Case Report

Pitfalls in the diagnosis and treatment of fat-poor angiomyolipoma of the renal pelvis mimicking urothelial carcinoma: report of three rare cases

Fang Xie¹², Jiming Zhao³, Fajuan Cheng⁴, Zhigang Yao⁵, Bin Zheng¹², Zhihong Niu¹³, Wei He³

¹Department of Urology, Shandong Provincial Hospital Affiliated to Shandong University, Jinan, Shandong, China; ²Department of Urology, Weihai Municipal Hospital, Cheeloo College of Medicine, Weihai, Shandong, China; ³Department of Urology, Weihai Municipal Hospital, Cheeloo College of Medicine, Weihai, Shandong, China; ⁴Department of Urology, Shandong Provincial Hospital Affiliated to Shandong First Medical University, Jinan, Shandong, China; ⁵Department of Pathology, Shandong Provincial Hospital Affiliated to Shandong First Medical University, Jinan, Shandong, China

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Abstract: Angiomyolipoma (AML) represents the most frequent benign neoplasm of the kidney. It arises mostly in the cortex and protrudes into the perirenal space. It is extremely rare for a fat-poor AML to originate from the renal sinus, invade the pelvis, and present with hematuria. Because of the rarity of this lesion, differentiating it from a urothelial carcinoma is difficult, thereby making a preoperative diagnosis and management complex and challenging. We report three cases of fat-poor AML centered within the renal pelvis mimicking a urothelial carcinoma that underwent radical nephroureterectomy. The clinical characteristics, surgical management, and prognosis are discussed to achieve better preoperative evaluation of these entities. This is the first report of fat-poor AMLs involving the renal pelvis and presenting with hematuria. Nephron-sparing treatment is crucial for patients with these entities. Accurate diagnosis may allow partial resection or kidney-preserving treatment.

Keywords: Angiomyolipoma (AML), renal pelvis, diagnosis, kidney, case report

Introduction

Angiomyolipomas (AMLs) are the most common benign renal neoplasms. They are composed of variable amounts of three components: blood vessels, smooth muscles, and fat. AMLs account for approximately ~3% of renal tumors [1-3].

AML belongs to a family of perivascular epithelioid cell neoplasms (PEComas), which arise by clonal proliferation of epithelioid cells distributed around blood vessels [4, 5]. While most of these lesions are sporadic (80%), the remaining 20% are diagnosed as part of tuberous sclerosis complex (TSC). There are differences regarding the clinical presentation and management between these two subtypes [6]. Most patients are asymptomatic and are diagnosed incidentally. The blood vessels in the lesion lack an elastic lamina, which makes the tumor prone to aneurysm formation and rupture [7]. Symptomatic presentation, related to spontaneous hemorrhage in the retroperitoneum, is seen in <15% of patients. This scenario can lead to the development of hypovolemic shock in one-third of patients presenting with sudden flank pain, a palpable mass, and gross hematuria [1, 8].

AML occurs in kidney and, rarely, other organs. Classically, a renal AML arises from the renal parenchyma and extends outwards into the perirenal space. Benign triphasic AML is divided into “classic AML” and “fat-poor AML”; the latter does not contain sufficient fat to be detected by imaging [9, 10]. A fat-poor AML originates from the renal pelvis rather than the renal cortex, and presentation with bleeding is extremely rare. Therefore, a fat-poor AML is difficult to differentiate fromurothelial carcinoma of renal pelvic urothelial carcinoma.
Fat-poor angiomyolipoma in the renal pelvis mimicking urothelial carcinoma

Here, we present three rare cases of AML centered within the renal pelvis presenting with hematuria, mimicking a renal pelvic urothelial carcinoma and resulting in radical nephroureterectomy. The clinical characteristics, surgical management, and prognosis are discussed to achieve better preoperative evaluation of this entity.

Case presentations

Case 1

A 64-year-old woman presented to Shandong Provincial Hospital (Jinan, China) with the chief complaints of left-flank pain and gross hematuria of 2 months duration along with passage of “worm-like” blood clots. She denied urgency or frequent urination. She did not have hypertension or diabetes mellitus. Physical examination did not reveal a clinical abnormality. Urinalysis showed a few red blood cells (RBCs; 26-38 per high-power field (HPF)). Urine was negative for nitrites or malignant cells. Levels of tumor biomarkers were normal. Ultrasonography suggested a hypoechoic mass of 20 mm within the left renal pelvis. Non-contrast enhanced computed tomography (CT) demonstrated a lesion in the left renal pelvis of soft tissue density 52 Hounsfield units (HU), which was of higher attenuation than that of the renal parenchyma, and no stone was seen (Figure 1A). The lesion was insinuating around the collecting system. Contrast-enhanced cortical-phase CT images revealed mild enhancement of the tumor (70 HU), which was less than that of the renal cortex (Figure 1B). CT urography revealed a filling defect in the middle calyx with distortion and the “goblet sign” (Figure 1C). Magnetic resonance imaging (MRI) showed a 2-cm soft-tissue mass in the left renal pelvis. The lesion had low signal intensity on T1-weighted images, intermediate signal intensity on T2-weighted images, and enhancement on contrast images. Cystoscopy confirmed that the bleeding was from the left ureteral orifice, and a visible mass was not found in the bladder. Cytologic examination of the urine collection revealed no evidence of malignancy.

With suspicion of a urothelial carcinoma in the renal pelvis, a left laparoscopic nephroureterectomy (LRNU) was undertaken. The left renal pelvic mass was well-circumscribed and situated in the middle calyx. Histology showed a tumor comprising well-differentiated smooth muscle, mature blood vessels, and scattered adipose cells (Figure 1D). Immunohistochemical (IHC) analysis revealed positivity for HMB-45 (Figure 1E), melanA (Figure 1F), and SMA (smooth muscle actin), but negativity S-100. Fewer than 1% of
Fat-poor angiomyolipoma in the renal pelvis mimicking urothelial carcinoma

Figure 2. Case 2. A fat-poor AML in a 44-year-old woman. (A) Non-contrast enhanced CT shows an 18-mm iso-attenuating mass (33 HU) compared with the renal parenchyma. (B) The arterial phase of contrast-enhanced CT demonstrates homogeneous and mild enhancement. (C) Excretory phase CT shows a filling defect in the upper calyx. (D) Histologic features of the tumor show a fat-poor angiomyolipoma composed of mostly smooth muscle with fat cells (×200, hematoxylin & eosin). (E) Tumor cells are positive for HMB-45 and melan A (F). CT, computed tomography; HU, Hounsfield units.

cells were Ki-67 positive. The patient was in good condition and was discharged after 5 days.

Case 2

A 44-year-old woman was referred to our institute complaining of intermittent gross hematuria of 10 days’ duration. She did not smoke tobacco or consume any drugs or alcohol. She denied a history of hypertension, coronary heart disease, diabetes mellitus, or weight loss. She did not take any medication, and had no family history. She had not undergone surgery previously. There was no history of fatigue, fever, or dysuria. The abdominal examination was normal. Urinalysis revealed RBC count of 187-239/HPF, and negativity for leukocytes and nitrites. There were no abnormal findings for other laboratory indices. Transabdominal sonography demonstrated a hypoechoic occupying lesion of 20 mm located within the dilated upper calyx. CT showed a soft-tissue mass of 18 mm in diameter centered on the upper calyx with mild enhancement (Figure 2A, 2B). CT urography revealed a filling defect with amputation of the upper calyx of the left kidney (Figure 2C). Blood oozed from the left ureteral orifice, and the worm-like blot clots were found in the bladder during cystoscopy. Malignant cells were not present in urine.

She was diagnosed with a urothelial carcinoma of the left renal pelvis and underwent LR-NU. Gross pathology revealed a well-encapsulated and uniform whitish mass located in the upper calyx. Microscopically, the lesion was composed of a few adipose cells, smooth muscle, and thick-walled blood vessels (Figure 2D). Tumor cells stained positively for CD34, SMA, HMB-45, and melan A (Figure 2E, 2F). Fewer than 1% of cells were Ki-67-positive. Histopathology revealed a renal AML of the calyx. Postoperative recovery was uneventful, and she was discharged on postoperative day 7.

Case 3

A 60-year-old woman was admitted to our institute due to intermittent, massive, gross hematuria of ~8-month durations. There was no history of urinary tract infection, renal calculi, or pyelonephritis. Her medical history was unremarkable. She had undergone cesarean section for her only child 38 years earlier. She did not suffer from any chronic medical ailment or bleeding disorders. There was no history of tobacco consumption. No significant abnormalities were seen on routines blood analyses, coagulation, or biochemical examinations. A
Fat-poor angiomyolipoma in the renal pelvis mimicking urothelial carcinoma

Urinary test demonstrated RBCs at 134/HPF, pus cells 6-10/HPF. Physical examination was normal. Ultrasonography showed a 55-mm hyperechoic lesion in the left renal pelvis. CT of the abdomen and pelvis revealed a mass of approximately 75 mm × 41 mm in the renal pelvis extending to the ureteropelvic junction with enhancement after contrast administration (Figure 3A-C). Cystoscopy did not reveal pathologic findings. Urine cytology was negative for urothelial malignancy. Subsequently, left LRNU with bladder-cuff removal was undertaken.

Gross examination of the specimen revealed a mass of 70 mm in maximum dimension in the renal pelvis extending to the ureter. The resection showed a well-circumscribed tumor. Hematoxylin & eosin staining showed smooth muscle and scattered adipose cells (Figure 3D). IHC staining of HMB-45, CD34, and melan A were positive (Figure 3E, 3F). Fewer than 2% of cells were Ki-67-positive. Based on histological and IHC findings, an AML was diagnosed. The patient recovered uneventfully and was discharged in good condition after 5 days.

Discussion

Angiomyolipoma represents the most common benign neoplasm of the kidney, with a prevalence varying between 0.2% and 0.6% in the general population, and a strong predilection in women [11]. Owing to increased use and advances in imaging modalities, AMLs are found incidentally. Most patients are asymptomatic when they are diagnosed. The symptomatic presentation is most frequently associated with spontaneous retroperitoneal hemorrhage [1], which can lead to hypovolemic shock. Based on different pathologic features, imaging findings, and clinical behavior, renal AMLs can be classified into several subtypes [12]. Most renal AMLs occur sporadically. The remaining 20% of AMLs are associated with tuberous sclerosis complex. The sporadic type of AML is divided into the benign triphasic type and potentially malignant epithelioid AML [13, 14]. The benign triphasic subtype is further divided into classic AML and fat-poor types.

Typically, renal AMLs can be identified accurately based on imaging findings. Detection of an adipose component within a lesion is the hallmark of all imaging modalities [1]. The radiologic characteristics of AMLs can help in making a definitive diagnosis. Ultrasonography is used commonly for screening AMLs. The typical appearance of a renal AML upon ultrasonography is a markedly hyperechoic lesion with a posterior “acoustic shadow” [15]. The hyperechoic effect is the result of the mixture of fat,
Fat-poor angiomyolipoma in the renal pelvis mimicking urothelial carcinoma

blood vessels, and muscle content. However, hyperechogenicity is not a constant feature. As the proportion of fat deceases, so does the echogenicity of the mass. The shadow is due to the interface between different components [16]. CT is the most commonly used modality for diagnosing AMLs. The classic triphasic AML shows predominately fatty attenuation with variable density [17]. Pre-contrast CT depicts a region of interest (ROI) of the hypoattenuating area (less than -10 HU), which is fat in a classic AML [12, 18]. The CT manifestation of a classic triphasic AML varies due to the proportion of the three components in the lesion. MRI has high sensitivity for detecting the fat component, so it can also be used to diagnose a classic AML [19]. Frequency-selective fat suppression and suppression of chemical shifts are, in general utilized to identify fat signals [20]. A typical AML shows a T1-hyperintense fatty lesion with an abundant “Indian ink” artifact surrounding the kidney.

Renal AML mostly arises in the cortex and protrudes into the perirenal space. This benign renal neoplasm can be diagnosed readily preoperatively based on intratumoral fat [21]. However, it is extremely rare that a renal AML originates from the renal sinus. To date, only 19 renal pelvic AMLs have been described in the literature [22-25].

The unusual location of this entity hampers the preoperative diagnosis. However, if intratumoral fat is visualized, a renal AML should be considered. The clinical manifestations of a renal AML involving the pelvis are non-specific; patients may be asymptomatic or present with lumbago and gross hematuria [22]. If an AML is diagnosed, the size and clinical manifestations determine the type of treatment [7]. Asymptomatic patients can be observed if the diameter is <4 cm; the surgical intervention is unnecessary. For those with apparent symptoms or a diameter >4 cm, surgery or embolization may be carried out [2]. Nephron-sparing surgery or selective artery embolization is the first option. Nephron-sparing surgery is technically challenging due to the difficulty of exposure, prolonged warm ischemia time, violation of the collecting system, and perioperative complications [26].

CT and MRI facilitate detection of the AML in the renal sinus. However, the diagnosis and management of this entity is challenging because of the uncertainty of the nature of the lesion, which is often indistinguishable from a urothelial carcinoma (especially since the tumor is fat-poor variant and associated with hematuria). Our three patients presented with variable degrees of hematuria. CT revealed soft masses centered in the renal pelvis; a hypoattenuating area was not identified on preoperative non-contrast CT or MRI. CT urography or retrograde pyelography showed filling defects in the calyx collecting system and “goblet sign”. The imaging diagnosis was not a classic AML and, along with its unusual location and hematuria, the possibility of urothelial carcinoma could not be excluded. Considering the diagnosis of urothelial carcinoma, flexible ureteroscopy or percutaneous biopsy was not employed, and LRNU was employed subsequently. Finally, histopathology and IHC staining revealed fat-poor renal AMLs. During follow-up period, the patients remain in good renal function and show no symptoms or images suggesting recurrence.

Conclusion

To our knowledge, this is the first case report of fat-poor renal AML involving the renal pelvis and presenting with hematuria. The rarity of these lesions hinders differentiating them from the renal pelvic urothelial carcinoma. The preoperative diagnosis and management are complex and challenging. Nephron-sparing treatment is crucial for the treatment for patients with renal pelvic AMLs.

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Disclosure of conflict of interest

None.
Fat-poor angiomyolipoma in the renal pelvis mimicking urothelial carcinoma

**Abbreviations**

AML, angiomyolipoma; CD, cluster of differentiation; TSC, tuberous sclerosis complex; HPF, high-power field; CT, computed tomography; HU, Hounsfield units; MRI, Magnetic resonance imaging; LRNU, laparoscopic nephroureterectomy; IHC, Immunohistochemical; ROI, region of interest; RBC, red blood cell.

**Address correspondence to:** Wei He, Department of Urology, Shandong Provincial Hospital Affiliated to Shandong First Medical University, 324, Jingwu Road, Huaiying District, Jinan 250021, Shandong, China. E-mail: heweilejmu.edu.cn

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Fat-poor angiomyolipoma in the renal pelvis mimicking urothelial carcinoma


