

Case Report

Renal transplant malakoplakia: case report and review of the literature

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Introduction

Malakoplakia is a rare inflammatory disorder that affects predominantly the urinary tract and kidneys. Isolated renal parenchymal involvement occurs in 16% of all cases [1]. Urinary tract and digestive malakoplakia have been reported in transplant recipients but involvement in transplant tissue is rare.

We report a case of renal allograft parenchymal malakoplakia and present a brief review of kidney transplant malakoplakia cases from the literature.

Case report

A 56-year-old woman was hospitalized on 25 October 2006 with a 5-day history of asthenia, fever, vomiting and diarrhoea. In 1996, she had developed end-stage renal disease due to undetermined glomerulopathy and received a first cadaveric renal transplant. In April 2004, she then presented with chronic allograft nephropathy and terminal renal failure. There was no sign of urinary tract infection. A second cadaveric kidney transplantation was performed on 18 November 2005. Immunosuppression treatment included anti-thymocyte globulins followed by tacrolimus and mycophenolate mofetil. The preservation fluid culture was sterile. A urinary tract infection due to *E. coli* was detected and treated on Day 14 post-transplantation; creatinine was 155 $\mu\text{mol/L}$ at Day 21.

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On admission, blood pressure was 120/80 and temperature was 38.5°C. She was oliguric for 2 days and had lost 2 kg of weight. Physical examination revealed a swollen but non-painful kidney transplant.

She had acute renal failure that was ascribed to extra cellular dehydration and acute pyelonephritis without clinical evidence of septic shock. Serum urea nitrogen was 48.5 mmol/L and creatinine 688 $\mu\text{mol/L}$. Urinalysis showed proteinuria of 0.7 g/24 h, haematuria ($10^5/\text{mL}$) and leucocyturia ($10^5/\text{mL}$). Other laboratory results revealed total serum protein 69 g/L, potassium 4.3 mmol/L, sodium 136 mmol/L, haemoglobin 8.7 g/dL, white blood cells 13 700/mm³, platelets 222 000/mm³ and CRP 204 mg/L. Blood and urine cultures were positive for *E. coli*. Abdominal ultrasound showed an enlarged 13-cm kidney transplant without pyelocaliceal dilatation.

The patient was treated with isotonic serum saline and intravenous gentamycin for 3 days combined with oral levofloxacin. Despite treatment, she remained oliguric and we suspected an acute rejection episode. On Day 7, intravenous methylprednisolone (500 mg/day \times 3) was administered. Percutaneous graft biopsy was performed on Day 8.

Histological examination showed interstitial inflammation with infiltration of neutrophils and histiocytic cells having abundant eosinophilic cytoplasm. Many of these cells contained periodic acid-Schiff (PAS) positive inclusions (Figure 1) consistent with Michaelis–Gutmann bodies. The patient was diagnosed with renal transplant malakoplakia.

Prednisone was immediately stopped. Levofloxacin was continued for 10 weeks and the tacrolimus dose was decreased to obtain residual levels between 4 and 6 ng/mL. Kidney function improved rapidly but did not return to anterior levels (serum creatinine: 225 $\mu\text{mol/L}$ versus 150 $\mu\text{mol/L}$).

The patient did not develop any recurrent urinary tract infection, but was admitted to the hospital at months 4 and 7 for functional acute renal failure. On each occasion, she presented with extracellular dehydration with elevated

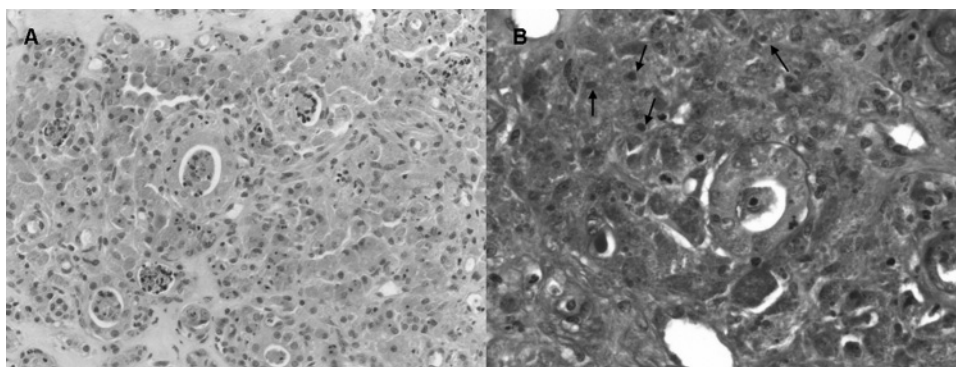


Fig. 1. (A) Kidney graft biopsy (HPS stain) the interstitium of the renal medulla was densely infiltrated by histiocytic cells (von Hansemann cells). These cells infiltrated the tubules. (B) (PAS stain), some cells contained strongly positive PAS rounded bodies: Michaelis–Gutmann bodies, black arrows.

urinary sodium concentration (>120 mmol/L). We suspected a salt-losing nephropathy secondary to malakoplakia. One year later, she has tubular proteinuria (0.78 g/day) and chronic kidney failure (creatinine 250 μ mol/L, GFR 30 ml/min).

Discussion

Malakoplakia is a rare inflammatory condition that most commonly involves the urinary tract, colon and rectum, and less frequently skin, lungs and other organs. The disease is associated with urinary tract infections in 80% of cases. An impaired macrophage bactericidal ability appears to be the underlying defect [1]. Involved tissues are characterized by accumulation of histiocytes with granular acidophilic cytoplasm (von Hansemann cells). The cytoplasm of these cells contains PAS positive granules, the Michaelis–Gutmann bodies, which are pathognomonic and are derived from phagolysosomes containing incompletely destroyed bacteria [1].

An immunodeficient state favours the development of malakoplakia since 40% of patients who have developed this condition had immunosuppressive drugs [1]. A complete or partial recovery of phagocytic cell function has been demonstrated in monocytes from patients with malakoplakia after immunosuppressive drug withdrawal [2].

Malakoplakia has been described in transplanted patients. The more frequent localizations are the bladder, the ureter and prostate, sometimes leading to obstructive nephropathy, but skin and digestive malakoplakia have also been reported.

We performed a MEDLINE search and analysed all cases reporting kidney transplant involvement (Table 1). Only 10 previous cases of renal transplant malakoplakia were reported [3–12] from 1977 to 2007. Patients' age ranged from 30 to 56 years, the sex ratio was 9/1 (F/M) and *E. coli* was detected in 80% of cases. Azathioprine plus prednisone

was the immunosuppressive regimen used in 6/10 patients. All patients had renal failure and biopsies indicated acute interstitial nephropathy with the pseudo-tumoral form in two of the cases. A retrospective analysis in our patient of all urine samples from the first year following transplantation showed that leucocyturia was continuously present after the sixth month post-transplantation. Laboratory results displayed either aseptic leucocyturia or presence of bacteria $<10^4$ /mL. The inflammatory process probably developed progressively.

In the first five cases reported before 1985, transplantectomy and patient death occurred in all five patients. In the more recent cases, renal function improved in two cases, transplantectomy was performed in one patient, renal function worsened in one case and renal outcome was not specified in one case. The improved outcomes were probably due to the lowering of immunosuppressive regimens and the use of antibiotics with intracellular penetration such as quinolones. In a review of all renal parenchymal malakoplakia cases after 1990 in nontransplanted patients, Tam *et al.* [13] reported a low mortality rate ($<10\%$) but a frequent diminution in renal function leading to haemodialysis.

Despite prolonged levofloxacin treatment and reduction in immunosuppression, graft function did not completely recover in our patient. We diagnosed chronic salt-losing nephropathy secondary to renal malakoplakia, which has not been previously described.

In our case, acute renal rejection was suspected at Day 7 and the patient was treated with high corticosteroid doses. We observed that renal function improved rapidly at 48 h following methylprednisolone treatment and hypothesized that high-dose steroid slowed the parenchymal inflammatory process.

Malakoplakia that affects renal transplant tissue is associated with severe morbidity. This pathologic condition must be considered in transplanted patients presenting with acute renal failure associated with urinary tract infection. Graft biopsies should be taken immediately to establish the diagnosis and to allow for prolonged antibiotherapy.

Table 1. Graft malakoplakia cases reported in the literature

Study	Age/sex	Bacteria identified	Immunosuppressive regimen	Malakoplakia treatment	Presentation form	Outcome
Osborn <i>et al.</i> [3]	48/F	<i>E. coli</i>	Prednisone/azathioprine	Ampicilline	Parenchymal	Haemodialysis 3 months later. Transplant nephrectomy Death 5 month later
Arnesen <i>et al.</i> [4]	37/F	<i>E. coli</i>	Prednisone/azathioprine	Antibiotics (not specified)	Parenchymal/Bladder involvement	Haemodialysis shortly after Transplant nephrectomy Death
Mullan <i>et al.</i> [5]	42/F	<i>E. coli</i>	Not specified	Not specified	Parenchymal	Hemodialysis shortly after Transplant nephrectomy Death
Nathan <i>et al.</i> [6]	30/F	<i>Corynebacterium hofermannii</i>	Prednisone/azathioprine	Several antibiotics	Parenchymal/Urethral/Bladder involvement	Transplant nephrectomy Death
Barker [7]	43/F	<i>E. coli</i>	Prednisone/azathioprine	Post-mortem diagnosis	Parenchymal/Quadriceps abscess	Death 6 month later
Melloul <i>et al.</i> [8]	56/M	<i>E. coli</i>	Prednisone/azathioprine	Not specified	Pseudo-tumoral	Not specified
McKenzie <i>et al.</i> [9]	29/F	Not specified	Prednisone/azathioprine	Antibiotic (not specified)	Parenchymal	Impaired renal function 3 years later (serum creatinine 400 µmol/L)
Husek <i>et al.</i> [10]	44/F	<i>E. coli/citrobacter</i>	Prednisone/ciclosporin A	Piperacillin/pefloxacin	Parenchymal	Survival renal function improvement
Puñl <i>et al.</i> [11]	43/F	<i>E. coli</i>	Mycophenolic acid/tacrolimus	Antibiotic (not specified)	Parenchymal	Survival renal function improvement
Puerto <i>et al.</i> [12]	45/F	<i>E. coli</i>	Not specified	Post-transplant nephrectomy diagnosis	Pseudo-tumoral	Survival transplant nephrectomy

Conflict of interest statement. None declared.

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