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Original Article

ORIGINAL ARTICLE

Renal allograft malakoplakia mimicking malignancy: the value of combined morphological and functional imaging

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ABSTRACT

Background. Malakoplakia is a rare, chronic granulomatous inflammatory condition that primarily affects the genitourinary tract, albeit rarely renal allografts. This article highlights the clinical presentation and radiological features of renal allograft malakoplakia and aims to identify knowledge gaps by a pooled analysis of case reports.
Methods. This study contains a detailed case report focusing on the presentation and radiological evolution of renal allograft malakoplakia, followed by a pooled analysis of 38 histologically confirmed cases, extracted from 34 publications. Descriptive statistics were applied.
Results. Malakoplakia of the renal allograft generally affects female (79%), middle-aged (mean 48 years) kidney transplant recipients in the first 2 years after transplantation (68.4%, mean 19 months), with a history of recurrent *E. coli* UTIs (87%) and considered at high immunological risk (70%). Acute kidney injury (AKI) was the most common presentation of allograft malakoplakia (84% of cases). Three main patterns can be differentiated on imaging: parenchymal lesions (40%), abscess-like formations (34%), and pseudotumoral masses (26%). Ultrasound, CT, MRI, and FDG-PET-CT can result in initial detection, assess disease extent, and treatment response. However, these imaging modalities cannot reliably differentiate malakoplakia from malignant or other infectious processes, making histopathological confirmation essential for definitive diagnosis. There are no standardized treatment protocols, nor guidelines concerning antibiotic duration, reduction of immunosuppression, and definition of remission. Despite treatment, one-fifth of cases result in graft failure and one-fifth in death.
Conclusions. Renal allograft malakoplakia is a rare but serious condition that in worst cases leads to graft loss and death. Prospective studies are needed to establish standardized diagnostic and therapeutic approaches, including the potential role of FDG-PET-CT in monitoring treatment response.

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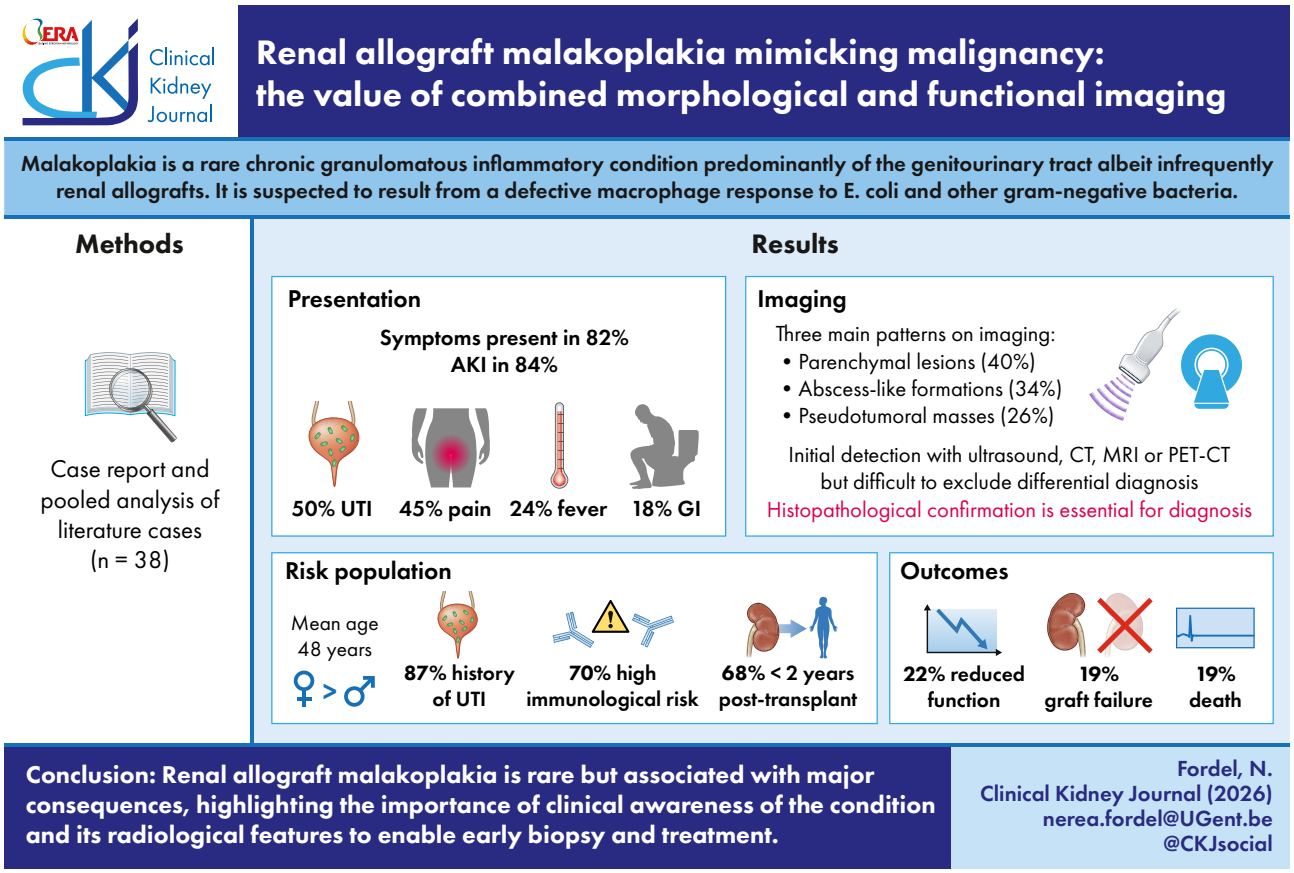
GRAPHICAL ABSTRACT



Keywords: allograft malakoplakia, malakoplakia, renal transplant, transplant malakoplakia

KEY LEARNING POINTS

What was known:

- Malakoplakia is a chronic granulomatous inflammatory condition that primarily affects the genitourinary tract, rarely renal allografts, sometimes leading to graft loss, dialysis, and even death.
- An underlying defective macrophage response to bacterial infection is suspected, usually to *E. coli* or other Gram-negative bacteria, resulting in accumulation of pathognomonic Michaelis–Gutmann bodies within histiocytes (von Hansemann's histiocytes).
- Diagnosis is frequently delayed because of a non-specific clinical and radiological presentation and the requirement for tissue confirmation.

This study adds:

- To prevent diagnostic delay, clinicians should maintain a low threshold for considering malakoplakia when faced with persistent urinary infections, unexplained deterioration of graft function, and/or allograft masses.
- Acute kidney injury (AKI) was the most common presentation of allograft malakoplakia (84% of cases). Only in 40% of AKI cases a full recovery to baseline kidney function was observed.
- Almost 60% of allograft malakoplakia cases present with pseudotumoral or abscess-like lesions on imaging, often mimicking malignancy. Although not conclusive in diagnosis, FDG-PET-CT has a potential role in treatment decisions and follow-up.

Potential impact:

- We increase awareness of renal allograft malakoplakia and its most common clinical and radiological presentations, hopefully prompting vigilance in KTRs at risk, earlier recognition and treatment, and stimulating close follow-up with FDG-PET-CT.
- We highlight the importance of immune dysfunction in the pathogenesis of allograft malakoplakia, underscoring the need for further investigation into the pathogen-specific abnormal macrophage response and alternative immunomodulatory therapies, such as mTOR inhibitors, cholinergic agents, and ascorbic acid.

INTRODUCTION

Malakoplakia is a rare, chronic granulomatous inflammatory condition that primarily affects the genitourinary tract, particularly the kidneys and bladder, but can occur in any solid organ [1]. The pathophysiology is not well understood but an underlying defective macrophage response to bacterial infection is suspected, usually to *Escherichia coli* or other Gram-negative bacteria. This results in accumulation of pathognomonic Michaelis–Gutmann (M–G) bodies within histiocytes (von Hansemann's histiocytes), leading to the formation of yellowish plaques or deposits [2–5]. This mechanism is particularly relevant in kidney transplant recipients (KTRs), in whom chronic immunosuppression and recurrent urinary tract infections (UTIs) thereby predispose to the development of malakoplakia [6–8]. Particularly in the renal allograft, malakoplakia's distinctive histopathology translates into highly variable clinical and radiological appearances, ranging from asymptomatic graft dysfunction and recurrent UTIs to the development of a renal mass or abscess, sometimes mimicking malignancy on imaging. Nonetheless, renal allograft malakoplakia may lead to severe outcomes such as graft loss, return to dialysis, and death, making early recognition crucial [9–11].

Ultrasound, computed tomography (CT), or magnetic resonance imaging (MRI) are essential for the initial detection of structural anomalies and disease extent but lack specificity [12, 13]. Advanced functional imaging, including 18F-FDG-PET-CT, may complement anatomical imaging by assessing metabolic activity, thereby providing additional insight into disease extent and treatment response [14, 15]. However, despite these advances, definitive diagnosis continues to rely on histopathological confirmation [1, 3, 16].

In this report, we describe a case of renal allograft malakoplakia, illustrating how the characteristic histological substrate of malakoplakia underlies its deceptive radiological presentation. We highlight the benefit of combining morphological imaging, functional FDG-PET, and histopathological analysis in the diagnostic strategy, therapeutic decision-making, and non-invasive monitoring of treatment. In addition, we present a pooled analysis of published cases to contextualize clinical presentations, radiological patterns, diagnostic strategies, and outcomes, with particular emphasis on the evolving role of imaging in this under-recognized condition.

CASE REPORT

A 79-year-old female, first diagnosed with membranoproliferative glomerulonephritis in 1977 and requiring haemodialysis by 1981, underwent her first deceased cadaveric kidney transplant in 1987. The post-transplant period was complicated by recurrent *E. coli* UTIs, escalating to an *E. coli* bacteraemia in 1993. Over the course of 33 years, a slow decline of graft function was observed, resulting in a return to haemodialysis in February 2020. In October 2020, at age 74, she received a second cadaveric kidney transplant in the left iliac fossa. No episodes of rejection were reported; however, the patient remained colonized with pan-susceptible *E. coli* and experienced occasional recurrent UTIs.

Four and a half years post-transplant, in October 2024, she presented to the emergency department because of progressive pain in the left lower quadrant, present since 1 to 2 months although significantly worsening over the preceding week. On examination, the patient was subfebrile [37.9°C (100°F)] with a noticeable induration at the level of the upper pole of the second renal allograft and blanchable erythema (Fig. 1a). Laboratory results revealed stable haemoglobin (12.4 g/dl), moderate inflammatory markers (leucocytosis 12 400/μl, CRP

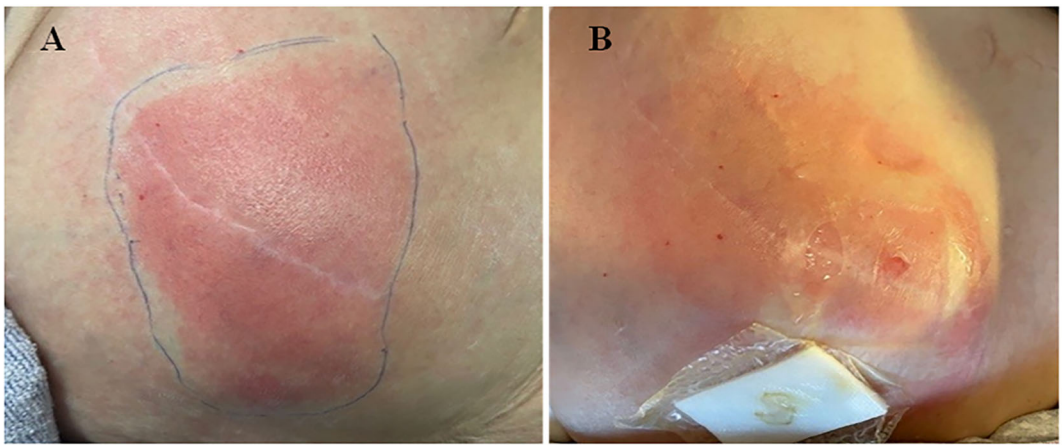


Figure 1: (a) At first presentation: noticeable induration at the level of the upper pole of the renal allograft and blachable erythema. (b) Readmission after <2 weeks: progression of the erythema to large blisters atop of the graft site.

44 mg/l), preserved graft function (creatinine 0.66 mg/dl, eGFR 86.6 ml/min/1.73 m^2), and slightly elevated LDH (303 U/l). The tacrolimus level was within therapeutic range (8.2 ng/ml). Urinalysis showed microscopic pyuria and haematuria, *E. coli* was cultured. Initial outpatient ultrasound suggested an abdominal wall hematoma extending into the renal allograft (Fig. 2a). Subsequent contrast-enhanced CT imaging visualized a subcapsular hematoma of the renal allograft extending through the abdominal wall musculature, most likely originating from an interpolar cortical cyst, but without signs of active bleeding (Fig. 2b).

Considering her stable clinical status, no signs of active bleeding and absence of other alarm signs, she was discharged with close follow-up and without antibiotic therapy. After just 2 weeks, she was readmitted due to persistent low-grade fever, anorexia, and worsening pain. Examination revealed progression of the erythema to large blisters atop of the graft site (Fig. 1b). Laboratory studies showed stable renal function, spontaneous decrease in inflammatory markers (leukocytes 9800/μl, CRP 26 mg/l) and persistent *E. coli* bacteriuria.

Repeat ultrasound now demonstrated an evolutive, vascularized solid mass, rather than the first established haematoma. MRI showed a 7.7-cm lesion arising from the allografts upper pole, going through the abdominal wall with extended subcutaneous infiltration (Fig. 2c). This finding raised concerns about a rapidly developing neoplasm, given the context, such as post-transplant lymphoproliferative disorder or Kaposi sarcoma. Retrospectively, a small nodule could already be identified on a previous CT angiography (of the lower extremities) in July 2024. FDG-PET-CT confirmed a hypermetabolic mass infiltrating the abdominal wall (Fig. 2d).

Since a percutaneous biopsy was not attainable because of isoechogenicity of the lesion, surgical biopsy was carried out. Perioperatively and macroscopically the lesion resembled an abscess-like structure for which broad-spectrum antibiotics (Piperacillin-Tazobactam IV) were initiated, and subsequently downgraded to oral levofloxacin based on *E. coli* positivity on intraoperative cultures. Pathological inspection showed no evidence of malignancy, but diffuse infiltration of foamy histiocytes with copious amounts of eosinophilic cytoplasm and prominent M–G bodies [positive on Periodic acid–Schiff (PAS) staining], consistent with malakoplakia (Fig. 3).

Immunosuppression was reduced (mycophenolate discontinued, tacrolimus target lowered to 6–8 mcg/l), and oral levofloxacin was continued for a prolonged time. Malakoplakia was still present on follow-up biopsy after 8 weeks of antibiotic treatment. Mass volume and metabolic activity gradually decreased according to serial FDG-PET-CT scans performed at 5 and 14 weeks (Fig. 4b and c). Owing to favourable evolution on imaging and the development of antibiotic-induced diarrhoea, antibiotics were discontinued at 14 weeks. Follow-up imaging at 26 weeks (and 11 weeks after termination of antibiotics, Fig. 4d) revealed further regression of the lesion and resolution of the abdominal wall infiltration.

This case underscores the diagnostic challenge posed by renal allograft malakoplakia and highlights the added value of a combined radiological and functional imaging strategy, particularly FDG-PET, for longitudinal assessment and treatment monitoring. Successful management was achieved through reduction of immunosuppression and prolonged targeted antibiotic therapy, with preservation of graft function and (to date partial) metabolic resolution of the mass on FDG-PET-CT.

POOLED ANALYSIS OF PUBLISHED CASES

Materials and methods

A thorough literature review was conducted to identify and analyse case reports and case series describing malakoplakia of the renal allograft. The primary literature search was performed in PubMed using ‘Malacoplakia’ and ‘Kidney transplantation’ as MeSH-terms. A detailed methodological search is described in the Supplementary data. In total, 33 publications were included in the review, comprising 37 cases (references in Supplementary data). Including our mentioned case report, this review evaluates 38 individual patients.

For each patient described in the included publications, data were extracted (see Supplementary data). Clinical findings were recorded in a binary manner (present/absent, yes/no, etc.), and time intervals were rounded to the nearest week, month, or year as appropriate.

General descriptive statistics were applied to the dataset. The frequency of each clinical finding was calculated based only on cases that reported the presence or absence of that finding. For

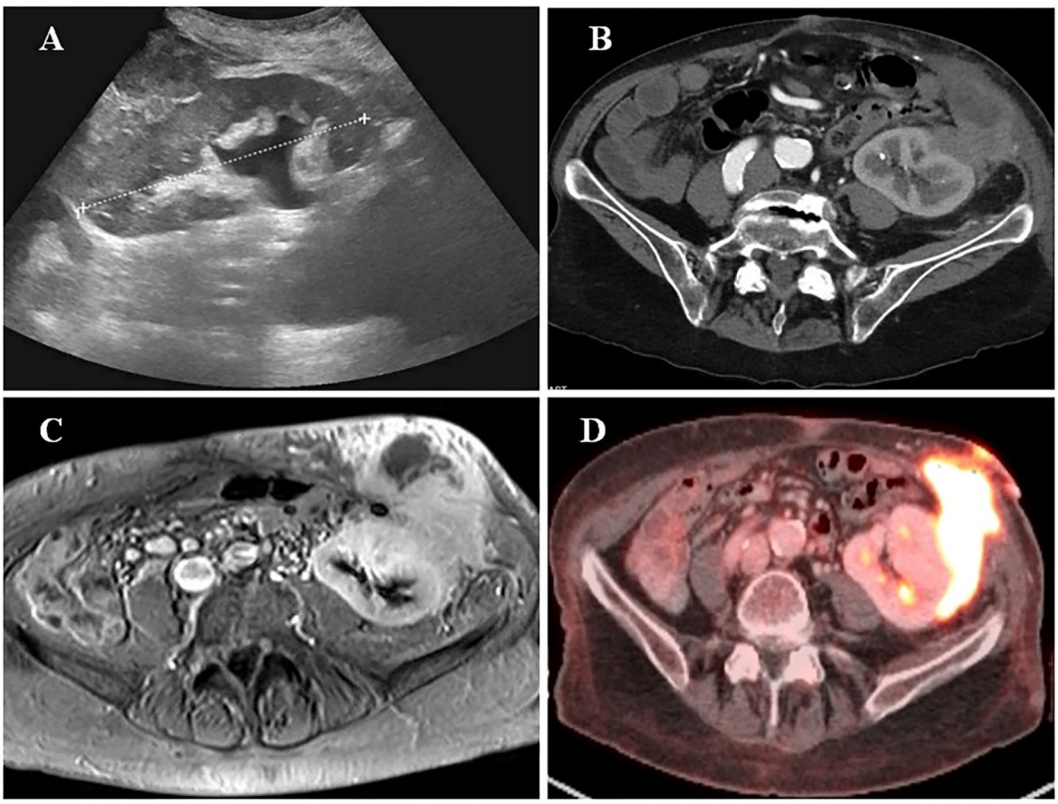


Figure 2: (a) Ultrasound at first presentation. (b) Contrast-enhanced CT, venous faze: according to initial protocol strong resemblance to large abdominal wall hematoma adjacent to the left oblique abdominal wall musculature, bordering the renal allograft. (c) MRI T1 TFE sequence: Mixed hyper- and hypo-intense signal on the T1- and T2-weighted images. Diffuse, predominantly late, enhancement of the lesion with heterogeneous, strand-like enhancement of the subcutaneous component. Diffuse, fairly homogeneous, pathological diffusion restriction throughout the entire lesion. On imaging suspect for sarcomatous origin, and fast evolutive in comparison to CT (b). (d) Intensely hypermetabolic mass in the left abdominal wall, extending to the skin, adjacent to the descending colon and the renal allograft, and appears to be connected to the haemorrhagic cyst interpolar in the renal allograft: based on imaging preference for malignant lesion.

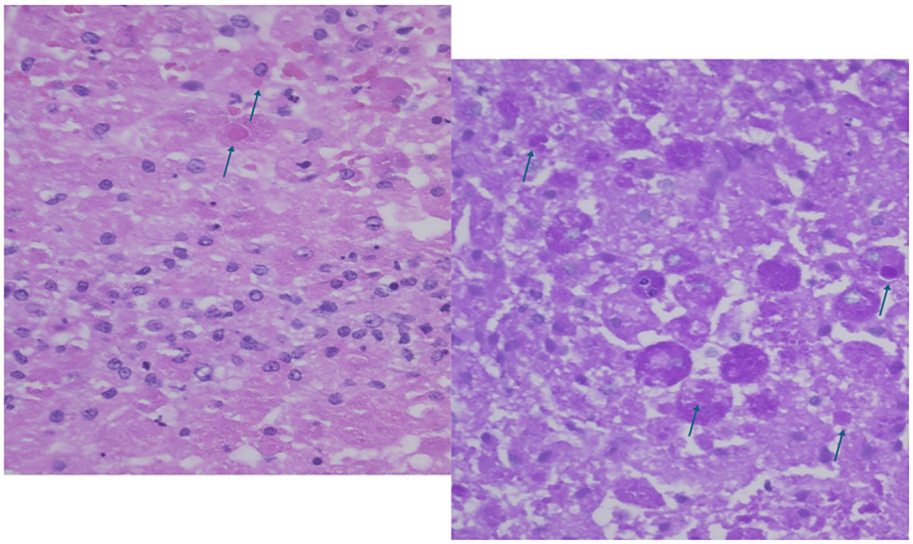


Figure 3: H&E stain ×400, showing the proliferation of histiocytes loaded with smaller and bigger eosinophilic granules (arrows). The granules are PAS positive (arrows, right panel).

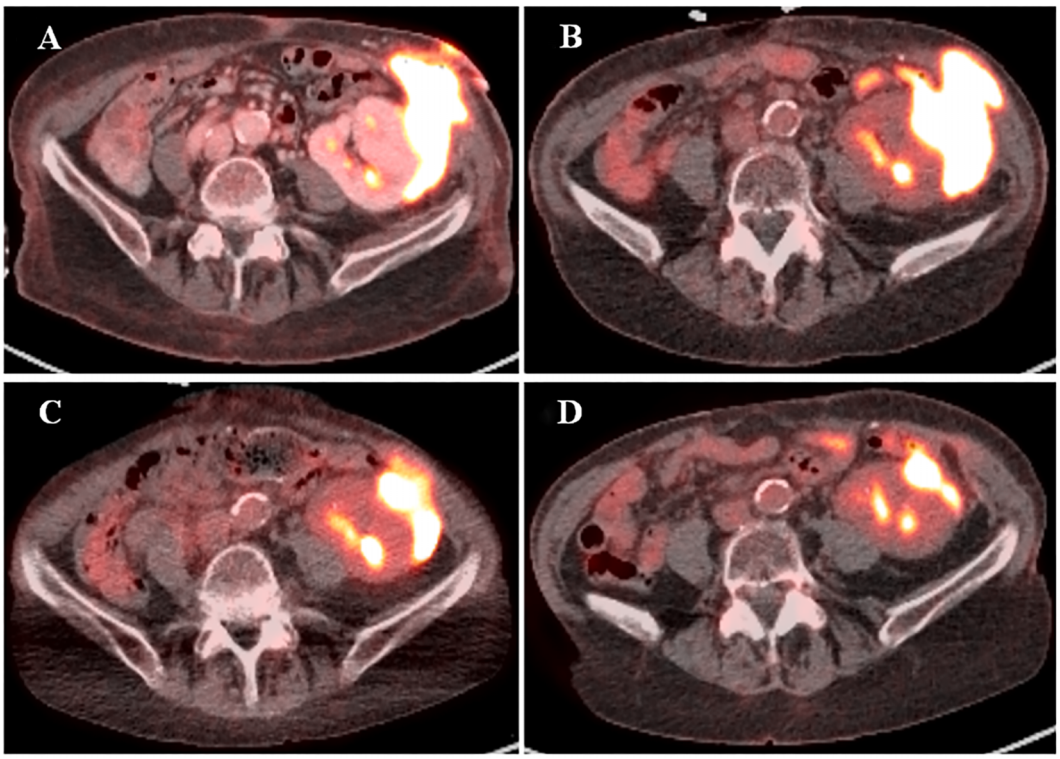


Figure 4: Evolution of renal allograft malakoplakia by FDG-PET CT imaging. (a) On 5 November 2024, initial presentation: baseline. (b) 10 December 2024, after 5 weeks of antibiotic treatment, resulting in a resolution of skin involvement. (c) 10 February 2025, after 14 weeks of antibiotic treatment, resulting in a significant reduction of the metabolic mass. (d) 2 May 2025, 26 weeks after initial presentation and 11 weeks after antibiotic cessation, further reduction of the metabolic mass with resolution of the abdominal wall infiltration.

example, if 31 cases reported AKI at presentation and seven reported its absence, then AKI was considered present in 82% of reporting cases. Cases in which a specific finding was not reported were considered 'non-reporting', and the number of such cases was noted when applicable.

RESULTS

Demographics, transplant characteristics, and native kidney disease

The study included 38 patients with histologically confirmed malakoplakia of the renal allograft. The mean age at diagnosis was 48 years (SD 14.32, range: 14–79 years). Females represented 79% (30/38) of cases, highlighting the female predominance in genitourinary malakoplakia, compared to 1:1 male–female ratio in other affected sites [9, 10, 18], presumably due to the higher prevalence of recurrent *E. coli* UTIs in women. The median time from transplantation to malakoplakia onset was 19 months (mean: 32 months, SD 39.27; range: 1–168 months), reflecting a right-skewed distribution. Cadaveric transplants comprised 63% (19/30) of cases, with glomerulonephritis being the most common underlying disease (26%, 8/31). A history of recurrent UTIs was reported in 87% (26/30) of patients (Table 1).

Immunological risk

Previous rejection episodes occurred in 52% (12/23) of recipients, including T-cell-mediated (17%, 4/23) and antibody-mediated (35%, 8/23) rejection. Including patients with multiple transplants (13%, 5/38), a total of 70% of the patient population was classified as 'high immunological risk' (e.g. rejection, previous transplantation, or sensitization). The most common immunosuppressive regimen was the triad of mycophenolate mofetil (MMF), tacrolimus (TAC), and prednisolone (66%, 21/32) (Table 1).

Clinical presentation and diagnosis

Symptoms were documented in 82% (31/38) of patients, meaning seven patients were asymptomatic, and the indication for renal biopsy was deterioration of the graft function on routine laboratories (suspecting rejection) or abnormalities on routine imaging. When symptomatic, classic symptoms of lower UTI were the most common presentation (50%, 19/38). Not a clinical symptom, but acute kidney injury (AKI) was the most common overall presentation of renal allograft malakoplakia (84%, 32/38). Among these, KDIGO staging can be calculated in 26 cases: stage 1 (50%, 13/26), stage 2 (15%, 4/26), and stage 3 (35%, 9/26). Cutaneous involvement with abdominal abscesses (as in the present case) was not uncommon (11%, 4/38).

The median duration of symptoms before diagnosis was 7 weeks (mean: 19 weeks; SD 30.8; range: 1–130 weeks), although this was reported in only 50% (19/38) of cases. In addition, it was often difficult to pinpoint the beginning of symptoms as they were non-specific and often wrongly contributed to other causes. (Table 2)

Three main patterns can be differentiated on imaging: parenchymal lesions (e.g. renal allograft enlargement or no abnormality on imaging, 40%, 14/35), abscess-like formations (34%, 12/35), and pseudotumoral masses (26%, 9/35). Ultrasound was the most utilized modality (75%, 27/36), followed by CT (50%,

Table 1: Descriptive data on demographic and transplant characteristics, native kidney disease, immunological risk and immunosuppressive regimens in renal allograft malakoplakia.

	N (%)
Age, years (mean—SD)	48.05–14.32
Gender	
Female	30 (79)
Male	8 (21)
Time after transplantation, months (mean—median)	32–19
Type of transplant	
Cadaveric	19 (63)
Living-donor	5 (17)
Live-related	6 (20)
Native disease	
Glomerulonephritis	8 (26)
Diabetic nephropathy	6 (19)
ADPKD	3 (10)
Chronic pyelonephritis	3 (10)
Hypertensive nephropathy	2 (7)
Undetermined	3 (11)
Others (atypical hemolytic uremic syndrome, lithium nephropathy, membranous nephropathy, analgesic nephropathy, Goodpasture's Syndrome)	5 (25)
Recurrent UTI	26 (87)
Previous rejection	
No	10 (48)
Antibody-mediated	8 (35)
T-cell mediated	4 (17)
Multiple transplantations	5 (13)
High immunological risk (2° transplant, previous rejection, sensitization)	17 (71)
Immunosuppressant regimen	
MMF/TAC/prednisolone	21 (66)
MMF/TAC	2 (6)
MMF/prednisolone	1 (3)
Azathioprine/prednisolone	7 (22)
Cyclosporin A/prednisolone	1 (3)

Table 2: Descriptive data on the clinical presentation of renal allograft malakoplakia.

	N (%)
Time from onset of symptoms to diagnosis, weeks (mean—SD)	18.74–30.8
AKI	32 (84)
Stage 1	13 (50)
Stage 2	4 (15)
Stage 3	9 (35)
UTI	19 (50)
Flank/abdominal pain	17 (45)
Fever	9 (24)
GI symptoms	7 (18)
Cutaneous involvement	4 (10)

18/36), MRI (11%, 4/36), and FDG-PET-CT (8%, 3/36). Interestingly, our case is the only one describing all four image modalities at presentation; and using FDG-PET-CT in the monitoring of treatment response. (Supplemental Table 3).

Microbiological findings and diagnostic approaches

E. coli was isolated in 87% (32/37) of cases, confirming its predominant role in renal allograft malakoplakia. Other cultured organisms, predominantly Gram negatives, were *Klebsiella pneumoniae* (4/37), *Pseudomonas aeruginosa* (3/37), *Enterobacter cloacae* (3/37), and more rare bacteria (*Acinetobacter*, *Enterobacter aerogenes*, *Staphylococcus aureus*, *Corynebacterium hofmannii*, *Proteus vulgaris*). Microbiological diagnosis was most frequently established by urine culture (86%, 32/37). Additional evidence of microbial pathogens was found in haemocultures (19%, 7/37) and cultured biopsy of the renal allograft (30%, 11/37). Notably, 8% (3/37) of cases remained culture-negative, with diagnosis

Table 3: Descriptive data on the outcomes and follow-up of renal allograft malakoplakia.

	N (%)
Timing for follow-up, months (mean—SD)	4.25–1.49
Outcome of kidney function	
Recovery to baseline	11 (40)
Persistent reduced graft function	6 (22)
Graft failure	5 (19)
Death	5 (19)
Evolution on imaging	
Reduction in mass size	7 (47)
Resolution of lesions	8 (53)

established solely through histopathological findings. (Supplemental Table 4).

Therapeutic strategies

Treatment regimens varied within the cohort, as can be seen in Supplemental Table 4 and 5. The most common combination approach was antibiotics with reduction of immunosuppressive therapy, used in 37% of cases (13/36). Fluoroquinoles and betalactam antibiotics were used with similar frequency. The duration of antibiotic treatment was prolonged, with a mean of 16 weeks (SD 16.39). This is probably an underestimation as in five cases antibiotic therapy was described as 'long-term' without clear indication of treatment duration.

Outcomes and follow-up

The mean follow-up period was 4.25 months (SD 1.49). At last follow-up contact, recovery of kidney function to baseline was observed in 40% (11/27) of patients with AKI (reminder: 32/38 patients had AKI at presentation). Persisting reduced graft function was present in 22% (6/27) of cases. Graft failure was documented in 19% (5/27), and death occurred in 19% (5/27) of cases.

In the categories of abscess-like and pseudotumoral lesions (in total 21 of the patient cohort) evolution on imaging was recorded in 15 cases, showing reduction in the size of malakoplakia lesions in 47% (7/15), while complete resolution of lesions was noted in 53% (8/15). Follow-up imaging consisted of US or CT; our case is the first describing the evolution on FDG-PET-CT. A negative follow-up biopsy, confirming histological resolution, was documented only in one case; as in our case follow-up biopsy at 8 weeks still confirmed the presence of malakoplakia. (Table 3, and Supplemental Table 5).

DISCUSSION

Renal allograft malakoplakia remains a rare but clinically significant complication, and this review of 38 cases provides the most comprehensive synthesis to date. The precise pathophysiology behind malakoplakia remains poorly understood. An immune-mediated defect in macrophage bactericidal activity is presumed, secondary to a defective lysosomal function and abnormal tubular assembly due to reduced cyclic guanosine monophosphate to cyclic adenosine monophosphate ratio within phagocytes. Collectively, these defects result in incomplete intracellular killing of bacteria, persistence of bacterial fragments, and chronic activation of macrophages. This proposed mechanism is closely reflected in the characteristic histopathological findings, as malakoplakia is defined by the presence of M–G bodies. These are targetoid, intra- and extracellular, mineralized [PAS, von Kossa (calcium); Perls' Prussion blue (iron) positive] remnants of incompletely digested phagosomes. In addition, bacilliform structures, bacterial fragments, and DNA can be demonstrated in these M–G bodies, further supporting the concept of defective intracellular bacterial clearance [2–7].

Our findings reinforce known epidemiological patterns, including the female predominance in genitourinary sites, the role of recurrent *E. coli* UTIs, and the high immunological risk profile of affected KTRs. The marked predominance of *E. coli* suggests a pathogen-specific abnormal innate immune response. This may partly reflect its prevalence as the most common uropathogen. However, back in 1977 Abdou *et al.* incubated mononuclear cells from patients with confirmed malakoplakia with *E. coli* and *S. aureus*. Only those exposed to *E. coli* had decreased bactericidal macrophage activity and low levels of cyclic-GMP [2]. While the precise mechanism remains unclear, parallels can be drawn with the intracellular bacterial community (IBC) pathway, first discovered in uropathogenic *E. coli*. The IBC pathway enables bacterial intracellular survival and replication in urothelial cells, and has been described in other uropathogens (e.g. *K pneumoniae*, *Enterococcus faecalis*, and *Staphylococcus saprophyticus*) albeit at lower levels (IBC-like) [19, 20]. Although the IBC pathway and malakoplakia occur in fundamentally different cells (urothelial epithelium vs. macrophages), they share a central pathogenic theme: the ability of *E. coli* to persist intracellularly by evading normal bactericidal mechanisms, providing a plausible biological link for further investigation.

This study endorses the typical disease onset in the first two years after transplantation, probably reflecting higher immunosuppressive exposure in the early post-transplant period resulting in macrophage function impairment and generally increased infection risk [9, 21]. Notably, 52% of patients had prior rejection: higher than previously reported cohorts (22%–41%) and the general kidney transplant population (10%–20%) [9, 18, 22]. When adding patients with multiple transplants and sensitization, 70% was considered high immunological risk. This reinforces the established role of immunosuppression and immune dysfunction in the pathogenesis, warranting higher vigilance in KTRs considered at high immunological risk. Although some previous reviews on the topic of malakoplakia in transplantation claim that current immunosupressive therapy may reduce the number of malakoplakia cases (compared to Azathioprine/Cyclosporin A regimens) [7, 8], this was not evident from our data. Nonetheless, alternative immunosuppressive regimens with mTOR inhibitors may potentially be associated with a lower risk of malakoplakia by enhancing macrophage autophagy and phagolysosomal maturation, improving intracellular bacterial clearance and preventing M-G body accumulation.

To our knowledge, this pooled analysis is the first to characterize the clinical presentation of renal allograft malakoplakia in detail. In 82% of cases diagnosis of malakoplakia was preceded by non-specific symptoms, including classic symptoms of lower UTI, flank/abdominal pain, fever and gastrointestinal complaints. These can be easily attributed to other causes, resulting in a significant delay in diagnosis (median 7 weeks, range 1–130 weeks). Clinicians should maintain a low threshold for considering malakoplakia when faced with persistent urinary infections and otherwise unexplained

Table 4: Possible radiological findings for renal allograft malakoplakia, main strengths and limitations of diagnostic approaches.

Imaging modality	Typical findings	Main strengths	Key limitations
Ultrasound (US)	Hypoechoic or heterogeneous parenchymal areas; solid or ill-defined mass-like lesions; graft enlargement; variable internal vascularity on Doppler [9, 12, 13]	Widely available; first-line tool; detects structural abnormalities and guides biopsy	Low specificity; cannot reliably distinguish infection from malignancy
CT	Hypodense or mildly enhancing lesions; abscess-like collections or infiltrative pseudotumoral masses; possible perinephric or abdominal wall extension; hyperdense or calcified components (e.g. M-G bodies) [9, 12, 13]	Good spatial resolution; evaluates disease extent and complications	Radiation; contrast exposure; cannot reliably distinguish infection from malignancy
MRI	T1 hyperintensity, T2 hypointensity; diffusion restriction; heterogeneous contrast enhancement; better soft-tissue delineation [12, 13]	Superior soft-tissue contrast; useful when CT is equivocal or contrast is contraindicated	Limited availability; still non-specific; fewer reported cases
18 FDG-PET-CT	Marked FDG uptake reflecting inflammatory macrophage activity [14, 15]	Functional assessment; evaluates disease extent, enables longitudinal monitoring of therapy	FDG uptake is non-specific (infection vs malignancy); fewer reported cases
Histopathology (gold standard)	Von Hansemann histiocytes with M–G bodies (PAS, von Kossa positive) [1, 3, 16]	Definitive diagnosis	Invasive; sampling error possible

symptoms. Nevertheless, eight out of 38 patients were strictly asymptomatic. In these cases, the diagnosis was established following a biopsy prompted by deterioration of graft function or by an incidental finding of a renal mass on imaging. Acute deterioration of graft function was present in 84% of the cohort, ranging from mild to graft failure, suggesting unexplained AKI (or any new renal mass should) should indeed prompt early biopsy.

Radiological assessment plays a pivotal yet often underestimated role in the diagnostic work-up of renal allograft infections in general [23]. Around 60% of renal allograft malakoplakia cases present with abscess-like formations or pseudotumoral masses. Ultrasound typically shows a hypoechoic, poorly defined, and often hypervascular lesion. On CT imaging, lesions may appear as solid-cystic masses with septations, hyperdense or calcified components (e.g. calcified M–G bodies), and contrast enhancement. MRI demonstrates T2 hypointensity, T1 hyperintensity, heterogeneous contrast enhancement, and restricted diffusion, secondary to the presence of calcium and iron in the M–G bodies [12, 13]. PET-CT reveals pronounced hypermetabolic (FDG-avid) lesions [14, 15]. In addition, malakoplakia lesions are often rapidly progressive, in combination with the described imaging features, raising suspicion of primary malignancies (such as renal cell carcinoma), sarcomas (such as Kaposi in the context of immunosuppression), and post-transplant lymphoproliferative disorder. Nevertheless, other infectious aetiologies (abscesses, tuberculosis, xanthogranulomatous pyelonephritis) should be included in the differential diagnosis. Although the described imaging modalities have their practical strengths and limitations, all of them lack the ability to discern malakoplakia from neither malignant nor infectious processes, definitive diagnosis generally requiring a targeted biopsy. Still, FDG-PET may provide incremental value by enabling longitudinal assessment of metabolic response to therapy, and potentially avoiding unnecessary graft nephrectomy (Table 4). Therapeutic strategies lack prospective evidence. They are largely theoretical, based on the proposed pathophysiological mechanisms, as evidence remains anecdotal and derived from small case series. Management strategies in this review mirrored those outlined in the literature: long-term antibiotic therapy with intracellular concentration and Gram-negative spectrum (such as fluoroquinolones, macrolides, and trimethoprim-sulfamethoxazol) to target bacteria sequestered within macrophages; and tapering of immunosuppression to correct the presumed intracellular signalling defect. In addition, use of bethanechol, a cholinergic agonist, and ascorbic acid, or vitamin C, has been suggested since these respectively increase cyclic guanosine monophosphate and reduce cyclic adenosine monophosphate levels, altering macrophage redox state [24–26]. The enigma remains on the duration of antibiotic treatment, varying from 3 weeks up to 18 months in the analysed cases. It remains unsure as to whether treatment should be titrated to clinical, radiological, microbiological, metabolic (as in FDG avidity), or histological remission. In our case, similarly to the native kidney malakoplakia case by Vanbrabant *et al.* [14], discontinuation of antibiotic therapy was based on favourable evolution on FDG-PET-CT, resulting in further regression of FDG uptake 11 weeks after antibiotic cessation.

In the end, outcomes seem guarded with most patients either not fully recovering kidney function, progressing to graft loss, or even to death. These numbers must be nuanced as all deaths occurred before 1985 and (related or not) before the development of second-generation fluoroquinolones. Still, renal allograft malakoplakia carries a significant morbidity and

mortality burden to this day, prompting the need for fundamental research into underlying pathophysiological mechanisms as well as prospective clinical investigations.

ETHICS COMPLIANCE

This study on organ transplantation was conducted in compliance with the Declaration of Helsinki and the Declaration of Istanbul. The participant concerning the case report provided informed consent, and the research was approved by the ethics committee EC Research UZ/KU Leuven (S71451).

AUTHORS' CONTRIBUTIONS

Research idea and study design: N.F., V.N., C.S., R.S., and M.N.; data acquisition: N.F., V.N., C.S., R.S., T.T., H.V., C.V., N.S., D.K., P.J., E.V.D.H., and M.N.; data analysis/interpretation: N.F., V.N., R.S., and M.N.; statistical analysis: N.F.; supervision or mentorship: V.N., R.S., T.T., D.K., P.J., E.V.D.H., and M.N. Each author contributed important intellectual content during manuscript drafting or revision and agrees to be personally accountable for the individual's own contributions and to ensure that questions pertaining to the accuracy or integrity of any portion of the work, even one in which the author was not directly involved, are appropriately investigated and resolved, including with documentation in the literature if appropriate.

SUPPLEMENTARY DATA

Supplementary data are available at *Clinical Kidney Journal* online.

CONFLICT OF INTEREST

None declared.

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DATA AVAILABILITY STATEMENT

The data underlying this article are available in the article and in its online supplementary material.

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