributed mostly in obtaining the radiological images. All authors have agreed on the final version of the manuscript, prior to submission.

Informed consent

A written informed consent was obtained from the patient himself for the publication of this case report, along with all corresponding figures. A copy of the written consent is available for review by the Editor-in-Chief of this journal, upon his request.

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