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Acute kidney injury secondary to obstructive bladder malakoplakia: a case report

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Abstract

Background Malakoplakia is a rare granulomatous inflammatory condition that can affect immunosuppressed patients. The genitourinary system is the most involved organ. We present a case of kidney failure caused by obstructing bladder lesions, clinically suspicious for malignancy and pathologically proven to be malakoplakia.

Case presentation A 70-year-old woman presented with acute kidney injury and *Escherichia coli (E.coli)* bacteremia. Investigation showed bilateral hydronephrosis with thickening of the renal pelvises suggestive of urothelial malignancy. Cystourethroscopy revealed multiple bladder lesions completely obliterating both ureteral orifices. Pathology of the resected lesions confirmed the diagnosis of malakoplakia. Patient was treated with a prolonged antibiotic course over 6 months with recovery of her kidney function.

Conclusion Malakoplakia can mimic invasive tumors, and the diagnosis is only attained through histopathology which uniquely demonstrates the pathognomonic Michaelis–Gutmann inclusions inside sheets of histiocytes. Treatment is largely dependent on prolonged antibiotics therapy that must cover the most common isolated pathogen, *E.coli*.

Keyword Bladder, Malakoplakia, Michaelis–Gutmann bodies, Rare disorder, Urinary tract infection

1 Background

Malakoplakia is a granulomatous inflammatory condition, affecting mainly middle aged immunosuppressed patients, with higher prevalence among women. It was first described more than a century ago by the German oncologist Von Hansemann, and by Michaelis and Gutmann, during postmortem examination of their patients [1]. Since that time, there have been several case reports and case series of patients with malakoplakia, and the awareness of this rare condition has increased tremendously. Malakoplakia classically occurs in females in their 5th decade. However, the literature of malakoplakia that was built over the past one century had reported patients having malakoplakia as young as 8 weeks and as old as 90 years [1, 2].

The genitourinary system is the most affected organ followed by the gastrointestinal tract [2]. The first four cases of malakoplakia in the literature were actually of bladder origin [3]. Malakoplakia can mimic invasive tumors

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causing inevitable worry, until the diagnosis is attained through histopathology which uniquely demonstrates the pathognomonic Michaelis–Gutmann inclusions inside sheets of histocytes. Treatment is largely dependent on prolonged antibiotics therapy that must cover the most common isolated pathogen, *Escherichia coli (E-coli)* [3]. We hereby present an interesting case of bladder malakoplakia in an elderly lady with obstructive nephropathy, secondary to tumor-like bladder lesion(s) causing bilateral hydroureteronephrosis, managed successfully with endoscopic resection and prolonged antibiotic therapy. A description of the entity with a brief literature review was followed.

2 Case presentation

A 70-year-old woman was admitted to the hospital with symptoms of fatigue, generalized weakness and decreased oral intake. Her past medical history was significant for uncontrolled diabetes mellitus type II, hypertension, chronic kidney disease stage 3 and chronic anemia. She was a non-smoker, and she denied any history of genetic diseases or history of malignancies, from either maternal or paternal sides. Two weeks prior to presentation, she had also one episode of fever and chills that subsided spontaneously. She denied any current urinary or gastrointestinal symptoms.

Initial workup was pertinent for an acute kidney injury with a creatinine of 5.0 mg/dl (baseline 1.1 mg/dl), significant anemia with hemoglobin of 6.9 g/dL, and leukocytosis with a WBC count of 13,900/mm^3 (Neutrophils: 92%). Blood and urine culture later grew *E. coli*, resistant to quinolones, and was treated with ceftriaxone. She had not had any previous recurrent urinary tract infections. Pertinent laboratory data are detailed in Table 1.

Further workup for her acute kidney injury (AKI), an ultrasound of the kidneys and pelvis showed unexplained moderate bilateral collecting systems dilatation/hydronephrosis, and a thickened but under distended bladder with surrounding fat streaking. Following that, an unenhanced computed tomography (CT) scan of the abdomen and pelvis showed bilateral moderate hydronephrosis with thickening of both renal pelvises and mild bilateral ureteral fullness (Fig. 1 A, B). Findings were initially suspicious for urothelial malignancy. Twice urine cytologies were negative for high grade urothelial carcinoma.

As no intravenous contrast could be administered, completion of her workup was made by performing a cystourethroscopy with bilateral retrograde pyelography, revealing multiple polypoid and velvety lesions over the bladder trigone and lateral walls, with complete obliteration of both ureteral orifices. Transurethral resection of those suspicious bladder lesions was performed until both ureteral orifices were visualized. Bilateral retrograde pyelography was then performed with no suspicious filling defects noted neither in the renal pelvis nor in the ureters (Fig. 1 C, D). Bilateral ureteral stents were inserted.

Histopathology of the resected tissue showed sheets of epithelioid histiocytes highlighted by CD68 (Fig. 2 A, B) and occasional small intracytoplasmic basophilic inclusions (Michaelis–Gutmann bodies) (Fig. 2 C, arrows). Numerous neutrophils and CD38-positive plasma cells were also present. These findings were consistent with malakoplakia with no evidence of malignancy.

The patient was shifted to cefixime on discharge; however, she developed lower urinary tract symptoms 2 weeks later. Urine culture grew *Enterococcus faecalis* 100,000 orgs/ml, and she was switched to amoxicillin-clavulonate which she received for 3 months. Her creatinine dropped to 1.5 mg/dl, and the ureteral stents were removed. Antibiotic therapy was changed to trimethoprim/sulfamethoxazole for its better concentration into phagocytes.

At month 5 of therapy, her kidney function went back to baseline with a creatinine of 1.2 mg/dl. Follow-up enhanced CT scan revealed significant resolution of the renal pelvis and ureteral wall thickening (Fig. 3 A, B). Antibiotics were stopped.

Table 1 Laboratory data upon presentation

Parameter	Value	Reference range
BUN, mg/dL	96	8–25
Creatinine, mg/dL	5	0.5–1.0
WBC, (/µl)	14,300	4000–11000
Neutrophils, %	87	50–70
Hemoglobin, g/dL	6.9	12–15.5
Urinalysis	PH 5, specific gravity 1.005, protein + 1, glucose negative, ketone negative, bilirubin negative, RBCs numerous, WBCs numerous, leukocyte esterase 500, nitrite positive	

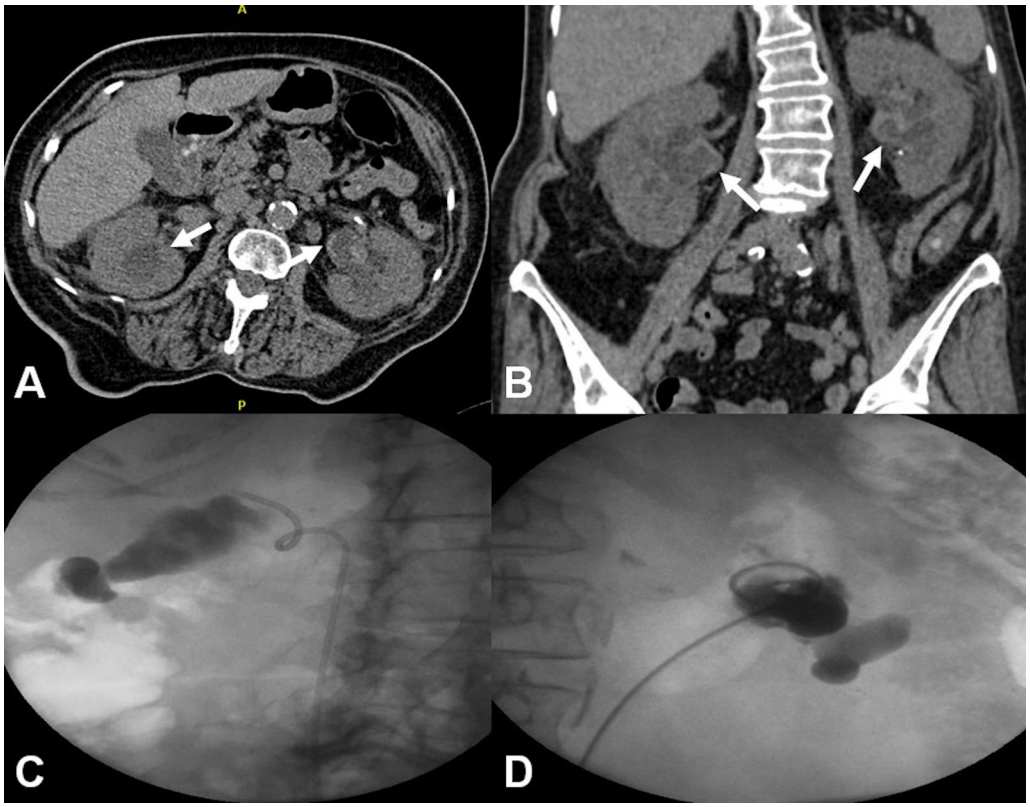

Fig. 1 **A** Unenhanced computed tomography (CT) scan of the abdomen and pelvis, axial view, showing bilateral hydronephrosis with urothelial thickening of the renal pelvis (*arrow*) that may represent urothelial malignancy. **B** Coronal view of the unenhanced CT scan of abdomen and pelvis showing similar dilatation and thickening (*arrow*). **C** Fluoroscopic view of the retrograde pyelography, right side, showing no filling defects within the right renal pelvis suggestive of any malignancy, along with a right double J ureteral stent, seen in good position. **D** Left-sided fluoroscopic view of the retrograde pyelography showing as well no filling defects within the left renal pelvis suggestive of any malignancy, along with a left-sided double J stent, seen in good position

3 Discussion

Malakoplakia is a rare granulomatous inflammatory condition, affecting many organs, with variable predilection [4].

The true incidence of malakoplakia is unknown. It is considered an uncommon condition, with the majority of reported cases in women. The bladder is usually the most commonly affected part, followed by prostate, ureters and kidneys. The second most common site of involvement is the gastrointestinal tract followed by others like bone, lungs, lymph nodes, endometrium, brain, peritoneum, thyroid, conjunctiva and the skin [4, 5]. One interesting feature of malakoplakia is its ability to mimic malignancy [6]. In our case, malakoplakia manifested as an obstructing pseudo tumor of the urinary tract, causing kidney failure, with a fortunate outcome of recovery of kidney function. This is greatly attributed to timely diagnosis and targeted therapy.

The clinical presentation of patients with malakoplakia is variable and nonspecific depending on the affected organ. When the urinary tract is involved, malakoplakia can present with fever, flank pain, palpable mass, hematuria, dysuria, frequency, urgency and other voiding symptoms. On the other hand, malakoplakia of the GI tract, the second most commonly affected system after genitourinary can manifest with abdominal pain, diarrhea, or even GI bleed [7].

Importantly, the ability of malakoplakia to mimic malignancy is fascinating [8, 9]. Aggressive lesions of malakoplakia presenting as invasive pseudo tumors and causing urinary tract obstruction with renal failure, as in our reported case, are considered an uncommon presentation with few similar reported cases in the literature [1, 10].

A state of immunosuppression and debilitation has been implicated in the development of malakoplakia, with diabetes, transplant, malignancy, HIV/AIDS, tuberculosis, autoimmune disease, immunosuppressive therapy and alcohol intake, making the most common predisposing risk factors. Another observation that is worth mentioning is that malakoplakia has been linked to a concurrent diagnosis of malignancy. Reported cases

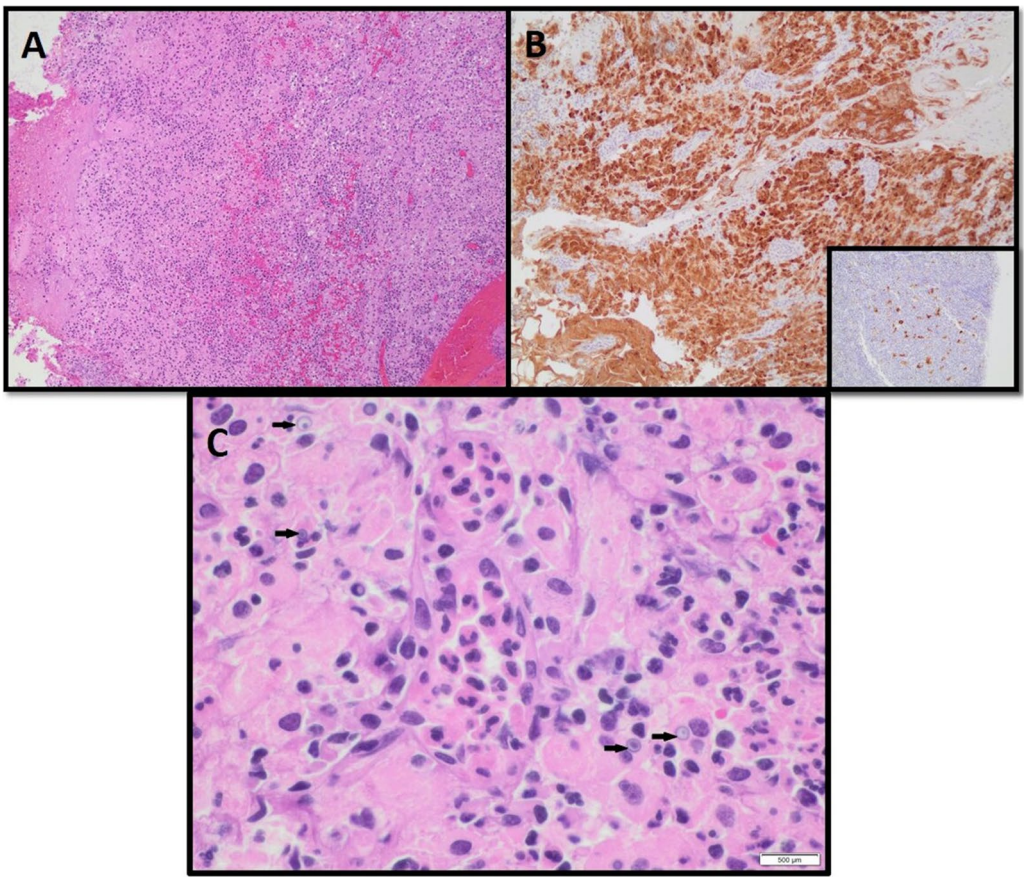

Fig. 2 **A** Sheets of epithelioid histiocytes with admixed neutrophils and plasma cells (hematoxylin–eosin staining; original magnification × 10). **B** CD68 immunohistochemical stain highlighting the histiocytes; original magnification × 10 (Inset: CD68 positive control). **C** Michaelis–Gutmann bodies (arrows) (hematoxylin–eosin staining; original magnification × 60)

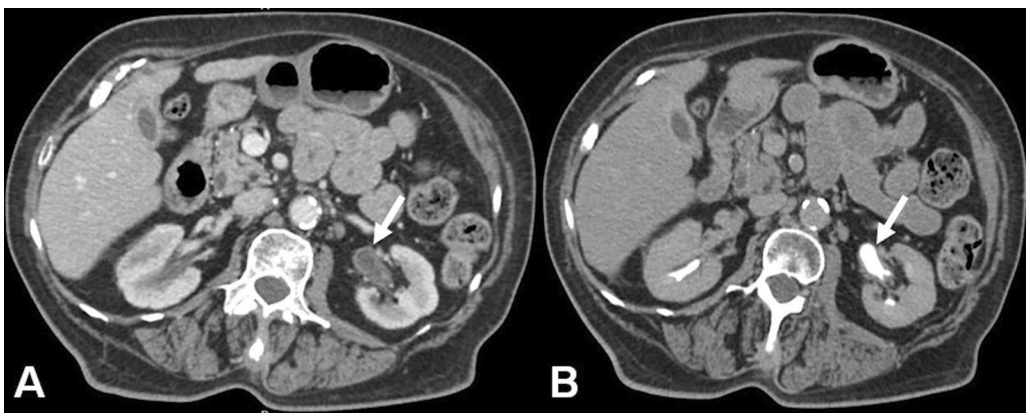

Fig. 3 **A** Enhanced CT scan of the abdomen and pelvis, axial cross section during the nephrogenic phase, showing significant decrease in the pelvicalyceal and ureteral wall thickening bilaterally, with almost complete resolution (arrow). Note as well the significant decrease in perinephric fat streaking after antibiotics administration. **B** Another axial view during the delayed phase also showing complete resolution of urothelial thickening with absence of any filling defects (*arrow*)

include urothelial carcinoma, bladder tumors, colon and prostate adenocarcinoma [11, 12].

Our knowledge of the pathophysiology of malakoplakia remains incomplete. It has been speculated that malakoplakia is caused by impaired phagolysosomal function, leading to inadequate killing of phagocytosed microorganisms by monocytes and macrophages [13]. The underlying mechanism of this defective bactericidal function is attributed to the low intracellular levels of cyclic guanosine monophosphate (cGMP) and decreased release of β glucuronidase by macrophages. Consequently, this abnormal cGMP/cAMP ratio negatively affects the microtubular role which is necessary for the lysosomal activity, resulting in incomplete elimination of bacteria from the phagocytes. Ultimately, the accumulated bacterial fragments in the lysosomes get mineralized by iron and calcium depositions, forming the characteristic pathognomonic Michaelis–Gutmann bodies [4, 13]. This most likely explains why malakoplakia is more seen in immunocompromised patients, due to their altered immune system [12].

Most patients diagnosed with malakoplakia have a history of recurrent urinary tract infection. A number of coliforms have been associated with malakoplakia, with *E. coli* representing the most frequently identified bacteria. Other organisms include *Staphylococcus aureus*, *Proteus*, and *Klebsiella*. It is prudent to be aware of the relationship between malakoplakia diagnosis in HIV patients and the isolation of *Rhodococcus equi* bacteria in this population [14].

Malakoplakia has proved to be a diagnostic challenge as the clinical presentation and radiologic features are not specific. The same issue applies to the gross appearance of malakoplakia which lacks peculiar characteristics. Malakoplakia can appear as a soft yellow lesion, but it can also be seen as solitary or multifocal papules, nodules, plaques, ulcers, polyps, umbilicated or fungating masses imitating malignant tumors and invading other organs [15].

The definitive diagnosis of malakoplakia is achieved by the recognition of its distinguishing histopathology. The characteristic lesions of malakoplakia specimens classically show aggregations of foamy ovoid histiocytes known as Von Hansemman cells which are cytokeratin negative, CD 68 positive with an eosinophilic cytoplasm. Importantly, Von Hansemman cells contain the pathognomonic basophilic, PAS positive Michaelis–Gutmann bodies which are laminated, 5–10 μm, targetoid or owl's eye-like cytoplasmic inclusions. The iron content of these distinctive mineralized bodies makes them stain positively by Perls' Prussian blue. Similarly, the calcium content helps in uncovering the diagnosis by highlighting these bodies with von kossa stains [16].

Malakoplakia is considered of good prognosis. The treatment of malakoplakia consists of prolonged antibiotic course using agents that achieve high intracellular penetration and bioavailability in the macrophages like floroquinolones, trimethoprim-sulfamethoxazole. Unfortunately, there is no evidence to support the optimal treatment duration [17].

Surgical intervention may be necessary in some cases to hasten the resolution of the lesions. However, this is based on case reports with no randomized clinical trials to guide its real indication [18]. Other therapeutic measures include HIV antiretroviral therapy, treating the underlying predisposing condition, and immunosuppression reduction, as reported in previous cases of malakoplakia in solid organ recipients [19].

4 Conclusion

In summary, we present a case of acute kidney injury secondary to malakoplakia simulating obstructing bladder malignancy that was successfully treated. This case illustrates the need to raise the differential of Von Hansemann disease in the immunocompromised patients. Malakoplakia can mimic invasive tumors, and the diagnosis is only attained through histopathology which uniquely demonstrates the pathognomonic Michaelis–Gutmann inclusions. Treatment is largely dependent on prolonged antibiotic therapy that must cover the most common isolated pathogen, *E. coli*. More evidence-based data are needed in terms of the optimal therapeutic approach to this uncommon inflammatory condition.

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Author contributions
SJ contributed to the conception of the work in addition to the acquisition of data. MM contributed to the conception of the work in addition to the acquisition of data. CM participated in the writing of the paper. JD participated in acquisition of data, images, and in the writing of the paper. CK participated in acquisition of data. AZ participated in the writing of the paper and supervision. All authors read and approved the final manuscript.

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Availability of data and materials
All data generated or analyzed during this study are included in this published article [and its supplementary information files].

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
We have obtained consent for publication from the person involved in this case.

Competing interests
All authors declare no conflict of interest.

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