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Case Report

Multimodal imaging appearance including cinematic rendering of renal malakoplakia in a patient with *E. coli* bacteremia ☆,☆☆

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ABSTRACT

Renal malakoplakia is a rare inflammatory disorder that predominantly affects the bladder, but has also been known to affect the kidneys. We present a case of a young woman with renal malakoplakia and concomitant *E. coli* bacteremia. The patient underwent numerous imaging studies during her clinical evaluation including ultrasound, magnetic resonance imaging, and computed tomography with 3-dimensional and cinematic renderings. Diagnosis was ultimately confirmed with renal biopsy which demonstrated Michaelis-Gutman bodies, a pathognomonic pathological finding in malakoplakia. She was started on antibiotics as well as bethanechol and ascorbic acid. Although her renal function improved with this treatment, she continued to have signs and symptoms of infection and she is planned for upcoming left nephrectomy.

Introduction

Malakoplakia is a rare granulomatous inflammatory disorder that predominantly affects the urinary tract; however, involvement of other organ systems such as the gastrointestinal (GI) tract, lungs, lymph nodes, and skin has also been reported [1]. The bladder is the most likely portion of the genitourinary tract to be impacted by malakoplakia, followed by the kidneys [2]. Renal lesions are usually bilateral and multifocal [2].

Malakoplakia most often occurs in patients with immunosuppression and/or autoimmune disorders requiring steroid use, including solid organ transplant recipients [1,3]. It is frequently associated with underlying *Escherichia coli* (*E. coli*) infection [2,4]. Patients may present with signs and symptoms of urinary tract infection including fever, flank pain, and pyuria

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[2,5]. In some cases, a renal mass may be present on imaging [6]. Because of this, renal malakoplakia may initially be mistaken for other disease entities such as renal cell carcinoma [5]. Multiple studies have described the imaging appearance of renal malakoplakia on computed tomography (CT), with less information in the literature regarding the imaging features on magnetic resonance imaging (MRI) and ultrasound [7–11]. To date, this condition has not been characterized with cinematic and 3-dimensional (3D) renderings of cross-sectional imaging data. We present the case of a young woman with biopsy-proven renal malakoplakia and concomitant *E. coli* bacteremia who underwent multimodal imaging, including CT with 3D and cinematic renderings.

Case report

A 32-year-old female with a past medical history of Raynaud's phenomenon and recurrent urinary tract infection (UTI) presented to an outside hospital with a 5-day history of UTI symptoms. Two days prior to presentation she developed shortness of breath. Upon initial evaluation, she was found to be hypotensive and altered.

Pressors and broad spectrum antibiotics (vancomycin, cefepime, and metronidazole) were initiated for treatment of presumed sepsis. Blood and urine cultures were obtained and grew *E. coli* and enterobacter. Antibiotic coverage was then narrowed down to cefepime. Further diagnostic workup revealed anemia, thrombocytopenia, and coagulopathy which required a transfusion of 3 units of platelets, 2 units of red blood cells, and fresh frozen plasma. The patient was also hyponatremic with a sodium of 117 mmol/L. A brain MRI and lumbar puncture were obtained and were unremarkable. During her hospital course, she developed acute respiratory distress requiring intubation. Laboratory studies revealed an elevated creatinine (Cr) of 6.4 mg/dL (baseline 0.6 mg/dL). Urinalysis was notable for 3+ blood, 3+ leukocytes, 3+ protein, and 4+ bacteria. Due to these findings, she was started on continuous renal replacement therapy with subsequent improvement in her renal function. CT of the abdomen and pelvis was obtained which demonstrated enlarged kidneys and hepatosplenomegaly. While receiving treatment at the outside hospital, she developed persistent agitation that prompted transfer to the medical intensive care unit at our institution, a large tertiary academic medical center.

Upon arrival, the patient was found to be anemic and thrombocytopenic with a hemoglobin of 7.6 g/dL and platelet count of 15,000 k/cu mm. She also had a profound leukocytosis with a white blood cell count of 30.78k/cu mm. She also was found to have an anion gap metabolic acidosis (bicarbonate = 20 mmol/L, anion gap = 18) and an elevated lactate (lactate = 5.6 mmol/L). She continued to be hyponatremic with a sodium of 128 mmol/L and her creatinine improved but was still elevated (Cr = 1.8 mg/dL). Based on her clinical presentation, differential considerations included infiltrative diseases that may involve the kidneys, such as idiopathic Castleman disease, malignancy, IgG4-related disease, or granulomatous disease.

Repeat CT of the abdomen and pelvis with intravenous (IV) contrast was obtained to further characterize the renal findings, which demonstrated bilateral nephromegaly as well as heterogeneous renal parenchymal enhancement and loss of corticomedullary differentiation (Fig. 1a). Focal wedge-shaped hypodensities were also noted in the subcortical left kidney suggesting superimposed necrosis (Fig. 1b).

Cinematic rendering of the CT data further demonstrated the extent of the inflammatory changes in both kidneys as well as bilateral renal abscesses (Figs. 1c and d). Based on the imaging findings, differential considerations now included infiltrative bilateral renal disease, glomerulonephritis, and less likely lymphoma. Renal cell carcinoma was felt to be less likely given the imaging features.

Renal biopsy was obtained following recovery of platelet counts. A total of 7 slides were examined, including 4 hematoxylin-eosin stains, 1 periodic acid-schiff stain, 1 silver stain, and 1 trichrome stain. Tissue cores demonstrated diffuse infiltration by histiocytic cells with focal abscesses. Gram stain and Gram Weigert stains were negative for bacteria. The Von Kossa stain was positive in sparse small round formations within the histiocytic infiltrate, suggestive of Michaelis-Gutman bodies. Additionally, immunostain for CD163 was diffusely positive in the renal cortex suggesting an infiltration of macrophages or histiocytes. Based on these findings, the diagnosis of pyelonephritis with focal micro-abscesses and malakoplakia was made.

Ultrasound imaging was obtained during the left renal biopsy and during a right upper quadrant ultrasound performed several days after the renal biopsy due to suspicion for biliary tract obstruction. Ultrasound demonstrated left greater than right nephromegaly with multiple renal abscesses (Fig. 2). MRI (Fig. 3) was also obtained and demonstrated bilateral nephromegaly with intrarenal and perinephric fluid collections as well as mild left hydronephrosis secondary to thickening of the left renal pelvis. Thickening of the left perinephric fascia with extension to the retroperitoneal soft tissues was also noted.

After obtaining the biopsy results, treatment options were weighed including administration of antibiotics with intracellular penetration capabilities due to the macrophage dysfunction associated with malakoplakia. Tigecycline was chosen due to the resistance profile of the patient's bacterial isolate and the mechanism of resistance compared to the other tetracyclines [14]. Ceftriaxone was also used to treat the patient as bacterial cultures showed sensitivity to this medication. The patient was also started on bethanechol and vitamin C due to potential to aid in intracellular bacterial destruction in macrophages through increasing the intracellular conversion of cyclic guanosine monophosphate (cGMP) to cyclic adenosine monophosphate (cAMP). She was also later switched to minocycline due to her sensitivity panel showing susceptibility and its ability to be taken by mouth. A nephrectomy was considered but was deferred due to possible liver involvement.

A liver biopsy was obtained which did not show evidence of hepatic malakoplakia. In order to prevent significant morbidity, nephrectomy was forgone. Over the course of her hospital stay, the patient's creatinine returned to normal range. However, she continued to have leukocytosis and low-grade fevers despite receiving additional antibiotics. Subsequent

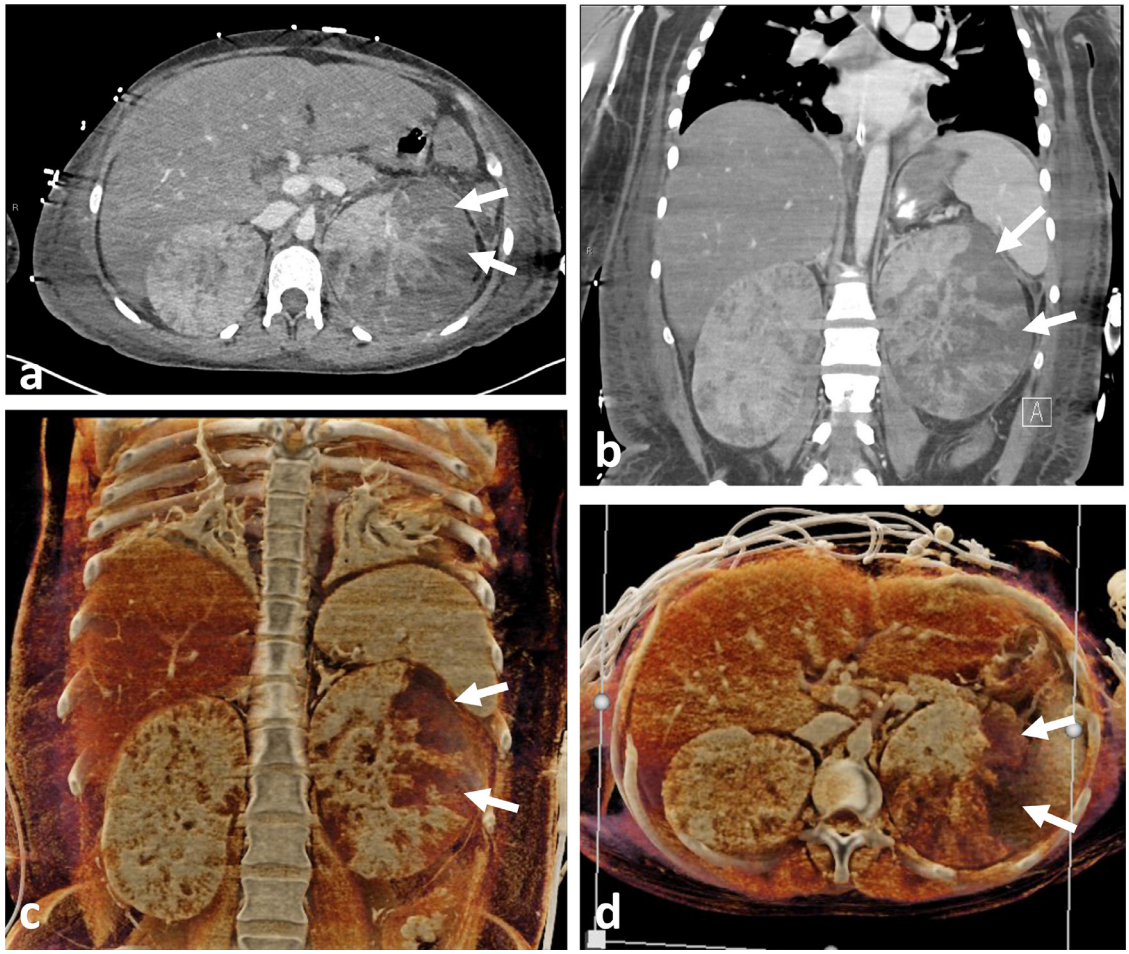

Fig. 1 – Axial (a) and coronal (b) venous phase CT scan at the level of the kidneys demonstrating bilateral nephromegaly with poor corticomedullary differentiation and multifocal hypoattenuation, most pronounced in the left kidney. Confluent regions of parenchymal hypoattenuation (arrows) may reflect abscesses and/or infarcted tissue. Coronal (c) and axial (d) cinematic renderings which further define the extent of multifocal renal abscesses (arrows) by highlighting textural differences in the renal parenchyma.

MRI showed progression of the disease, with extension to the left perinephric space and retroperitoneum (Fig. 3e). The patient is scheduled to undergo radical left nephrectomy in the near future.

Discussion

In this report, we detail the case of a patient with renal malakoplakia and concomitant *E. coli* bacteremia who underwent multimodal imaging of the abdomen and pelvis. As is common with renal malakoplakia, this patient had a history of recurrent UTIs and presented with *E. coli* infection [2,4,12]. She later developed acute renal failure which has also been seen in other published cases of renal malakoplakia [4]. During her initial evaluation, multiple imaging modalities were employed to further characterize her urinary tract pathology.

Previous literature has described the imaging findings of renal malakoplakia using imaging modalities including ultrasound, CT, and MRI. In prior literature, findings such as diffusely increased renal parenchymal echogenicity, loss of corticomedullary differentiation, nephromegaly, and renal masses on ultrasound have been associated with renal malakoplakia [9,10]. In terms of CT findings, nephromegaly, mass-like lesions, abscesses, and inflammatory changes have been seen in renal malakoplakia patients [1,5,6,8]. MRI findings of renal malakoplakia include nephromegaly, irregular renal contours, lack of cortico-medullarity differentiation, and intervening fibrous tissue and ill-defined parenchymal nodularity that is T1 and T2 hypointense [11].

One unique aspect of our case report is that cinematic and 3D renderings of the patient's CT data were also generated as part of her imaging evaluation. To our knowledge, this is the first time that this technique has been used in a case of renal malakoplakia. Cinematic rendering incorporates a complex lighting model that traces the path of photons projected over materials within a specific volume to generate a 3D image [13]. Use of cinematic rendering can aid in characterization of pathology due to use of photorealistic lighting, more accurate vascular mapping, and estimation of organ and lesion characteristics including texture and density [13].

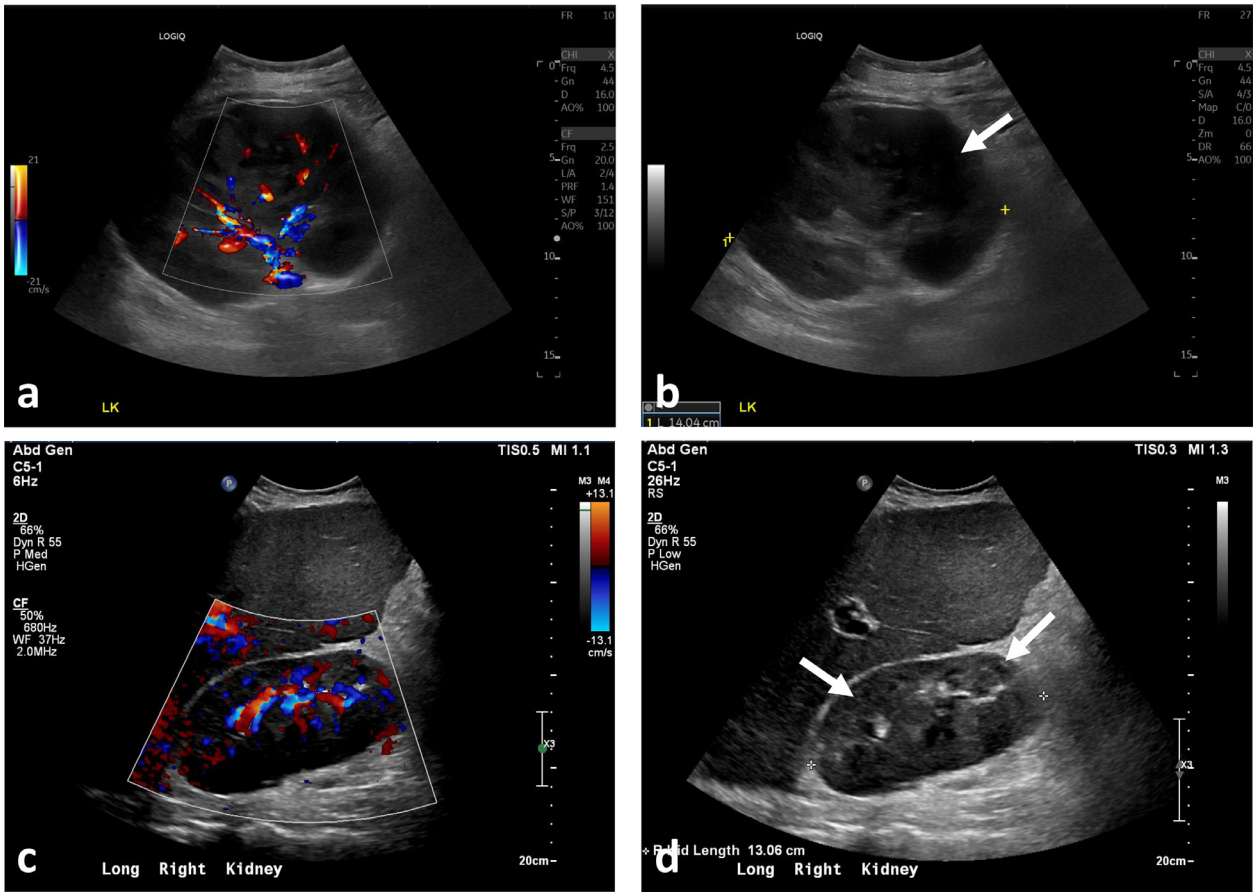

Fig. 2 – Ultrasound images of the left kidney (a, b) obtained at the time of renal biopsy and right kidney (c, d) at the time of right upper quadrant ultrasound demonstrate left greater than right nephromegaly with heterogeneous echogenicity of the renal parenchyma and scattered hypoechoic foci (arrows) consistent with abscesses. Heterogeneous renal perfusion is also present on color Doppler images (a, c).

Although imaging is often used in the initial evaluation of patients with renal malakoplakia, diagnosis cannot be confirmed without a biopsy. Renal malakoplakia is a disease that is associated with defects in macrophage and monocyte function [5]. It is currently believed that in malakoplakia, macrophages and monocytes inadequately digest bacteria after phagocytosis [5]. This defect in intracellular killing is thought to be due in part to a decrease in the intracellular cGMP:cAMP ratio. It has been shown that a low cGMP:cAMP ratio is associated with impaired lysosomal digestion in macrophages and monocytes [5]. Decreased cGMP levels are thought to impair microtubule assembly and beta-glucuronidase release leading to impairment in phagolysosomal digestion of bacteria [11].

Two key histologic characteristics of malakoplakia are von Hansemann Cells and Michaelis-Gutman bodies [4]. Von Hansemann cells are large polygonal shaped macrophages with foamy eosinophilic cytoplasm. Michaelis-Gutmann bodies are PAS-positive granules that are thought to be derived from abnormal calcium phosphate and iron deposition on incompletely digested bacteria within phagolysosomes of macrophages [4,11].

Due to macrophages' and monocytes' reduced ability to perform intracellular bacteriocidal activity, treatment options include administration of antibiotics that are capable of entering macrophages and aiding in intracellular killing of bacteria. Rifampin, trimethoprim-sulfamethoxazole and ciprofloxacin are agents effective agents for treatment of malakoplakia because they are capable of intracellular penetration which aids in the intracellular killing of bacteria in macrophages and monocytes [12]. Fluoroquinolones are especially effective at treating malakoplakia, perhaps due to achieving high intracellular concentrations achieved in macrophages [12]. Bethanechol and ascorbic acid have also been used as adjuvant therapy due to their ability to increase the intracellular cGMP:cAMP ratio and increase bacteriocidal activity of monocytes and macrophages [10–12]. These treatments generally have favorable outcomes [12]. In the event that antibiotic therapy is insufficient, nephrectomy may be pursued. Unilateral nephrectomy is an option for patients with predominant involvement of one kidney. Bilateral nephrectomy is associated with poor prognosis including significant patient mortality [12].

In conclusion, renal malakoplakia is a rare inflammatory disease that is characterized by macrophage dysfunction. Nonspecific imaging findings make diagnosis challenging, however, recognition of key imaging features and use of adjunct imaging modalities and postprocessing techniques

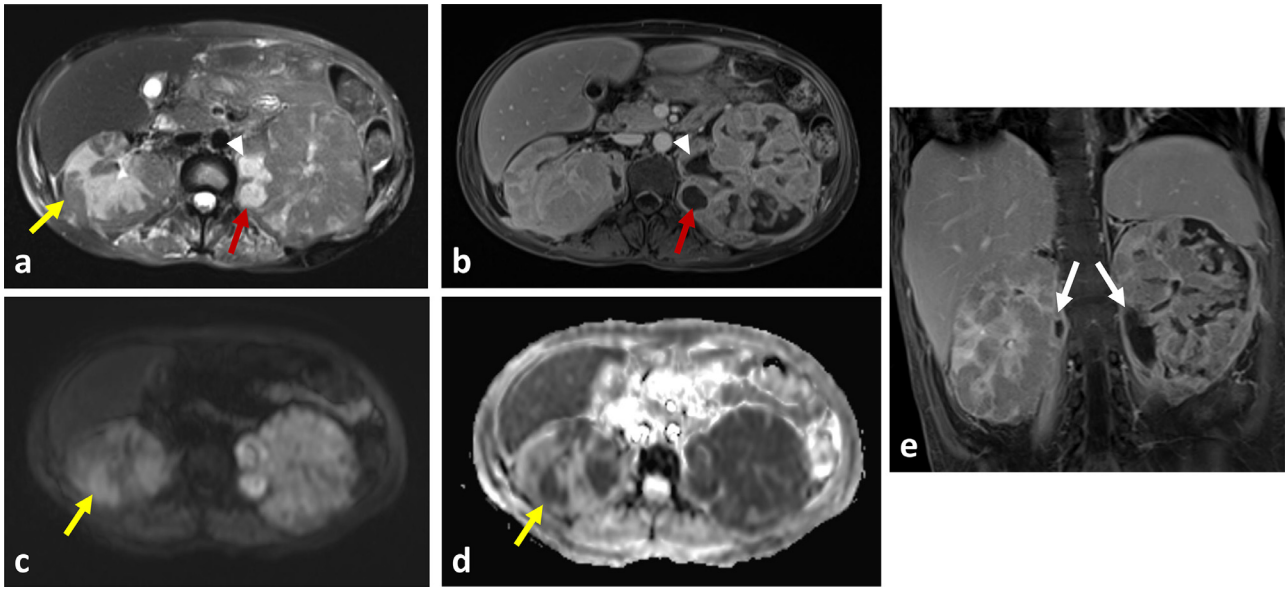

Fig. 3 – Axial T2-weighted (a) and T1 post-contrast (b) images of the abdomen demonstrate bilateral nephromegaly with heterogeneous hypoenhancement and signal intensity in the left greater than right kidney. Bilateral intrarenal and perinephric fluid collections are also present (red arrows). Mild left hydronephrosis with thickening of the left renal pelvis is also present (arrowheads), as well as thickening of the left perinephric fascia and retroperitoneal soft tissues. Diffusion-weighted images (c) and corresponding ADC map (d) demonstrate diffusion restriction in the areas of parenchymal hypoenhancement (yellow arrows). Coronal post-contrast images (e) demonstrate fluid collections extending into both psoas muscles (white arrows).

including 3D and cinematic rendering of CT data may aid in accurate characterization of imaging findings and that may facilitate accurate diagnosis.

Ethics approval

Not applicable.

Availability of data and material

All data and materials support the published claims and comply with field standards.

Consent to participate

Obtained.

Consent for publication

Obtained.

Code availability

Not applicable.

Authors' contributions

All authors contributed to the study conception and design. Material preparation and image collection were performed by Elliot Fishman and Erin Gomez. 3D and cinematic renderings generated by Elliot Fishman. The first draft of the manuscript was written by Nicholas Henlon and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Patient consent

The patient has given written informed consent to write and submit this case report.

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