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Anastomosing Hemangioma of the Kidney in End-Stage Renal Disease: A Case Report

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ABSTRACT

Background: Renal Anastomosing Hemangioma (AH) is a rare benign vascular neoplasm first described by Montgomery and Epstein in 2009 and later incorporated into the 2016 World Health Organization (WHO) classification of urinary system tumors. Histologically, AH is characterized by a unique anastomosing network of sinusoidal vessels lined with hobnail endothelial cells, often accompanied by extramedullary hematopoiesis. The tumor predominantly occurs in middle-aged individuals, with an average age of 50 years, and exhibits a slight male predominance. There is a significant clinical association between AH and renal failure, with approximately 32% of patients exhibiting some degree of renal dysfunction; of these, nearly two-thirds progress to end-stage renal disease. Differentiating AH from renal cell carcinoma preoperatively remains challenging due to substantial radiologic overlap, resulting in a high misdiagnosis rate of up to 80%, which highlights the difficulty in achieving an accurate preoperative diagnosis.

Case Description: A 39-year-old woman was admitted to the hospital following the detection of a left renal mass during a routine follow-up examination. Preoperative imaging identified a left renal neoplasm of indeterminate nature. In light of the patient's 8-year history of renal failure and the inconclusive imaging results regarding malignancy, the patient elected to undergo a radical nephrectomy. Postoperative pathological analysis confirmed the diagnosis of a left renal anastomosing hemangioma. The patient was discharged on the third postoperative day and has exhibited no abnormalities during six months of follow-up.

Conclusions: Considering the diagnostic challenges in accurately differentiating angiomyolipoma with hemorrhage (AH) from renal cell carcinoma prior to surgery, especially in patients with pre-existing renal failure, radical nephrectomy presents itself as a viable management strategy. This approach effectively reduces the risk of bleeding complications associated with the necessary anticoagulation during dialysis following a partial nephrectomy.

KEYWORDS: Renal anastomosing hemangioma, Renal cell carcinoma, Differential diagnosis, Radical nephrectomy, Renal failure.

ABBREVIATIONS

RAH: Renal Anastomosing Hemangioma; AH: Anastomosing Haemangioma; WHO: World Health Organization; CT: Computerized Tomography; MRI: Magnetic Resonance Imaging; CM: Centimeter; CD31: Cluster of Differentiation 31; CD34: Cluster of Differentiation 34; ERG: v-ets Avian Erythroblastosis Virus E26 Oncogene Homolog; CK: Cytokeratin; P53: Tumor Protein P53; Ki-67: Ki-67 Antigen (named after Kiel, Germany); PAX-8: Paired Box Gene 8; CA9: Carbonic Anhydrase IX; P504S: P504S / Alpha-Methylacyl-CoA Racemase; CD10: Cluster of Differentiation 10; VEGF: Vascular Endothelial Growth Factor; Inhibin-a: Inhibin-alpha; S-100: S-100 Protein; NSE: Neuron-Specific Enolase; CD56: Cluster of Differentiation 56; SMA: Smooth Muscle Actin; MelanA: Melanoma Antigen Recognized by T-cells 1; GLut-1: Melanoma Antigen Recognized by T-cells 1;PAX-8: Paired Box Gene 8; S-100: S-100 Protein (soluble in 100% saturation ammonium sulfate); ESRD :end-stage renal disease; HMB-45: Human Melanoma Black-45(Antigen); Melan-A: Melanoma Antigen Recognized by T-cells; SMA+: Smooth Muscle Actin (Positive); CAIX: Carbonic Anhydrase IX.

INTRODUCTION

Anastomosing hemangioma (AH) represents a distinct and rare morphological variant of hemangioma that has gained increasing recognition in recent years.[1-4] Histologically, AH is characterized by a unique sinusoidal, anastomosing growth pattern that closely resembles splenic parenchyma, thereby presenting a potential diagnostic challenge in distinguishing it from well-differentiated angiosarcoma.[5] Although initially identified in the genitourinary tract, particularly the kidney, AH has also been documented in various other anatomical locations. Preoperative diagnosis is notably challenging, as imaging features observed on CT or MRI are often non-specific and can be easily mistaken for more common malignant renal tumors.[6] In this report, we present a case of renal AH in a patient with end-stage renal disease. The objectives of this report are: (1) to contribute to the limited literature on this rare lesion; (2) to discuss its characteristic histopathological features essential for accurate diagnosis; (3) to underscore the importance of including AH in the differential diagnosis of renal masses to prevent misdiagnosis and overtreatment; and (4) to review the existing literature to summarize its typically benign clinical course.

CASE PRESENTATION

A 39-year-old female patient presented to our hospital with the primary concern of a left renal mass identified during a physical examination conducted two weeks prior. The patient reported that an abdominal ultrasound performed at that time revealed a hypoechoic nodule in the left kidney, which raised suspicion for a neoplasm and prompted recommendations for further investigation. Subsequent abdominal computed tomography (CT) confirmed the presence of a neoplasm in the mid-portion of the left kidney, measuring approximately 2.5 cm × 2.4 cm, with characteristics yet to be determined. The patient reported no symptoms of urinary frequency, urgency, dysuria, difficulty voiding, abdominal distension, diarrhea, nausea, vomiting, palpitations, chest tightness, shortness of breath, cough, sputum production, or chest pain.

The patient's medical history is significant for a 10-year history of hypertension, which has been managed with long-term administration of oral antihypertensive agents, including amlodipine, carvedilol, sacubitril/valsartan, and terazosin. Additionally, she was diagnosed with IgA nephropathy 15 years prior, which advanced to uremia 8 years ago, necessitating ongoing maintenance dialysis.

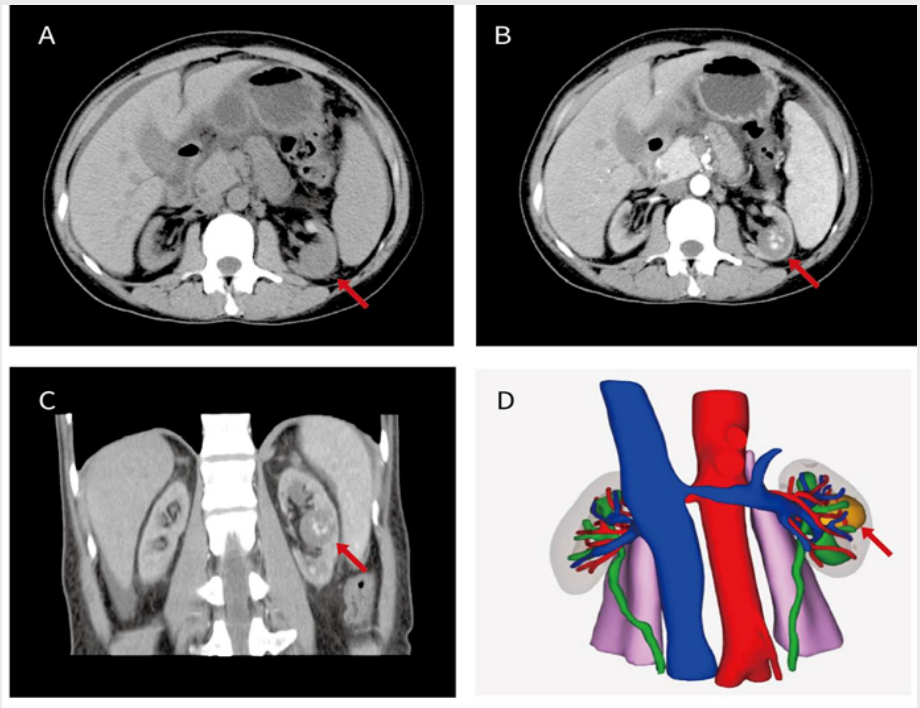
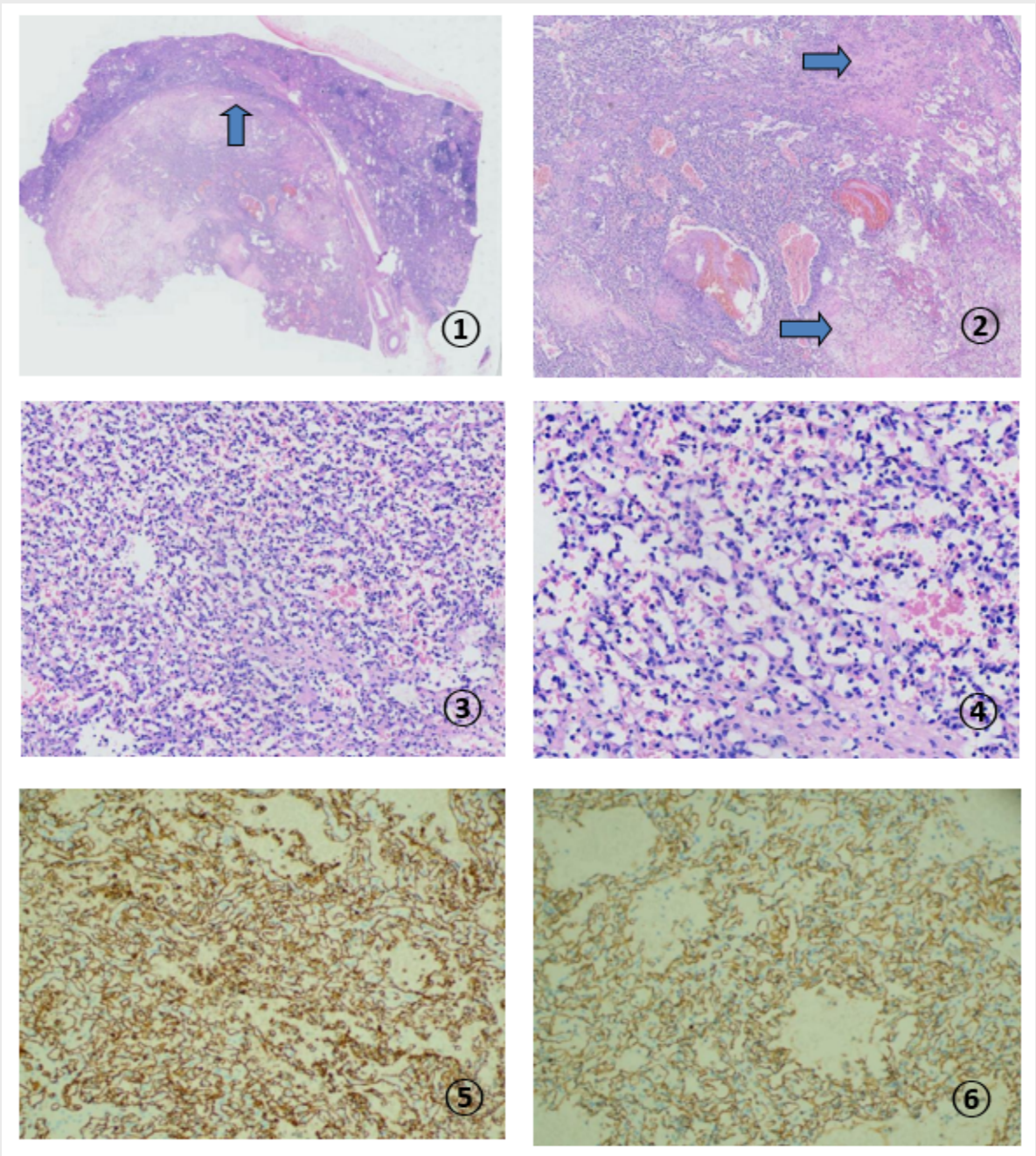


Figure 1. Computed tomography-based assessment strategy of anterior ankle soft tissue thickness using axial sequence

Preoperative laboratory assessments, encompassing a complete blood count, urinalysis, evaluations of liver and renal function, coagulation profile, and electrolyte panels, were conducted. Computed tomography imaging corroborated the presence of an endophytic tumor in the left kidney, with no significant exophytic extension beyond the renal surface (Figure 1). Following the exclusion of any contraindications to surgical intervention, the patient underwent a retroperitoneal laparoscopic radical nephrectomy of the left kidney. The surgical procedure was executed via the retroperitoneal approach, involving the sequential ligation of the renal artery, renal vein, and ureter, thereby facilitating the complete excision of the left kidney along with the perirenal adipose tissue. Hemodialysis was recommenced on the second postoperative day.

The postoperative pathological examination corroborated the diagnosis of anastomosing hemangioma in the left kidney. Immunohistochemical analysis revealed positive staining for CD31, CD34, ERG, and Vimentin, while negative staining was observed for CK, PAX-8, CA9, P504S, CD10, VEGF, Inhibin-α, S-100, NSE, CD56, Melan-A, and GLUT-1. The P53 protein exhibited a wild-type expression pattern, and the Ki-67 proliferation index was low, with less than 5% positivity. Smooth muscle actin (SMA) staining highlighted the presence of pericytes surrounding the vascular channels. The neoplasm was confined to the renal capsule, with no tumor involvement at the ureteral margin (Figure 2). No recurrence was detected during the six-month postoperative follow-up period.



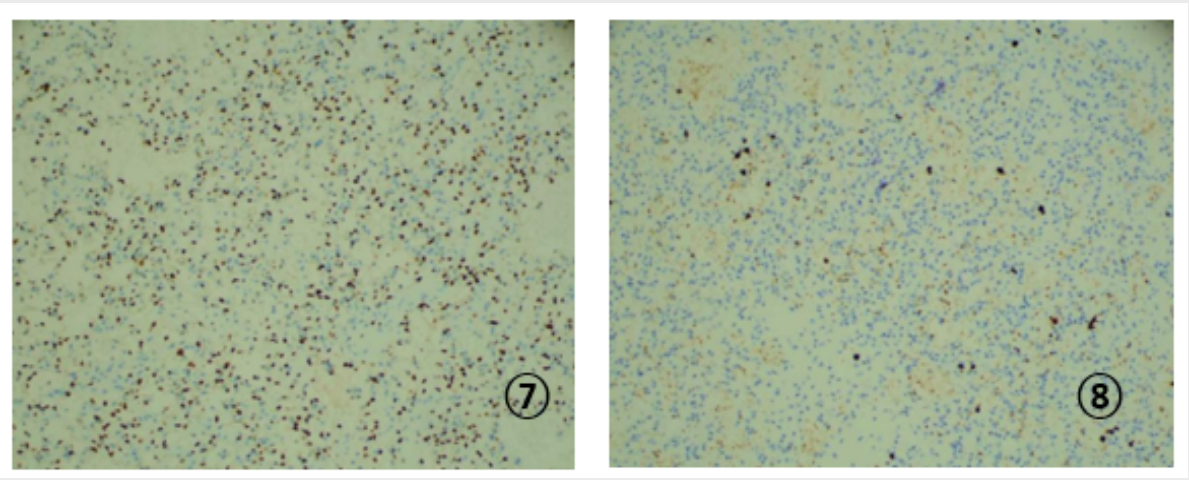


Figure 2. Microscopic and immunohistochemical images.

1. The tumor is clearly demarcated from the surrounding normal renal tissue, HEx20.

2. The tumor contains abundant edema and hyaline interstitial tissue, HEx40.

3. The tumor consists of tightly packed capillary lumens that are interconnected and communicate with each other, HEx200

4. Endothelial cells in the vascular lumen are arranged in a single layer, with some cells exhibiting a nail-like morphology resembling the red pulp structure of the spleen, HEx400

5-7. Endothelial cells showed positive expression for CD31, CD34, and ERG, IHCX200.

8. The Ki-67 index in tumor cells is approximately 5%, IHCX200.

DISCUSSION

Renal anastomosing hemangioma (RAH) is classified as a subtype of hemangioma that manifests within the renal tissue. According to the World Health Organization's 2020 classification of soft tissue tumors, hemangioma is formally recognized as a distinct tumor entity.7 RAH is characterized by an absence of specific clinical symptoms or signs, and its imaging characteristics are often indistinguishable from those of malignant renal tumors, which frequently results in preoperative misdiagnosis.8 As a rare benign vascular neoplasm, the nonspecific clinical and radiological presentations of RAH constitute the primary challenges in achieving accurate preoperative diagnosis.9

In the present case, the preoperative CT scan revealed a "left renal neoplasm of undetermined nature," which posed challenges in distinguishing it from renal cell carcinoma, particularly the chromophobe or papillary RCC subtypes, as documented in previous literature.[10] The conclusive diagnosis was entirely dependent on postoperative pathological and immunohistochemical analyses (Table 1). Microscopically, classic renal angiomyolipoma (RAH) is characterized by a diffusely distributed, anastomosing sinusoidal vascular network that mirrors the architecture of the splenic red pulp.[11] The vascular channels are lined by a single layer of unremarkable endothelial cells, which are typically flat or exhibit a hobnail morphology, without nuclear atypia or significant mitotic activity.[12] In this case, the low Ki-67 proliferation index (<5% positive) further corroborates its benign biological nature.

Immunohistochemistry is instrumental in the differential diagnosis process. The strong expression of vascular endothelial markers, including CD31, CD34, and ERG, confirms the vascular origin of the tissue. Conversely, the absence of staining for various epithelial markers (such as CK and PAX-8), renal cell carcinoma markers (such as CA9, CD10, and P504S), and other tumor markers (such as S-100 and Melan-A) effectively rules out malignancies such as renal cell carcinoma, angiosarcoma, and epithelioid hemangioendothelioma.[13] Additionally, the presence of smooth muscle actin (SMA) around the vessels underscores the pericytal support structure, a distinguishing feature of benign hemangiomas.[14]

The distinctiveness of this case is attributed to the patient's intricate medical history, characterized by a prolonged history of uremia necessitating dialysis and the presence of IgA nephropathy. An increasing body of evidence indicates a potential correlation between renal angiomyolipoma with hemorrhage (RAH) and end-stage renal disease (ESRD), particularly in patients undergoing long-term dialysis.[15] One hypothesis suggests that the metabolic disturbances and micro-environmental changes associated with chronic renal failure may stimulate reactive endothelial hyperplasia, thereby contributing to the development of this benign tumor.[16] Although the precise pathogenesis remains elusive, this case provides additional clinical evidence supporting this association. It underscores the importance for urologists to consider RAH in the differential diagnosis of renal masses identified in patients with ESRD, despite its infrequency.

In the context of management, radical nephrectomy continues to be the most commonly utilized strategy, primarily due to the substantial challenges associated with preoperative differentiation between renal angiomyolipoma (RAH) and renal cell carcinoma.[17]

Nonetheless, with heightened awareness and advancements in imaging techniques, nephron-sparing surgery (partial nephrectomy) or even active surveillance are emerging as viable options for small tumors exhibiting typical benign characteristics, such as well-defined borders and homogeneous enhancement. This is particularly relevant in scenarios involving bilateral tumors or pre-existing renal impairment.[18] In the case of this patient, radical nephrectomy was deemed an appropriate intervention, considering the patient's prolonged dialysis status and the lack of necessity for renal preservation. The prognosis is favorable, with no recurrence detected during short-term follow-up, consistent with the benign clinical trajectory reported in the literature.

Table 1. Postoperative pathological and immunohistochemical analyses .

Characteristics and Features	Renal Anastomosing Hemangioma	Angiomyolipoma	Angiosarcoma	Renal Cell Carcinoma (Hypervascular)
Clinical Biological Behavior	Benign	Benign (the epithelioid variant may exhibit malignant potential in rare cases)	Highly aggressive	Malignant
Histological Features	An anastomosing sinusoidal vascular network, Hobnail endothelial cells, Extramedullary hematopoiesis	Mature adipose tissue, Spindled smooth muscle, Thick-walled blood vessels	Infiltrative growth pattern, marked cytological atypia, and increased mitotic activity	Glandular arrangement, Clear or eosinophilic cytoplasm
Immunohistochemistry	CD31+/CD34+/ERG+, Ki-67 low	HMB-45+/Melan-A+/ SMA+, CD34-	CD31+/ERG+, Ki-67 high	PAX-8+/CAIX+/ CD10+
Radiological Characteristics	Demonstrates significant enhancement on contrast-enhanced CT/MRI, but shows no hypermetabolism on PET/CT	The lesion contains fat components (evidenced by negative attenuation values on unenhanced CT) and demonstrates significant enhancement after contrast administration.	Ill-defined borders, frequent necrosis, and marked heterogeneous enhancement	Solid mass with rapid wash-in and wash-out enhancement pattern
Association with renal failure	Approximately 30% of patients are accompanied by renal impairment.	A high incidence in individuals with tuberous sclerosis complex	Occurring independently	Occurring independently
Treatment Strategy	Nephron-sparing Surgery (Preferred Approach)	Embolization or Nephron-sparing Surgery	Radical Resection with Adjuvant Chemoradiotherapy	Radical or Partial Nephrectomy
Prognosis	The prognosis is favorable, with no reported cases of recurrence or metastasis following complete resection	Favorable (classic subtype)	Poor prognosis with high propensity for recurrence and metastasis	highly dependent on tumor stage and histological grade.

CONCLUSIONS

Renal anastomosing hemangioma is an infrequent benign neoplasm that is often preoperatively misdiagnosed as renal cell carcinoma. Accurate diagnosis necessitates histopathological examination and immunohistochemical analysis. Urologists should maintain a high degree of suspicion for this condition, especially when assessing small renal masses in patients with end-stage renal disease. Although surgical excision remains the primary therapeutic approach, the selection of the surgical procedure—ranging from radical nephrectomy to nephron-sparing surgery—should be tailored to the tumor's size, location, renal function, and the patient's overall health status. With heightened awareness, nephron-sparing surgery

is expected to become a viable option for an increasing number of patients in the future. The principal limitations of this case report include the relatively short duration of follow-up and the lack of genetic studies to explore potential pathogenic mutations.

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CONFLICTS OF INTEREST

All authors have completed the ICMJE uniform disclosure form. The authors have no conflicts of interest to declare.

DATA AVAILABILITY

The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

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