Angiomyolipoma of the Left Ureterovesical Junction

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Angiomyolipoma (AML) is a benign tumor that typically consists of 3 tissue elements: thick-walled blood vessels, smooth muscle cells, and adipocytes. The most common location for AML is renal; however, extrarenal AML has been described. Reports of extrarenal AML within the genitourinary tract are rare. We report a case of AML at the left ureterovesical junction and the evaluation and management decisions regarding this lesion.
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Key words: Angiomyolipoma • Immunohistochemical staining • Ureterovesical junction

Angiomyolipoma (AML) is a benign tumor that typically consists of 3 tissue elements: thick-walled blood vessels, smooth muscle cells, and adipocytes. Although the classic form of AML contains all 3 elements, different tissues can predominate, leading to categorization as epithelioid, leiomyoma-like, or lipoma-like AML. This tumor is found in 0.13% of the population when screened by ultrasound.[1] Though its origin is historically controversial, AML is considered clonal (neoplastic) rather than hamartomatous (resulting from a benign proliferation of mature tissues indigenous to a location).[2] It is thought to derive from a specific type of cell called the *perivascular epithelioid cell*.

The kidney is the most common site for AML, though extrarenal AML does occur. The liver is the second most common site for this tumor. Renal AML is typically diagnosed radiographically based on the presence of fat on computed tomography (CT) scan or ultrasound (thought to be pathognomonic for AML)[3]

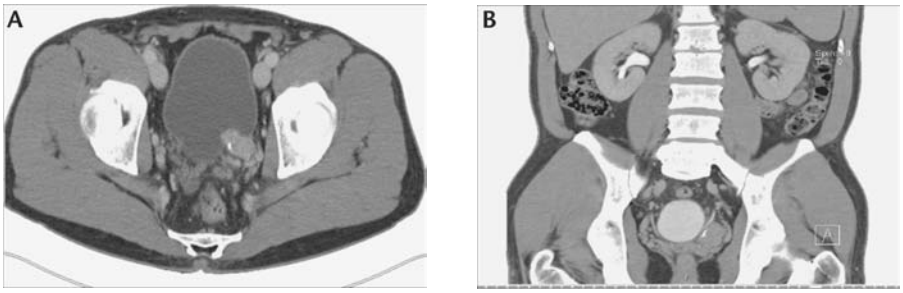


Figure 1. *Computed tomographic urogram revealing* (A) *a well–circumscribed, lobulated soft tissue mass measuring 3 × 2 cm adjacent to the insertion of the ureter at the left ureterovesical junction with no evidence of ureteral obstruction and* (B) *sagittal reconstruction revealing the perivesical mass with focal calcification.*

and on the lack of other suspicious characteristics for renal cell carcinoma (RCC). Renal AML may be sporadic (80%) or multifocal (20%); the latter is associated with tuberous sclerosis (TS), an autosomal dominant disorder characterized by mental retardation, seizures, and adenoma sebaceum.

The great majority of renal AML cases follow a benign course and thus may be observed radiographically. Lesions greater than 4 cm in diameter are more likely to become symptomatic[4,5] and have increased risk for bleeding, and thus may be removed or embolized. Malignant transformation of AML is exceedingly rare, though it has been reported.[6,7]

Extrarenal AML involving the genitourinary tract is rare, though there are scattered case reports. The case presented here is of AML of the left ureterovesical junction (UVJ) and our evaluation and management decisions regarding the lesion.

Case Presentation

The patient was a 47-year-old man with a history of chronic neutropenia who presented to his urologist's office with a single episode of gross hematuria that resolved spontaneously. He denied other voiding symptoms, flank or abdominal pain, fevers, or urinary tract infections. His only additional complaint was chronic mild left testicular discomfort.

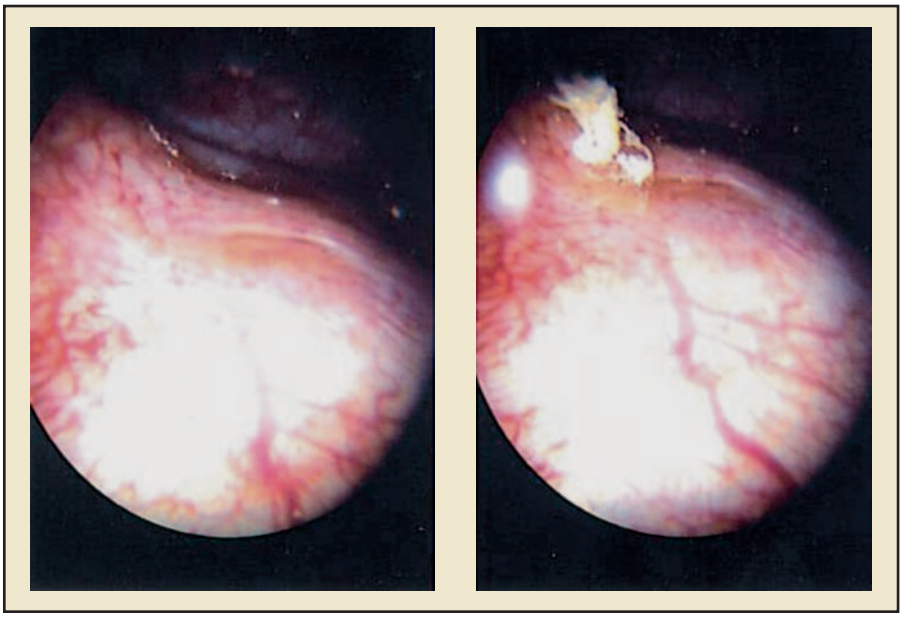
The patient had no significant past medical or surgical history, was taking the prescribed bupropion (Wellbutrin®; GlaxoSmithKline, Research Triangle Park, NC) and methylphenidate (Ritalin®; Novartis Pharmaceuticals Corp., East Hanover, NJ), and had no allergies. He denied history of tobacco use and denied any family history for stones or urologic malignancy.

His examination was within normal limits except for slight tenderness of the left epididymis and a small left hydrocele. His laboratory work-up included urinalysis and culture, which were negative. Other pertinent laboratory results included a white blood cell count of 1.9×10^9/L, hematocrit of 38%, and serum creatinine of 1.0 mg/dL. A hepatic panel and prothrombin time/partial thromboplastin time were within normal limits. His urine cytology revealed atypical urothelial cells and signs of inflammation.

A CT urogram was performed and revealed a well-circumscribed, lobulated soft tissue mass measuring 3 × 2 cm adjacent to the insertion of the ureter at the left UVJ with no evidence of ureteral obstruction (Figure 1). There was a focal calcification medially within the mass. The mass was described as extrinsic to the bladder though focally involving it. Prostate and kidneys were normal, with no evidence of stones or lymphadenopathy.

The patient then underwent cystoscopy. Although no intravesical lesions were noted, a raised area at the left UVJ was thought to be either a mass in the wall of the bladder or adjacent to the bladder, or an intramural ureteral tumor (Figure 2). A left

Figure 2. *Cystoscopic view of the raised area at the left ureterovesical junction.*



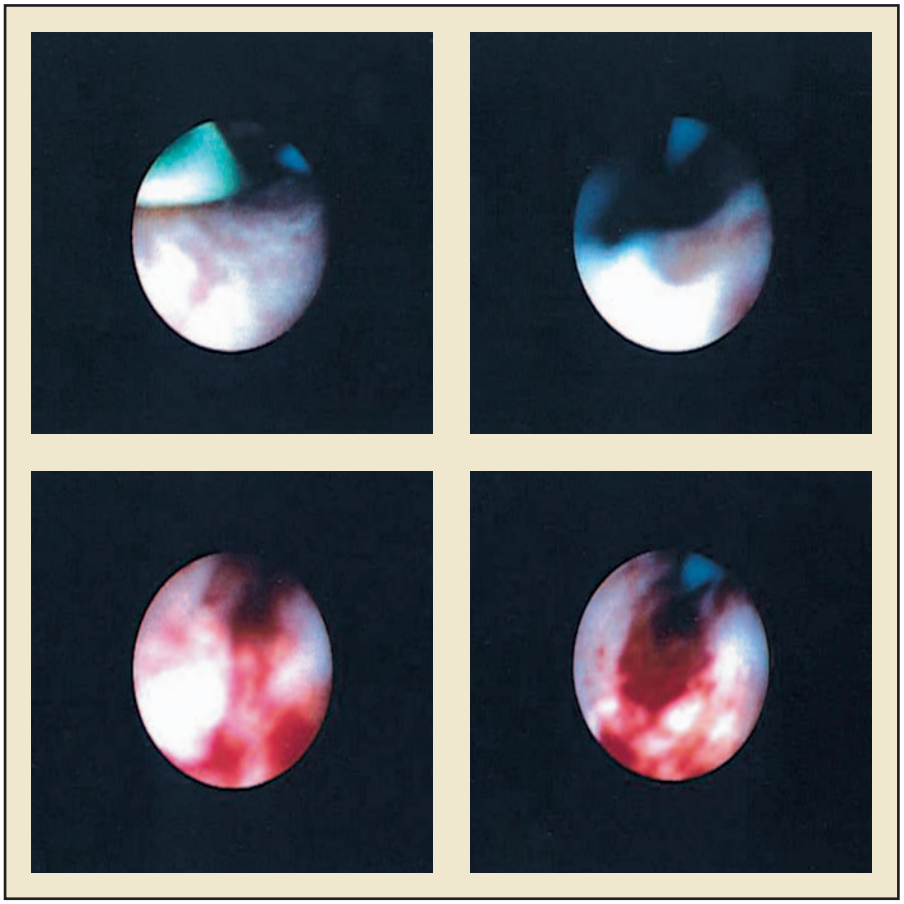


Figure 3. *Ureteroscopic view of the compressed posterior ureteral wall at the distal-most portion, with abnormal-appearing ureteral mucosa.*

retrograde pyelogram (RTGP) was performed, and it was normal. Rigid ureteroscopy was then performed, which revealed a compressed posterior ureteral wall at its distal-most portion with slightly abnormal ureteral mucosa possibly secondary to inflammation (Figure 3). Two cold cup biopsies were taken from the distal ureter. Also, bladder urine was sent for bacterial and fungal culture as well as for acid-fast bacilli staining. A second RTGP was performed and showed no extravasation. A left ureteral stent was placed without difficulty.

The ureteral biopsy revealed sparse urothelial cells and insufficient tissue. The intraoperative cultures were negative.

The patient was then taken for CT-guided biopsy of the left perivesical mass. Both fine-needle aspiration and core biopsies were taken. Pathology revealed an epithelioid and spindle cell infiltrate with scattered small thick-walled, hyalinized blood vessels. Abundant eosinophilic cytoplasm with fine chromatin and conspicuous nucleoli was noted. Immunohistochemical staining was positive for HMB-45, CD31, and CD34; focally positive for SMA; and negative for desmin, AE1/AE3, and S100. The diagnosis of AML was made in light of immunophenotype and morphology.

On the basis of the possibility of sampling error and the atypical location of the tumor, the patient was offered exploration and excision of the mass with the hope that the lesion was indeed benign and would peel off from adjacent structures, though there was the possibility of requiring a more extensive operation, such as partial cystectomy and ureteral reimplantation. The patient obtained a second opinion from another institution, where opinion was divided on whether to observe or resect. Ultimately, the decision was to maintain watchful waiting.

Discussion

This case report describes a rare extrarenal AML affecting the genitourinary tract, specifically the perivesical area near the left UVJ. On imaging, the lesion appeared extravesical, and cystoscopy confirmed that the lesion was either intramural or outside of the bladder causing extrinsic compression. Differential diagnosis included soft tissue lesions of the bladder and pelvis, including leiomyoma, fibroma, teratoma, and sarcoma. AML was not initially included on this list because of the location of the tumor in the pelvis. AML is indeed uncommon outside of the kidney. Although the second most common site is the liver, cases of AML have been reported in the heart, lungs, palate, vagina, colon, retroperitoneum, skin, penis, spermatic cord, and bladder.[8-10]

One other report confirmed the existence of AML at the left UVJ,[11] though this patient's tumor was associated with ipsilateral renal and ureteral agenesis. The tumor had no distinctive imaging characteristics; thus, definitive diagnosis was based on pathology characteristic for AML. The absence of an ipsilateral kidney and ureter led to the hypothesis that the tumor resulted from malformation of fetal mesenchymal elements along the ureteral bud during fetal development. This mass was completely excised, and the patient had no recurrence in short follow-up.

Another author reported an AML of the bladder wall, diagnosed incidentally by magnetic resonance imaging.[12] Pelvic ultrasound confirmed a heterogeneous mass in the left bladder wall, and transperineal biopsy made the diagnosis of AML based on immunohistochemical staining. The mass was resected, per the authors, because of rare cases of malignant degeneration of AML and to avoid possible future growth or hemorrhagic complications.

Last, there is a report of bladder AML in which a 55-year-old woman presented with lower abdominal pain.[2] Pelvic ultrasound revealed a 5-mm bladder-floor polyp that was subsequently resected cystoscopically. The lesion appeared smooth and solid on the bladder floor and was covered with normal urothelium. Pathology was characteristic for AML, and the patient was followed without recurrence for 4 years.

These cases illustrate the variable diagnostic and therapeutic options available for working up atypical bladder masses, as well as treating benign bladder and perivesical tumors. Importantly, it is not clear to what extent principles of diagnosis and treatment of renal AML translate to extrarenal lesions. In terms of diagnosis, for renal AML the presence of any fat (Hounsfeld units $\leq$ 10) is considered pathognomonic,[3] though additional findings, such as the presence of calcifications, may raise the suspicion of RCC. Notably, calcification was present in our patient's lesion.

Also, in rare cases of RCC, fat has been present on imaging.[13] The fat is thought to result from osseous metaplasia or necrosis of cells with high lipid content. Also, there have been rare cases of AMLs containing enhancing components on CT scan suspicious for RCC, though final pathology has revealed AML only.[14]

AML is more readily diagnosed radiographically when it contains abundant fat, though AML can have variable proportions of its 3 tissue elements. When fat cannot be recognized radiographically, diagnosis of AML and exclusion of RCC (in the case of renal tumors) require pathologic analysis. Pathologic analysis relies on characteristic cellular features as well as immunohistochemical staining. HMB-45 is a specific stain for the epithelioid elements in AML and is useful for diagnosis when patients present with atypical or fat-poor lesions.[2,12] Other microscopic findings of AML may include thick-walled blood vessels in an angiomatous arrangement, a disorganized adventitial cuff of smooth muscle, and lack of a capsule but good margination.[2] Absence of elastic tissue in tumor vessels predisposes to aneurysm formation within these lesions and the risk of spontaneous hemorrhage.

Regarding our patient, the risks and benefits of watchful waiting versus resection were discussed extensively.

Regarding our patient, the risks and benefits of watchful waiting versus resection were discussed extensively. Important issues included the possibility of sampling error from percutaneous biopsy, the risk of malignant transformation of AML, and the risk of growth leading to bleeding and/or ureteral obstruction.

Percutaneous biopsy of renal masses has been well studied, and this modality has a role in specific clinical situations—for instance, in a patient with a known cancer diagnosis or with known metastatic disease.[15,16] The risk of sampling error is certainly present; one study showed that there may be lower negative predictive value for both small (1 to 3 cm) and large (> 6 cm) lesions.[17] The former might be true because of greater technical difficulty with biopsy of smaller lesions. In our case, tissue might have been obtained via transurethral biopsy during cystoscopy, but this was considered problematic given the proximity of the lesion to the ureteral orifice, and thus was not performed.

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There are rare reports of malignant transformation of renal AML. One set of case reports describes 2 patients with epithelioid-predominant renal AML who developed metastases related to their primary lesions.[7] Patient 1 was status post radical nephrectomy for a 20-cm AML and developed splenic and retroperitoneal masses 3 years postoperatively. These masses were resected and found to contain malignant epithelioid cells that stained positive for HMB-45. This patient died from complications of liver metastases.

Patient 2 was status post radical nephrectomy for an 8-cm AML whose pathology revealed malignant epithelioid cells. This patient received 2 courses of chemotherapy but died from multiple pulmonary metastases. A separate case report described a high-grade liposarcoma arising from an otherwise typical AML.[6] This patient developed peritoneal metastases and expired.

Given the rarity of malignant transformation of AML, it is unclear what factors might raise suspicion for this process. In situations of atypical radiographic presentation of either renal or extrarenal AML, tissue diagnosis may be imperative to ensure that malignancy is excluded. Notably, AML has rarely been observed to extend into the renal vein and/or inferior vena cava, and to be present in regional lymph nodes; this is thought not to result from malignant spread but rather from multicentric disease.[18] Also, cellular atypia can be present within AML; thus, differentiating AML from sarcoma may rely on immunohistochemical staining, specifically HMB-45.[1]

Risk of hemorrhage from renal AML increases when diameter exceeds 4 cm.[4,5] Although it is unclear to what extent renal AML behavior translates to extrarenal lesions, our patient's tumor might be safely followed radiographically to ensure that it does not increase significantly in size, thus either increasing the risk for bleeding or potentially obstructing the left ureter. ■

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Main Points

- Angiomyolipoma (AML) is a benign tumor that typically consists of 3 tissue elements: thick-walled blood vessels, smooth muscle cells, and adipocytes.
- Renal AML is typically diagnosed radiographically based on the presence of fat on computed tomography scan or ultrasound and on the lack of other suspicious characteristics for renal cell carcinoma (RCC).
- The great majority of renal AML cases follow a benign course and thus may be observed radiographically.
- AML is uncommon outside of the kidney, and the liver is the second most common site.
- For renal AML, the presence of any fat is considered pathognomonic, though additional findings, such as the presence of calcifications, may raise the suspicion of RCC.
- AML is diagnosed more readily radiographically when it contains abundant fat, though AML can have variable proportions of its 3 tissue elements.
- In situations of atypical radiographic presentation of either renal or extrarenal AML, tissue diagnosis may be imperative to ensure that malignancy is excluded.
- Notably, AML has rarely been observed to extend into the renal vein and/or inferior vena cava, and to be present in regional lymph nodes; this is not thought to result from malignant spread but rather from multicentric disease.
- Risk of hemorrhage from renal AML increases when the diameter exceeds 4 cm.