



## Bilateral giant angiomyolipomas revealed after massive retroperitoneal hemorrhage – A case report

### Veliki bilateralni angiomiolipomi otkriveni posle masivne retroperitonealne hemoragije

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#### Abstract

**Introduction.** Angiomyolipomas (AML) are benign neoplasms composed of fat, smooth muscle and thick-walled blood vessels in varying proportions. These tumors have a significant female predominance. **Case report.** We reported a 61-year-old man with spontaneous rupture of AML. Computerized tomography revealed a change in morphology of both kidneys. Multiple lesions of fat density with dilated blood vessels were found in the left kidney. The right retroperitoneum was obliterated with a giant heterogeneous mass originating from the right kidney with a massive hemorrhage, active extravasations, compression of inferior the vena cava and intraperitoneal collections. After radical nephrectomy, histological examination revealed that the tumor was composed of relative proportions of fat, smooth muscle and blood vessels. We incidentally found small renal adenoma. **Conclusion.** The true nature of AML is unclear, but they are usually classified as hamartomas. Angiomyolipomas are generally benign lesions, although the epithelioid angiomyolipoma, a subtype that occurs in about 3% of cases, can behave aggressively.

**Key words:** kidney neoplasms; angiomyolipoma; diagnosis, differential.

#### Apstrakt

**Uvod.** Angiomiolipomi (AML) su benigni tumori, izgrađeni od masnog i glatkomišićnog tkiva i krvnih sudova u različitim odnosima. Ovi tumori češći su u ženskoj populaciji. **Prikaz bolesnika.** Predstavljen je bolesnik, star 61 godinu, sa spontanom rupturom AML. Kompjuterizovanim tomografijom uočena je izmenjena morfologija oba bubrega. U levom bubregu viđene su multiple lezije u masnom tkivu sa dilatiranim krvnim sudovima. Na desnom bubregu uočena je velika heterogena masa koja je ispunjavala desni retroperitonealni prostor, sa masivnim krvarenjem, aktivnom ekstravazacijom, kompresijom donje šuplje vene i intraperitonealna kolekcija. Posle radikalne nefrektomije, histološkom analizom utvrđeno je da tumor čini nejednak odnos masnog i glatko-mišićnog tkiva i krvnih sudova. Mali bubrežni adenom bio je uzgredan nalaz. **Zaključak.** Pravo poreklo ovih AML nije u potpunosti razjašnjeno, ali često se svrstavaju u hamartome. To su uglavnom benigni tumori, dok su epitelioidni angiomiolipomi varijanta koja se sreće kod oko 3% slučajeva, mogu da imaju agresivni tok.

**Ključne reči:** bubreg, neoplazme; angiomiolipom; dijagnoza, diferencijalna.

#### Introduction

Renal angiomyolipoma (AML) stands for mostly benign tumors originating from mesenchymal elements of the kidney<sup>1</sup>. They occur with an incidence of 0.3–3%, indicating that such lesions are present in more than 10 million people worldwide<sup>1,2</sup>.

AML may appear associated with tuberous sclerosis or as an isolated lesion with frequency of symptoms and risk of bleeding increasing with the size of the lesion<sup>3–9</sup>.

Ultrasonography (US), computerized tomography (CT) or magnetic resonance imaging (MRI) are usually sufficient for the diagnosis, so histological confirmation with biopsy is rarely needed<sup>10</sup>.

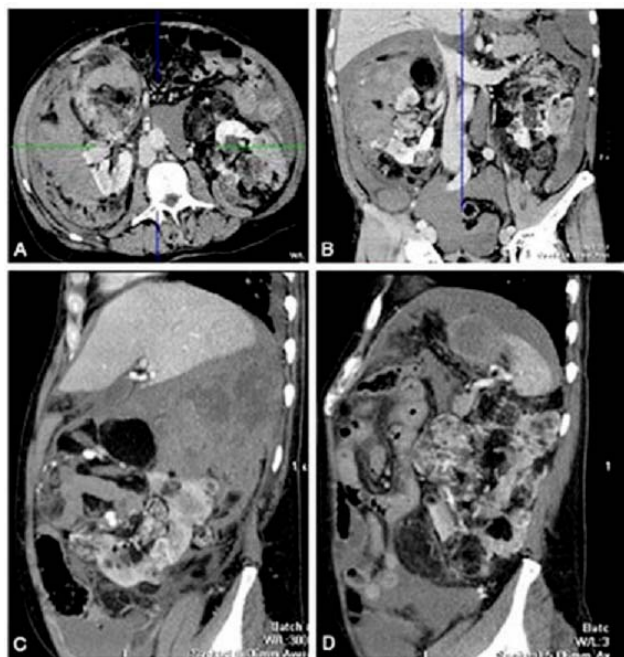
The main mortality from AML is spontaneous life-threatening hemorrhage<sup>11</sup>.

Herein we reported a case with bilateral multifocal renal angiomyolipomas and massive retroperitoneal hemorrhage resulting from the rupture of pseudoaneurysm of the renal artery branch.

### Case report

A 61-year-old patient presented with sudden abdominal pain, palpable right flank mass and weakness. During the transport to an emergency diagnostic center for suspected rupture of abdominal aorta aneurysm, the patient developed hypotension and developed shock.

CT of the aorta demonstrated normal findings. Incidentally, CT revealed a change in morphology of both kidneys. Multiple lesions of fat density with dilated blood vessels were found in the left kidney. The right retroperitoneum was obliterated with giant heterogeneous mass originating from the right kidney with massive hemorrhage, active extravasations, compression of the inferior vena cava and intraperitoneal collections (Figure 1).

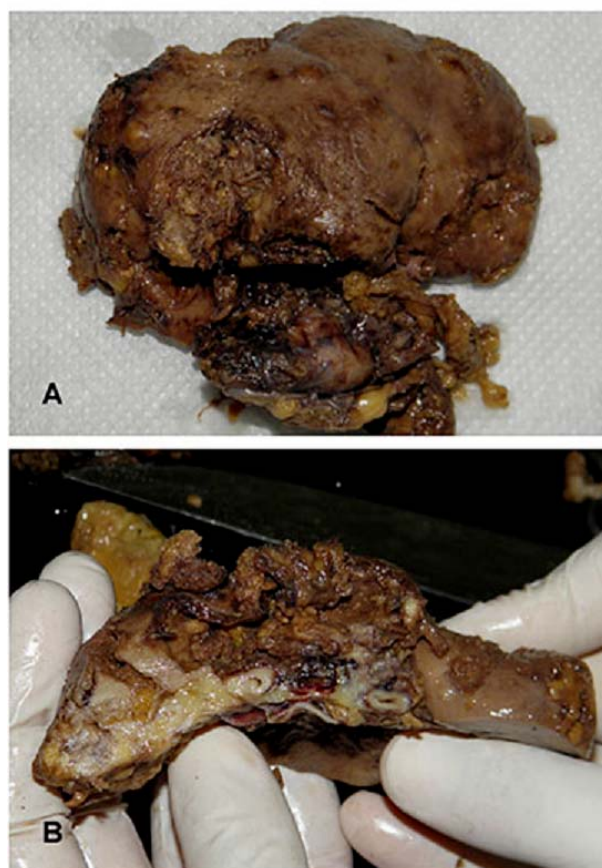


**Fig. 1 – Postcontrast multiple detector computed tomography (MDCT): A) Sagittal and B) Coronal plane, show bilateral angiomyolipomas of the kidney with right sided retroperitoneal haemorrhage; C) Right sided kidney angiomyolipoma with haemorrhage; D) Left sided kidney angiomyolipoma.**

Radical right nephrectomy was performed on the same day and samples were sent for pathological verification.

Grossly, the lesion was predominantly pale yellow, 7 cm in size with massive areas of hemorrhage (Figure 2).

Microscopically, the lesion had the relative proportions of fat, smooth muscles, and blood vessels. The adipose tissue was composed of uniform fat cells with large cytoplasmic vacuoles and small peripheral nucleus. The smooth muscle cells were typically spindle shaped but occasionally they were epithelioid and had abundant eosinophilic cytoplasm. The vascular components consisted of large thick walled tortuous blood vessels.



**Fig. 2 – A) The tumor measuring 7 cm in its maximum diameter, protruded from the renal capsule in the upper-pole; B) The cut surface exhibited yellowish solid and hemorrhagic degeneration zones.**

According to immunohistochemistry, tumor cells were positive for melan-A, HMB-45, CD117, CD68. Moreover, tumor cells were negative for S-100 protein, as well as for epithelial markers such as cytokeratin and epithelial membrane antigen (Figure 3).

Incidentally, we found a small renal adenoma. The cells had round to oval nuclei with chromatin that ranges from stippled to clumped, as well as inconspicuous nucleoli (Figure 4).

Because of the increase of nitrogen products in blood, the patient underwent dialysis. However, after dialysis creatinine values were still increasing.

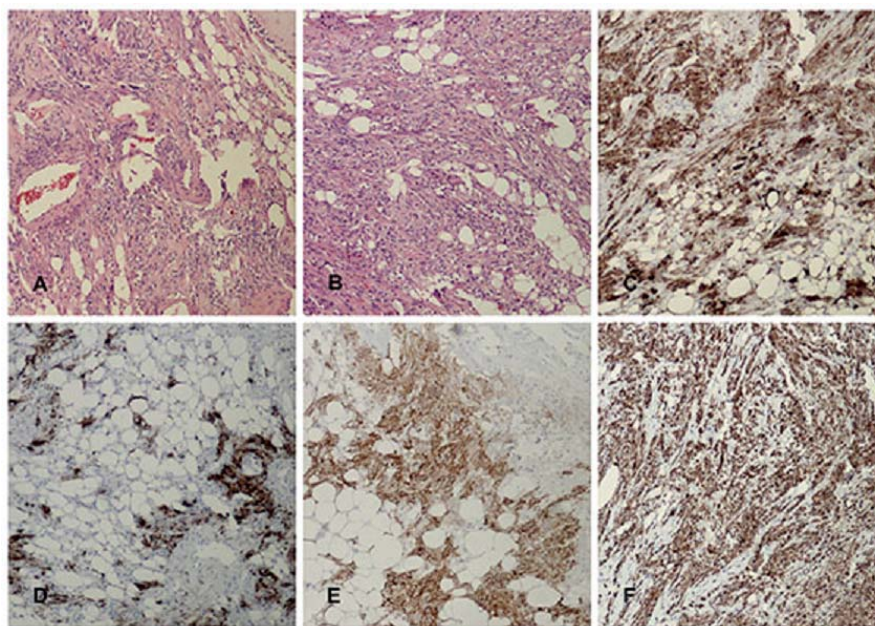
After achieving diuresis of 1,000 mL, on the postoperative day 4, control CT examination was performed.

CT of the abdomen presented completely distorted morphology of the left, remaining kidney, caused by multifocal angiomyolipoma, with patches of preserved renal parenchyma.

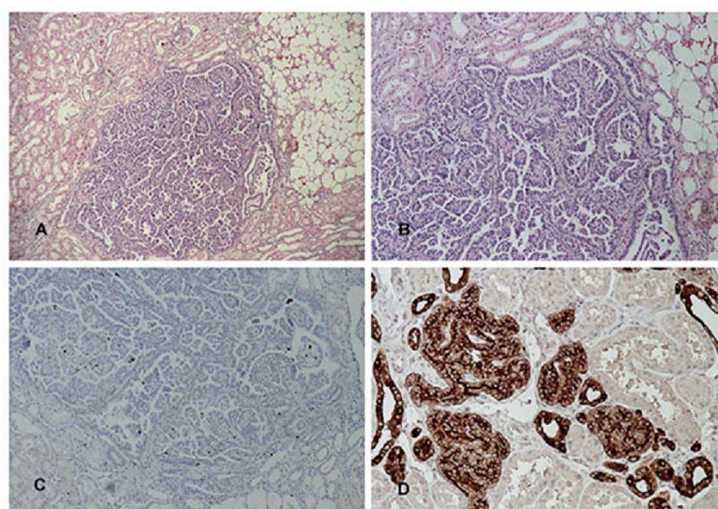
Considering high rate of comorbidity with tuberous sclerosis, especially in bilateral angiomyolipomas, the patient underwent CT of the brain, which demonstrated normal findings.

Ten months after the first intervention the patient underwent radical left nephrectomy. As suspected pathological diagnosis was also angiomyolipoma.





**Fig. 3 – A) and B) Angiomyolipoma composed of thick-walled blood vessels, smooth muscle, and fat (hematoxylin-eosin, original magnification  $\times 10$ ); C) Cytoplasmic granular diffuse immunopositivity for Melan-A in the tumor cells (original magnification  $\times 10$ ); D) Cytoplasmic granular focal immunopositivity for HMB-45 in the tumor cells (original magnification  $\times 10$ ); E) Cytoplasmic granular immunopositivity for CD-117 in the tumor cells (original magnification  $\times 10$ ); F) Cytoplasmic granular immunopositivity for CD-68 in the tumor cells (original magnification  $\times 10$ ).**



**Fig. 4 – A) Cortical adenoma (hematoxylin-eosin, original magnification  $\times 4$ ); B) Cortical adenoma (hematoxylin-eosin, original magnification  $\times 10$ ); C) Neoplastic cells are Ki-67 negative (original magnification  $\times 10$ ); D) Neoplastic cells are strong EMA positive (original magnification  $\times 20$ ).**

## Discussion

Renal angiomyolipoma is the second most common benign tumor of the kidney, and accounts for 3.7% of all renal masses<sup>12</sup>.

It is composed of variable amounts of mature adipose tissue, smooth muscle, and thick-walled blood vessels derived from perivascular epithelioid cells<sup>6,11</sup>.

AML occurs with overall female predominance of approximately 4 : 1 to 8 : 1, suggesting the role of female hormones in tumor growth<sup>4</sup>. There are two clinical forms: as isolated phenomenon or a part of the syndrome associated with tuberous sclerosis. Isolated AML occurs sporadically,

accounts for 80% of cases and is usually solitary, while those associated with tuberous sclerosis are typically larger, have multifocal or bilateral disease, tend to occur in younger patients and bleed more often than sporadic AMLs<sup>4,13</sup>.

At presentation, most patients are asymptomatic, with AML presenting as an incidental finding on imaging done for other reasons<sup>14</sup>. Although most AML are benign and asymptomatic, symptoms develop in 68–80% of patients when tumor size reaches 4 cm or more<sup>2</sup>. Symptomatic patients classically suffer from flank pain (53%), a palpable tender mass (47%) and gross hematuria (23%); this is known as “Lenk’s triad”<sup>15</sup>. Clinical manifestations less frequently include nausea or vomiting, fever, anemia and blood pressure changes<sup>2</sup>.

More than 51% of symptomatic cases are presented with haemorrhage<sup>2</sup>.

AML is the most common cause of spontaneous renal hemorrhage which, presented with the classic triad of symptoms – acute abdominal pain, palpable mass and hypovolemic shock, is referred to as Wunderlich syndrome. Wunderlich syndrome appears in up to 10% of patients with AML, thus considered the most severe complication of these lesions<sup>16–18</sup>.

The histological appearance of AML may vary. Nuclear pleomorphism may be pronounced and mitotic figures may be present. But these findings have no adverse prognostic significance in most cases. In some cases, angiomyolipomatous tissue has been found in regional lymph nodes and spleen. This finding should not be misinterpreted as metastatic sarcoma. Occasionally, angiomyolipoma invades the renal vein or vena cava; all these patients are cured surgically, so this does not indicate malignancy.

AMLs are typically positive for melan-A and HMB-45 antibody raised against melanosome-related antigen. They are also known to be positive for other melanocytic markers such as HMB-50, tyrosinase, and microphthalmia-associated transcription factor. Other markers for AML are CD117 and CD68<sup>19, 20</sup>. AMLs exhibit variable immunopositivity for myoid markers such as smooth muscle actin, musclespecific actin, desmin, and calponin. About 25% of AMLs express estrogen and progesterone receptors. Angiomyolipomas are typically negative for S100 protein and epithelial markers such as cytokeratin and epithelial membrane antigen<sup>21, 22</sup>.

Because of the benign nature of renal AML, the principles of management are resolution of symptoms and preservation of renal function. The choice between current management approaches (observation with monitoring of tumor size, selective arterial embolization, renal-conserving surgery and total nephrectomy) is made based on the following: size of the tumor; the presence of significant symptoms such as

pain, severe hemorrhage and risk of rupture; and suspicion of a malignant tumor<sup>23</sup>. Nephrectomy, partial or radical, is indicated if there are persistent hemorrhage, suspicion of malignancy, or failed embolisation<sup>24</sup>.

Incidental finding of bilateral AML, not associated with tuberous sclerosis, in an elderly male patient, developing symptoms only after spontaneous rupture and hemorrhage, is, in our opinion, considered extremely rare. On the other hand, considering positive correlation between the size of the lesion and risk of bleeding<sup>2, 4</sup>, giant AML of the right kidney in our patient was extremely prone to rupture. At the moment of presentation, AML was already complicated by rupture followed by Wunderlich syndrome, which is one of the most feared complications of renal AML and required aggressive management.

Surprisingly, beside histopathological verification of AML of the right kidney, adenoma was also found in tissue of the operatively removed kidney. To our knowledge, there are only two reported cases of concurred occurrence of adenoma with AML, both of them adrenal adenoma. One of them is in the homolateral adrenal gland, and the other one intrarenal, ectopic, adrenal adenoma<sup>25, 26</sup>.

## Conclusion

The true nature of AMLs is unclear, but they are usually classified as hamartomas. Angiomyolipomas are generally benign lesions, although the epithelioid angiomyolipoma, a subtype that occurs in about 3% of cases, can behave aggressively.

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