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# Renal malakoplakia with invasion of the liver and diaphragm: a patient case and literature review

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Accepted 1 September 2022

**SUMMARY**

Renal malakoplakia, a seldom seen chronic inflammatory condition, continues to elude medical, surgical, radiological and pathological specialists due to its mimicry of other renal pathologies and low incidence. The variable clinical manifestations and non-specific radiological findings of malakoplakia can be misleading, and ultimately require a pathological diagnosis. A literature review reveals an extremely low prevalence of renal malakoplakia, a handful of invasive renal malakoplakia cases and no reports of liver and diaphragmatic invasion. We present a case of a renal mass with liver and diaphragmatic invasion in a 59-year-old woman that deceived clinicians and radiologists until a pathological diagnosis of renal malakoplakia was performed. This case highlights the need of awareness for malakoplakia in the differential diagnosis for renal invasive and non-invasive masses. The need to await a surgical biopsy and pathological diagnosis is critical to ensure a correct diagnosis and avoid unnecessary surgery of the kidney.

**BACKGROUND**

Malakoplakia, Latin for ‘soft plaque’, is a chronic and rare inflammatory disorder that most commonly presents in immunocompromised patients. First delineated in the early 20th century by Michaelis and Gutmann, the pathogenesis is still not well understood.<sup>1</sup> This inflammatory reaction is thought to occur due to phagocyte function defects in response to bacterial infections. Primarily, the bacterial instigator is *Escherichia coli* as coliform bacteria have been found in nearly 90% of patients, more rarely the *Proteus* sp has been found as well.<sup>2,3</sup> It has been described in numerous case reports but occurs most commonly in the genitourinary (GU) tract.<sup>1</sup> On microscopic examination, this disorder is characterised by ‘von Hansemann cells’ or sheets of foamy macrophages that present along with ‘Michaelis-Gutmann bodies’, which are round basophilic scattered intracytoplasmic inclusions.<sup>1</sup>

Since the 1902 description of malakoplakia in a patient’s bladder, there have been over 400 case descriptions ranging from the most common GU occurrences to those in the pancreas, thyroid gland, lung, bone, skin and brain.<sup>1</sup> This disease is more common in men and presents at a median age of 53 years. The large majority of patients are immunodeficient due to causes such as HIV infection, neoplasia and kidney transplantation; there have been reported cases in healthy patients.<sup>4</sup> The most common symptom of malakoplakia is a recurring urinary tract infection (UTI), haematuria or renal

failure occurring at presentation.<sup>5</sup> Typically, *E. coli* would be grown in urine cultures or evidence could be seen on cystoscopy.

The clinical picture of those diagnosed with malakoplakia widely varies, and diagnosis is usually made after scrupulous workup. Culture, histopathology and 18-fluorodeoxyglucose positron emission tomography scan are critical to establish diagnosis and determine need for follow-up.<sup>6</sup> Additionally, the same characteristics that are pathognomonic for malakoplakia, Michaelis-Gutmann bodies, are why the von Kossa calcium stain is so critical. The von Kossa stain is a widely used histological technique which detects the presence of abnormal calcium deposits. This occurs from the breakdown of calcium salts into silver salts. Once placed under an ultraviolet source, the silver phosphates degrade and allow for counterstaining with nuclear red. In malakoplakia, the histiocytic inclusions stain positive for calcium, an important finding in malakoplakia.

The prognosis is positive as death has occurred very infrequently and individuals are cured in over 80% of cases. The primary treatment has been antibiotics with quinolones and trimethoprim/sulfamethoxazole with other modifying therapies including immunosuppressant discontinuation or bethanechol administration.<sup>3,7</sup> Importantly, these outcomes are derived from the common malakoplakia which is often benign. Here, we report a case of malakoplakia with unusual invasive features. The diagnostic workup, including specific pathological characteristics, and the management of the case are described.

**CASE PRESENTATION**

A female patient in her 50s had a history of tobacco use for over 30 years and no known immunodeficient conditions. She was previously admitted to the hospital 4 years prior for flank pain, haematuria and dysuria. Workup revealed a benign renal polyp with concurrent UTI. After that, she experienced intermittent haematuria every 2–3 months, and each episode would receive an antibiotic regimen from an outpatient physician without a standard UTI workup. Her last episode began 5 days prior to admission. She experienced haematuria and right upper abdominal pain with subsequent spread of pain to the right anterior groin and right flank.

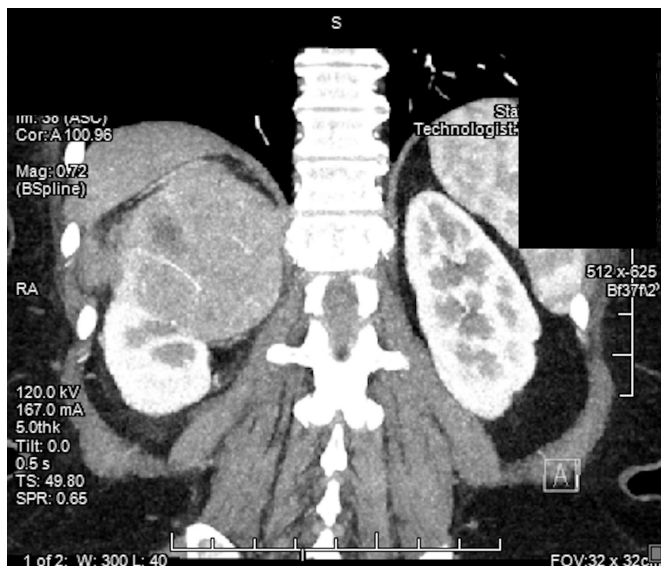
**INVESTIGATIONS**

Her creatinine level was 0.6 mg/dL (estimated glomerular filtration rate was >60 mL/min/1.73



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**To cite:** Grunhut J, Oroz R, Brown S, et al. *BMJ Case Rep* 2022;**15**:e251254. doi:10.1136/bcr-2022-251254



**Figure 1** Coronal CT of the abdomen demonstrating a renal mass of the right upper pole with adjacent invasion of the liver and diaphragm.

m<sup>2</sup>) and her white cell count was 8500/ $\mu$ L (neutrophil count was 82.0%). Urine culture grew *E. coli* organisms.

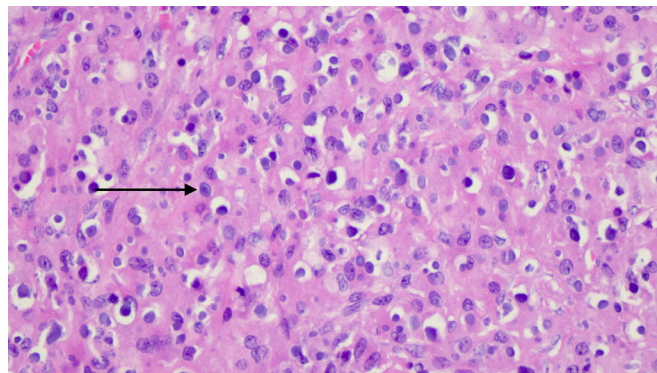
The heterogeneously enhancing mass (8.1 $\times$ 5.4 $\times$ 8.0 cm in size) at the right upper pole with extension to the renal pelvis causing renal pelvis dilation and extension into the diaphragm superiorly was noted on the enhanced MRI of the abdomen (figures 1 and 2); rupture of the right upper pole calyx with mixture of cystic and solid lesion within the perirenal fat and liver was noted (6.6 $\times$ 3.2 cm in size).

#### DIFFERENTIAL DIAGNOSIS

This was suspected to be an infected urinoma with tumour involvement and biopsy was performed. Biopsy for the lesion was performed, and pathological analysis revealed numerous macrophages with basophilic and eosinophilic granular cytoplasm containing intracellular and extracellular bacteria mixed with acute inflammatory cells and nearby fibrotic tissue containing



**Figure 2** Axial MRI of the abdomen further delineating the infiltration extension into the liver.



**Figure 3** Histiocytic cells with dense infiltrates containing the Michaelis-Gutmann bodies, which contain high PAS positivity and often show a targetoid appearance (arrow) (PAS stain, original magnification  $\times$ 400). PAS, periodic acid-Schiff.

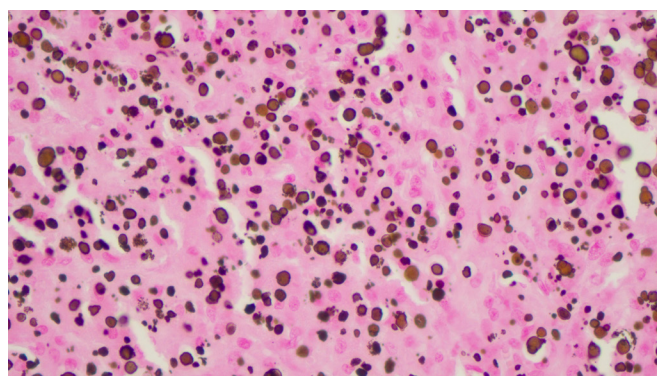
abundant plasma cells and lymphoid cells (figure 3). By special von Kossa stains, rare Michaelis-Gutmann bodies were identified as well as many eosinophilic globules (figure 4). These findings were consistent with malakoplakia.

#### TREATMENT

Radical nephrectomy was indicated due to the suspected permanent renal damage and concern for invasive damage to other tissues. After discussing with the patient and her family, right robotic radical nephrectomy with adrenal sparing was performed. The tumour was inflammatory and dissected off the liver capsule and diaphragm. The final pathology report was malakoplakia; the Gerota fascia was congested. The specimen weighed 495 g and measured 17.0 $\times$ 10.0 $\times$ 7.0 cm. The mass was 8.0 $\times$ 7.5 $\times$ 6.5 cm in the superior pole of the kidney and contained a cyst measuring 2 cm, filled with fibrinopurulent material (figure 2). Within the mass, diffuse histiocytic inflammation (highlighted by immunostaining CD68) was noted, with the histiocytes containing eosinophilic cytoplasm and round intracytoplasmic inclusions consistent with Michaelis-Gutmann bodies (figure 3).

#### OUTCOME AND FOLLOW-UP

After the surgical treatment, her clinical recovery and laboratory outcomes were satisfactory, and she no longer suffered from urosepsis. There was no adverse event or recurrence noted on follow-up images. The patient remained alive and free of disease 6 months after treatment (figure 5).



**Figure 4** Von Kossa-positive Michaelis-Gutmann bodies (von Kossa, 400 $\times$ ).

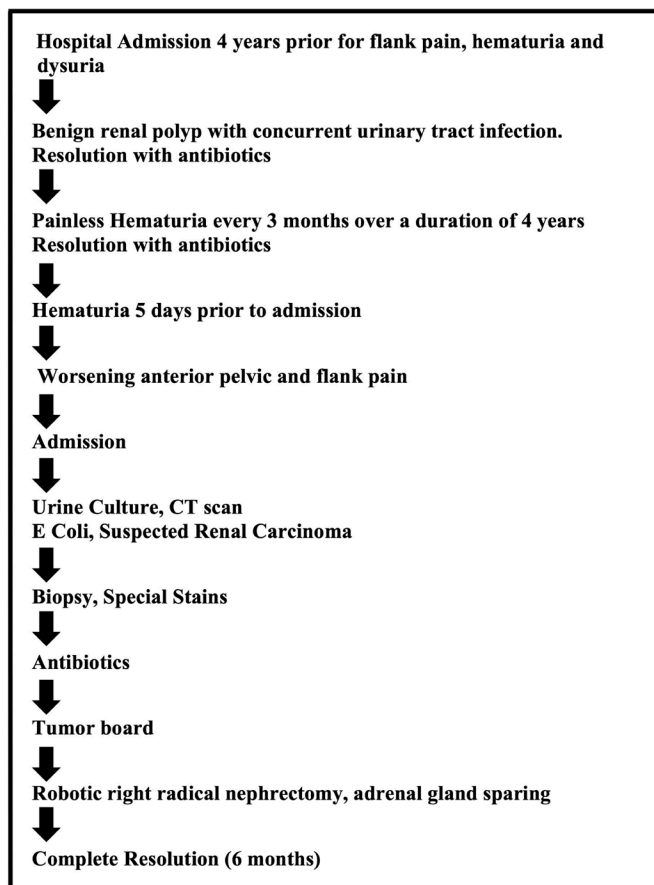


Figure 5 Diagnostic and treatment timeline.

## DISCUSSION

Malakoplakia is an inflammatory and chronic infectious condition usually associated with immunosuppression and is most commonly seen in renal transplant patients.<sup>8–10</sup> The current belief among researchers is it results from inadequate killing of phagocytosed microorganisms by monocytes and macrophages, leading to decreased levels of intracellular cyclic guanosine monophosphate and decreased release of  $\beta$  glucuronidase.<sup>11</sup> Microtubular function and lysosomal activity are not adequate due to decreased intracellular cyclic guanosine monophosphate

levels causing an incomplete elimination of bacteria from within the phagocytes.

Renal malakoplakia commonly presents with fever, flank pain and oftentimes a palpable mass.<sup>12</sup> Patients can present with recurrent signs of UTIs before accumulation of the bacterial macrophage complex is large enough to cause other symptoms. On rare occasions, when renal malakoplakia is invasive, it is easily mistaken for cancer. At presentation, symptoms can be easily and properly mistaken for neoplasms of the kidney or xanthogranulomatous pyelonephritis since workup of these pathologies is the same. Therefore, diagnosis of renal malakoplakia is difficult and requires a renal biopsy.<sup>13</sup> The presence of Michaelis-Gutmann bodies, basophilic structures that exist within clusters of macrophages, on histological examination is pathognomonic for the diagnosis.<sup>5</sup>

Although malakoplakia resembles carcinoma on imaging and gross pathology, its treatment can be very different. In the past, bilateral renal malakoplakia was treated with antibiotics, whereas unilateral was dependent on extension of the inflammation and the patient's condition.<sup>14</sup> If the malakoplakia is invasive and the kidney structure is damaged, treatment is typically nephrectomy.<sup>15</sup>

Renal malakoplakia is an extremely rare pathology. The incidence of renal malakoplakia is one of the lowest among renal pathologies. A PubMed literature review revealed 237 total publications with mention of renal malakoplakia in a timespan of over 60 years. Of these, only 192 were case reports, 11 were reported to have local advancement beyond the kidney and ureter, 2 were reported to advance into the liver and there were no reports of advancement to the diaphragm.

In this case, the first reported of its kind, the patient's malakoplakia extended from the upper 2/3 of the kidney to the diaphragm. The patient also had no known immunosuppression. This patient presented an exceedingly challenging case both for diagnosis and for treatment. From a radiological perspective, this presentation was highly singular and would normally be defined as a malignancy to be confirmed with pathology after nephrectomy. Our team decided to perform biopsy first, which proved to be transformative.

From a surgical point, this case proved challenging to preserve intact liver capsule and make sure all tumour was preserved on the kidney. Part of the tumour was also densely adherent to the duodenum and carefully dissected until risk of bowel perforation outweighed reason to excise the mass. Fortunately, this patient continued to remain symptom free, suggesting minor amounts of remaining mass were not significant enough to cause disease recurrence.

## Learning points

- ▶ Malakoplakia is an inflammatory and chronic infectious condition usually associated with immunosuppression and is most commonly seen in renal transplant patients. It commonly presents with fever, flank pain and oftentimes a palpable mass.
- ▶ Inadequate destruction of phagocytosed bacteria is thought to contribute to the pathogenesis of malakoplakia. This is commonly seen in immunocompromised individuals.
- ▶ Although the use of antibiotics is the standard treatment for malakoplakia, in cases of extensive invasion of other tissue and organs, nephrectomy is indicated.
- ▶ Radiological studies are often deceptive and suggestive of renal cell carcinoma. Pathological diagnosis is necessary and is proven with the presence of Michaelis-Gutmann bodies and von Kossa stain.

**Contributors** JG was involved in the planning, conduct, reporting, conception and design, acquisition of data or analysis and interpretation of data, manuscript preparation, review and final approval. SB was involved in the planning, conduct, reporting, conception and design, acquisition of data or analysis and interpretation of data, manuscript preparation, review and final approval. RO was involved in the planning, conduct, reporting, conception and design, acquisition of data or analysis and interpretation of data, manuscript preparation, review and final approval. RN was involved in the planning, conduct, reporting, conception and design, acquisition of data or analysis and interpretation of data, manuscript preparation, review and final approval.

**Funding** The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

**Competing interests** None declared.

**Patient consent for publication** Obtained.

**Provenance and peer review** Not commissioned; externally peer reviewed.

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Case reports provide a valuable learning resource for the scientific community and can indicate areas of interest for future research. They should not be used in isolation to guide treatment choices or public health policy.

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### REFERENCES

- 1 Kohl SK, Hans CP. Cutaneous malakoplakia. *Arch Pathol Lab Med* 2008;132:113–7.
- 2 Netto GJ, Amin MB. The lower urinary tract and male genital system. In: *Robbins & Cotran Pathologic Basis of Disease*, 2021: 953–83.
- 3 Stanton MJ, Maxted W. Malakoplakia: a study of the literature and current concepts of pathogenesis, diagnosis and treatment. *J Urol* 1981;125:139–46.
- 4 Flann S, Norton J, Pembroke AC. Cutaneous malakoplakia in an abdominal skin fold. *J Am Acad Dermatol* 2010;62:896–7.
- 5 Diwakar R, Else J, Wong V. Enlarged kidneys and acute renal failure-why is a renal biopsy necessary for diagnosis and treatment? *Nephrol Dial Transplant Off Publ Eur Dial Transpl Assoc - Eur Ren Assoc* 2008;23:401–3.
- 6 Vanbrabant P, Drieskens O, Blockmans D. 18-fluoro-deoxyglucose positron emission tomography may contribute to the diagnosis and follow-up of malakoplakia. *Acta Clin Belg* 2004;59:138–42.
- 7 van der Voort HJ, ten Velden JA, Wassenaar RP, et al. Malakoplakia. two case reports and a comparison of treatment modalities based on a literature review. *Arch Intern Med* 1996;156:577–83.
- 8 Patel MR, Thammishetti V, Agarwal S, et al. Renal graft malakoplakia masquerading post-transplant lymphoproliferative disorder. *BMJ Case Rep* 2021;14. doi:10.1136/bcr-2021-244228. [Epub ahead of print: 16 Aug 2021].
- 9 Nieto-Ríos JF, Ramírez I, Zuluaga-Quintero M, et al. Malakoplakia after kidney transplantation: case report and literature review. *Transpl Infect Dis* 2017;19. doi:10.1111/tid.12731. [Epub ahead of print: 12 Jul 2017].
- 10 Augusto J-F, Sayegh J, Croue A, et al. Renal transplant malakoplakia: case report and review of the literature. *NDT Plus* 2008;1:340–3.
- 11 Purnell SDK, Davis B, Burch-Smith R, et al. Renal malakoplakia mimicking a malignant renal carcinoma: a patient case with literature review. *BMJ Case Rep* 2015;2015. doi:10.1136/bcr-2014-208652. [Epub ahead of print: 15 Jul 2015].
- 12 Kajbafzadeh A, Baharnoori M. Renal malakoplakia simulating neoplasm in a child: successful medical management. *Urol J* 2004;1:218–20.
- 13 Gillenwater JY. *Adult and pediatric urology*. Vol 1. Lippincott Williams & Wilkins, 2002.
- 14 Abolhasani M, Jafari AM, Asgari M, et al. Renal malakoplakia presenting as a renal mass in a 55-year-old man: a case report. *J Med Case Rep* 2012;6:379.
- 15 Ayllon J, Verkarre V, Scotté F, et al. Renal malakoplakia: case report of a differential diagnosis for renal cell carcinoma. *Am J Case Rep* 2012;13:38–40.

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