Centrally Thrombosed Renal Angiomyolipoma: A COVID-Induced Pathology?

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ABSTRACT

Renal Angiomyolipomas (AMLs) are benign neoplastic entities paradigmatically composed of smooth muscle, blood vessels, and adipose tissue. The cornerstone of renal AML identification fundamentally entails imaging; however, findings may rarely resemble malignancy and subsequently obfuscate diagnosis. Compellingly, the comorbid effect of viral diseases such as COVID-19 on neoplasm integrity and morphology remains incompletely understood. The following case reports a 46-year-old female presenting with intermittent right flank pain persisting for three weeks. Preliminary sonographic studies revealed a predominantly echogenic, space-occupying lesion with well-defined margins in the right renal cortex undergoing angiogenesis. Shortly thereafter, the patient contracted COVID-19, and the right flank pain progressed to a debilitatingly constant nature described as sharp, stabbing, and aggravating to an eight on a scale of ten. Recovery was uncomplicated; however, the patient presented with mild thrombocytopenia. Contrast-enhanced CT scans elucidated a compelling hypodense mass center suggesting the presence of an encapsulated thrombus accompanied by further invasion of Morison's pouch 25 days post-initial identification. Histopathological examination of the surgically excised specimen confirmed the likely diagnosis of a centrally thrombosed renal angiomyolipoma. Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) infection may have ostensibly contributed to neoplasm morphology alterations and subsequent thrombosis, as intrinsic renal cell damage is well-documented in the literature. Consequently, clinicians must remain vigilant that radiographic abnormalities may emerge secondary to comorbid viral diseases such as COVID-19 via incompletely understood mechanism(s).

INTRODUCTION

Renal Angiomyolipomas (AMLs) are benign mesenchymal neoplasms classically comprising assorted proportions of smooth muscle cells, adipose tissue, and blood vessels. Renal AMLs are the most frequent benign renal tumor, with oscillating prevalence between 0.2% and 0.6% and a reported female preponderance [1]. Renal AML etiology is sporadic in 80% of cases; therefore, yielding heterogenous radiologic features and pleomorphic pathologic findings [2,3]. In rare occasions, imaging of a renal AML may resemble histopathological signs of malignancy due to frequent bleeding, necrosis, perirenal extension, and myomatous pleomorphism [4,5]. Inevitably, an accurate preoperative elucidation is fundamental to minimizing dubious nephrectomies and preserving renal function [6]. In the following case report, a retrospective medical record examination revealed a centrally thrombosed renal AML, ostensibly secondary to COVID-19 infection.
CASE PRESENTATION

A 46-year-old Venezuelan woman presents to an outpatient clinic with the chief complaint of non-traumatic intermittent right flank pain starting three weeks ago. The pain did not radiate distally but was described as stabbing and rated a three on a scale of ten. The patient had no significant past medical or family history, including allergies. She denied any alcohol intake, tobacco, or substance abuse. On presentation, the patient was afebrile with a blood pressure range of 115/74, a heart rate of 71 beats/minute, a respiratory rate of 20 breaths/minute, an oxygen saturation of 98% on room air, and a BMI of 26.

Physical examination was unremarkable; however, sonographic studies dating from December 19, 2020, revealed a 2.33 x 1.89 cm predominantly echogenic, marginally regular mixed mass located in the right renal cortex and intruding anterosuperiorly into Morison’s pouch (Figure 1.A). Notably, Doppler ultrasound evaluation unraveled intussusceptive-like angiogenesis in the superior third of the renal cortex (Figure 1.B). The remainder of the sonographic studies for the liver, gallbladder, biliary tree, pancreas, spleen, bladder, uterus, retroperitoneal structures, and vessels were unremarkable. Initial laboratory workup encompassed a comprehensive metabolic panel, complete blood count with differential, and a urinalysis, which failed to reveal any abnormalities except for an incidental finding regarding fasting glucose levels of 75 mg/dL. Notably, leukocyte counts were 8.2 x 10⁹/L, RBCs 4.9 x 10¹²/L, hemoglobin 13.5 g/dL, hematocrit 41%, MCV 83.7 fl, MCH 27.6 pg, MCHC 32.9 g/dL, and platelets 250 x 10⁹ μ/L.

A CT urogram was ordered to elucidate the mass; however, qRT-PCR analysis confirmed the patient had contracted COVID-19. Her symptomatology included fever, headache, anosmia, cough, mild dyspnea, and myalgias; nevertheless, the etiology did not result in respiratory complications. The right flank pain rapidly progressed to a debilitatingly constant nature described as sharp, stabbing, and aggravating to an eight on a scale of ten. The patient denied fever, macrohematuria, dysuria, emesis, or nausea. Medical records indicate that emergency room physicians ordered contrast-enhanced abdominal and pelvic CT scans on January 13, 2021, revealing an appreciable surface area

Figure 1: Ultrasound 1.A reveals a space-occupying lesion in the right renal cortex, whereas 1.B exhibits angiogenesis via Doppler ultrasound studies on a transverse plane.

Figure 2: Transverse view of contrast-enhanced CT scan elucidating a space-occupying mixed mass.
increase associated with a 2.6 x 2.4 cm space-occupying mixed lesion ostensibly invading the hepatorenal space but exhibiting mostly well-defined margins (Figures 2.A and 2.B). Notably, a striking finding comprises a prominently encapsulated hypodense mass center visible in coronal planes (Figures 3.A and 3.B).

Excretion of intravascularly administered contrast medium remained under normal parameters and the rest of the CT evaluation was unremarkable. Shortly thereafter, a fine-needle aspiration biopsy was collected; however, the results were inconclusive. Inevitably, a laparoscopic right radical nephrectomy was indicated due to concerns encompassing the rapidly growing mass exhibiting a seemingly necrotic or hemorrhagic center accompanied by architectural delving into Morison’s pouch, presumably suggesting early malignancy attributes resembling a small lipid-rich renal cell carcinoma.

Preoperative labs were unremarkable, with values comprising WBCs at 8.8 x 10^9/L, RBCs at 4.4 x 10^12/L, hemoglobin 13.3 g/dL, hematocrit 40%, MCV 90.9 fl, MCH 30.2 pg, and MCHC 33.3 g/dL, except for subtle thrombocytopenic results of 145 x 10^3 μ/L. The surgical intervention was a success, and there were no associated complications. Specimen examination by the pathology department found the renal parenchyma remained intact with conserved corticomedullary relation and absent tumor metastasis to the renal hilum. The report confirmed a 2.6 x 2.6 x 2.2 cm semi-firm mass located in the anterior aspect of the renal cortex (Figures 4.A and 4.B), which was subsequently analyzed microscopically.

The tumor predominantly consisted of spindle-shaped smooth muscle cells circumambient to clusters of proliferating cells undergoing hyalinization and exhibiting nuclear pleomorphisms such as irregular chromatin structure,
micronucleoli, and isolated mitotic activity assembling into a thick-walled capsule. Mature adipocytes and dysmorphic blood vessels lacking elastic lamina were also found; therefore, suggesting a classic triphasic angiomyolipoma as the responsible entity. Notably, the mass center revealed a proximal hemorrhagic focus accompanied by subtly localized necrosis: a compellingly rare manifestation. Microscopic examination of the thrombus with Masson’s trichrome revealed a fibrin-rich surface subject to dynamic structural permutations. Immunohistochemical studies were necessary to validate the angiomyolipoma diagnosis; however, cost constraints rendered the patient unable to undergo confirmatory studies.

**DISCUSSION**

AMLs are ordinarily benign neoplasms; however, life-threatening complications may stochastically develop due to retroperitoneal hemorrhage secondary to spontaneous ruptures [7,8]. Incidental discoveries account for approximately 80% of all cases; thus, imaging remains a fundamental diagnostic tool [9,10]. Paradigmatically, the cornerstone of renal AML diagnosis in all modalities is fat presence; nevertheless, the criterion may overlap with rare entities such as the so-called fat-containing renal cell carcinoma [11-16]. Malignant neoplasm suspicions are contingent on succinct guidelines comprising mass size, demarcation irregularities, invasive behavior, lymph node involvement, and histopathological features such as hemorrhagic signs, necrosis, or fat ratio [12].

Compelling studies demonstrate that Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2), the causative agent for COVID-19, may induce kidney damage [17-19]. Indeed, patients afflicted by COVID-19 pneumonia may present multiple types of kidney injuries, whereas histological studies from expired patients revealed profuse deterioration of renal integrity [20]. Nonetheless, the comorbid effect of COVID-19 immunopathology on previously existing renal neoplasms remains a mystery. Jocelyn Young et al. reported the case of a 22-year-old female diagnosed with a ruptured renal AML two weeks after COVID-19 infection, albeit the patient lacked risk factors associated with coagulopathic states such as pregnancy, aneurysm, or a mass greater than 4 cm [21]. The authors concluded that it is reasonable to speculate that COVID-19 may have induced the spontaneous AML rupture due to the conspicuous timing; however, additional evidence must validate the causal relationship.

The present case is unique, as COVID-19 infection may have kinetically contributed to neoplasm morphology abnormalities. Initial Doppler ultrasound examination revealed a marginally regular echogenic mass endowed with intussusceptive-like angiogenesis and seemingly invading Morison’s pouch. Subsequently, contrast-enhanced CT scans unraveled an appreciable surface area expansion post-COVID accompanied by exacerbated symptomology. Compelling evidence also revealed a hypodense center associated with the exophytic mass, suggesting an unenhanced encapsulated thrombus. Ascribable to inconclusive biopsy results, mixed tumor morphology, rapid growth, and invasive behavior, a minimally invasive radical nephrectomy was performed. Specimen examination by the pathology department confirmed the likely diagnosis of a triphasic renal angiomyolipoma presenting with a thrombotic center accompanied by localized necrosis.

The multifactorial mechanism remains in question; however, it is known that mild thrombocytopenia can exist in 40-55% of COVID-19-positive patients [22,23]. Moreover, thrombocytopenia severity is proportional to clinical outcomes since platelet reduction could be correlated to gas exchange parameter alterations dictated by the A-aO2 gradient from a systemic standpoint [24,25]. Our patient profile is consistent with thrombocytopenia as platelet levels were identified at 145 x 109 μ/L post-COVID. In a similar vein, the molecular mechanism(s) responsible for intrinsic renal cell damage is postulated to be via ACE2-rich kidney and bladder tissue [26,27].

Pro-inflammatory cytokine and chemokine secretion may further aggravate tissue damage and necrosis. Evidence reveals that exuberant COVID-induced interleukin-6 (IL-6) responses result in receptor-mediated activation of vascular endothelial growth factor and decreased E-cadherin expression to orchestrate vascular permeability, shock, and multiorgan dysfunction syndrome (MODS) [28]. Plausibly, cell-mediated responses may concurrently contribute to immunopathology. Kidney biopsies isolated from COVID-19 patients have identified tubulointerstitial infiltration of CD68+ macrophages, CD56+ natural killer cells, CD4+, and CD8+ T cells, potentially contributing to cytotoxicity [29]. Further studies might elucidate the combined mechanism(s) responsible for renal mass architectural abnormalities. In conclusion, clinicians must remain vigilant that comorbid viral infections such as COVID-19 may potentially alter neoplasm integrity, ostensibly resulting in thrombosis and increasing the risk for embolic episodes. Radiographic novelties may compound diagnosis, treatment modality, and case management; thus, clinical awareness in comorbid cases of immunopathology secondary to viral infections might enhance the clinical outcome.

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CONFLICT OF INTEREST

The author declares no conflict of interest.

References


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CONSENT FOR PUBLICATION

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