Bilateral renal malakoplakia with acute renal failure: a case report and literature review

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Malakoplakia involving the genitourinary tract is a rare inflammatory disorder that presents a diagnostic challenge. Renal parenchymal involvement is particularly uncommon. We report a case of bilateral renal malakoplakia that presented with acute renal failure and simulated xanthogranulomatous pyelonephritis (XGP). The etiology, clinical course, and management of malakoplakia are reviewed, emphasizing the distinct characteristics of the disease that lead to its accurate diagnosis.

Key Words: malakoplakia, xanthogranulomatous pyelonephritis, renal failure

Case report

A 71-year-old female with a history of hypertension and alcoholism was transferred to our hospital for management of new onset renal failure. The patient had been in stable health until 4 days prior, when she presented to an outside hospital with fatigue, dysuria and diarrhea. A careful history elicited an unintentional 30 pound weight loss over the past year. She denied any bony pain or hematuria.

The patient's medical history was significant for controlled hypertension and a remote history of alcoholism. Her only prior surgery was an abdominal hysterectomy and bilateral oopherectomy for fibroids performed over 15 years ago. Physical exam revealed a thin woman in no acute distress. Abdomen was soft, nontender, with a well- healed lower midline abdominal scar. Admission labs revealed acute renal failure with a creatinine of 6.1. She had a leukocytosis of 20,000.

In response to patient's leukocytosis, urine and blood cultures had been drawn at the outside hospital, both of which were positive for E.coli. Based on these culture results, the patient was started on ciprofloxacin for urosepsis. Despite antibiotic therapy, she remained persistently febrile with an elevated WBC, even after completing her ciprofloxacin course. Additional antibiotic treatment with Vancomycin and Aztreonam was started, with no clinical improvement.

Persistent fevers unresponsive to antibiotic therapy prompted a CT scan of the abdomen and pelvis. The CT scan revealed diffuse heterogeneous enlargement of both kidneys as well as multiple renal masses. No retroperitoneal adenopathy was noted. The bilateral enlarged appearance was suspicious for an infiltrative process such as lymphoma, leukemia or metastatic disease. A CT of the chest and a nuclear medicine scan ruled out any evidence of lung or skeletal metastases respectively.

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Our next step was a CT guided core biopsy of one of the renal masses in hopes of obtaining tissue diagnosis. Pathology results revealed foamy histiocytes and a polymorphous population of lymphocytes, with a final read of xanthogranulomatous pyelonephritis (XGP). As suspected by prior radiologic workup, there was no evidence of malignancy.

The patient's acute renal failure was initially treated with conservative measures. When creatinine did not show improvement she started hemodialysis. At the time of patient's tissue diagnosis with XGP, the patient had been dialysis dependent for over 1 month.

In this patient with an overall septic course despite lengthy antibiotic treatment, persistent renal failure, and a tissue diagnosis of xanthogranulomatous pyelonephritis, the decision was made to undergo bilateral nephrectomy.

Open bilateral nephrectomy was uneventful. Postoperatively, patient's leukocytosis gradually declined from her admission baseline of 20,000 to 9,000. Concurrently, the patient defervesced. Final pathologic diagnosis of the surgical specimen was bilateral renal malakoplakia, as evidenced by Michaelis-Gutman bodies.

Discussion

Malakoplakia is a rare inflammatory disorder originally described by Michaelis and Gutman in 1902. The urinary tract is the organ system most often affected by this rare disorder. Within the urinary system, invasion most commonly involves the bladder mucosa. Renal parenchymal malakoplakia is considered relatively rare, with only 14 published cases of bilateral involvement over the past 20 years.[1]

Clinical presentation of renal malakoplakia involves urinary tract infection, pyelonephritis, and kidney enlargement. It tends to occur at middle age, typically in patients with chronic urinary tract infections. Additionally, almost half of affected patients have systemic disorders that impair immune function.[2]

The pathophysiology of the disease is thought to be due to inadequate intracellular destruction of phagocytosed bacteria. Low intracellular levels of cyclic guanosine monophosphate seem to be the cause of this impaired destruction of bacterial debris.[2] Microscopically, concretions composed of partially digested and mineralized bacterial fragments can be seen within the cytoplasm of macrophages. These concretions, containing calcium phosphate and iron salts from bacterial breakdown, are called Michaelis-Gutmann (M-G) bodies.[3] Histologically, plaques containing large macrophages with concretions and occasional multinucleate giant cells can often be seen, Figure 1. The diagnosis of malakoplakia, is dependent on the demonstration of these pathognomonic M-G bodies.[4] In the presented case, the renal biopsy was misdiagnosed as XPG. However, pathology of the final surgical specimen revealed the presence of M-G bodies within the renal parenchyma, diagnostic of malakoplakia.

The clinical presentation of XGP has many similarities to that of renal malakoplakia, and they may be easily confused. Both occur in the setting of chronic infection and obstruction, and both have urine cultures almost invariably positive for E.coli.[3] Malakoplakia is even considered by some to exist in a diagnostic spectrum that includes XGP. Although the characteristic imaging of XGP is of a staghorn calculus within enlarged kidneys, the diagnosis of XGP versus malakoplakia cannot be made solely on radiologic findings. Histologically, both disease processes involve collections of macrophages in the setting of infection, but it is the histologic presence of M-G bodies that distinguishes malakoplakia from XGP. To date, there is no consensus for the pathologic classification of XGP. However, the microscopic progression of XGP been broadly grouped into three forms: nonspecific tubulointerstitial nephritis with rare foamy macrophages, followed by megalocytic tubulointerstitial nephritis with increased foamy macrophages, and finally xanthogranulomatous pyelonephritis as the final phase with foamy macrophages devoid of intracellular inclusions on light-microscopy.[4] Given the clinical similarities between the two diagnoses, it is easy to see why the core biopsy result, read as XGP, seemed plausible for our patient.

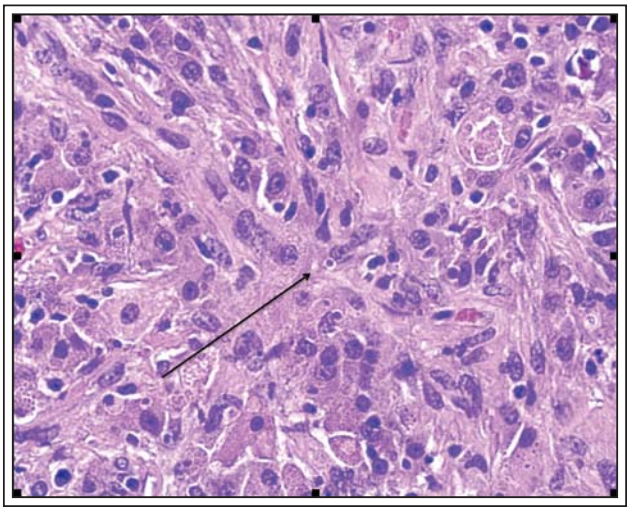

Figure 1. Presence of multiple Michaelis-Gutmann bodies in the renal surgical specimen (PAS stain, original magnification, x 100).

Other diagnoses that were appropriately considered based on the presenting triad of acute renal failure, fever and leukocytosis included acute interstitial nephritis (often as result of an allergic reaction to a drug), autoimmune disease, or an infiltrative process. Urinary tract obstruction with infection, particularly secondary to stone disease, involves a similar presentation, but would likely be seen with flank pain or nausea.

What is intriguing about this case, is not only the bilateral parenchymal involvement, but also that the course of renal deterioration was so rapid, and seemingly, so irreversible. When described in the literature in the 1970's, bilateral renal malakoplakia was understood to be a "progressive and destructive disease...and shown to be uniformly fatal".[5] Although no longer viewed as universally fatal, one of the consequences of bilateral renal malakoplakia is the progressive deterioration of kidney function, typically to the point of dialysis dependence. The recommendation for antibiotic treatment of the disease began in the 1970's. At this time, although antibiotics sterilized the urine, they had not been shown to alter the course of the disease.[5] More recent case reports, however, have shown preservation of function, and even reversal of acute renal failure, with antibiotic treatment. Flouroquinolones, because of their intracellular penetration, are the antibiotics of choice in clearing bacteria and halting interstitial damage. Patients treated with antibiotics promptly may be able to delay dialysis dependence for several years. In Tam et al's review of cases involving bilateral renal parenchymal malakoplakia only 6 of the 25 patients had significant impairment of renal function. Of these 6, only 3 ultimately required hemodialysis.[6] The patients who require dialysis have sustained such severe kidney damage prior to antibiotic treatment that despite destruction of bacteria, irreversible injury to the interstitium has already occurred. It is the prompt treatment of renal malakoplakia with antibiotics that is important for preservation of renal function.

An important question to consider is whether our surgical plan would have changed had the core biopsy results returned as renal parenchymal malakoplakia, rather than XGP. At the time of renal biopsy our patient had already been dialysis dependent for 1 month. She had a persistently elevated WBC and continued to be febrile despite IV antibiotic therapy. Her renal injury by the time of IV antibiotic treatment was already irreversible. In retrospect, despite an incorrect diagnosis by core biopsy, our surgical management would not likely have changed, because the patient's clinical status was already severely compromised.

Malakoplakia, as an infectious process, is a disease that targets the immunocompromised. In fact, over half of the patients affected by malakoplakia have systemic disorders that impair immune function.[2] Review of the literature revealed that alcoholism affected a large number of patients affected by bilateral renal malakoplakia with acute renal failure requiring dialysis. Our patient also had a history significant for alcoholism. Presumably, alcoholism interferes with the infection response, thereby allowing the development and progression of renal parenchymal malakoplakia.

Our understanding of renal malakoplakia has been a slow evolution since Michaelis-Gutman bodies were first reported in 1902. Renal parenchymal malakoplakia should be on the differential for patients presenting with chronic urinary tract infection, acute renal failure, and enlarged kidneys by imaging. The clinical and radiologic presentation of XGP and renal malakoplakia are quite similar, and may easily be confused. As learned in this case, as it is a spectrum disease, a diagnosis of renal parenchymal malakoplakia should be entertained in cases where XGP is considered. As malakoplakia is a histologic diagnosis, a timely renal biopsy improves chances of early antibiotic treatment and gives the best chances for preservation of renal function. □

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