

CASE REPORT

End stage renal disease due to bilateral renal malakoplakia

S Hegde, M G Coulthard

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Malakoplakia typically affects the bladders of immunocompromised adults who have defective intracellular killing of *Escherichia coli*. Renal malakoplakia is rare in children and generally has a good outcome. In the case presented, however, it caused end stage renal failure in a 5 year old girl. The management dilemmas surrounding renal transplantation are highlighted.

Malakoplakia, meaning soft plaque, is an uncommon chronic granulomatous inflammatory disorder primarily affecting the urinary collecting system in immunocompromised or debilitated adults. It can also affect renal parenchyma and other sites in adults, and rarely in children.¹ The underlying abnormality appears to be defective macrophage lysosomal digestion of phagocytosed bacteria, particularly coliforms. This leads to intracytoplasmic deposition of bacterial fragments within pathognomonic laminated basophilic calcospherules called Michaelis-Gutmann bodies.¹

We are aware of only eight paediatric case reports involving the renal parenchyma in the English literature (see table 1).²⁻⁸ *Escherichia coli* was cultured from the urine of all eight, and the blood of four. The first case died,² and two with unilateral involvement were successfully treated with nephrectomy.^{3,4} Of the five remaining bilateral cases, three were treated with antibiotics alone, of whom one died and two made a full recovery.^{5,6} Two additionally received prednisolone,^{7,8} plus azathioprine in one case;⁷ both recovered fully. We report a unique case of bilateral renal malakoplakia producing end stage renal disease in a 5 year old girl.

CASE REPORT

A 5 year old girl was febrile, shocked, and encephalopathic after three days of bloody diarrhoea and two days of anuria. This presentation, plus her biochemistry (plasma creatinine 448 µmol/l, urea 34 mmol/l, potassium 5.4 mmol/l, bicarbonate

7.3 mmol/l, ionised calcium 0.6 mmol/l, and phosphate 3.2 mmol/l) and her haematology results (haemoglobin 88 g/l, white cells $16 \times 10^9/l$, neutrophils $9 \times 10^9/l$, platelets $89 \times 10^9/l$) suggested haemolytic-uraemic syndrome, though she did not have a typical blood film. Investigations six months earlier for poor weight gain had shown normal urinalysis, full blood count, plasma creatinine, and blood pressure. Her older sister had had a ganglioneuroma resected at 5 years of age.

She was treated with fluid resuscitation, and intravenous cefotaxime before transfer to our unit for peritoneal dialysis. Computed tomography of her head, cerebrospinal fluid examination, and metabolic screen were normal. Blood culture grew *Escherichia coli*, but urine was not obtained before antibiotic treatment. Stool grew no pathogens. C reactive protein was raised at 459 mg/l. Renal ultrasound appearance changed over eight days from being slightly enlarged (78 mm long) with decreased corticomedullary differentiation, to being 88 mm long with a well defined right lower pole hypoechoic mass which distorted the internal architecture. These findings were confirmed on computerised tomography, and the mass was biopsied. Most of the glomeruli were sclerosed, the tubules contained neutrophils and necrotic debris, and the interstitium was massively expanded by a cellular infiltrate (fig 1A) including abundant large histiocytes with eosinophilic cytoplasm that contained Michaelis-Gutmann bodies, diagnostic of malakoplakia (fig 1B,C). In view of this she underwent the following immunological tests, all of which were normal: plasma immunoglobulin and subclass concentrations, lymphocyte subsets, neutrophil and monocyte oxidative burst tests, and phagocytosis assessments.

Fifteen months later she remains dialysis dependent and is on-call for a renal transplant. She takes daily cotrimoxazole which has intracellular antibacterial activity, but no other specific therapy. She remains clinically well with no signs of malakoplakia elsewhere, nor evidence of susceptibility to other infections.

Table 1 Nine reported cases of renal parenchymal malakoplakia in children, including the present case

References	At presentation		<i>E coli</i> cultured			Kidneys involved	Medical/surgical therapy*	Outcome
	Age (y)	Sex			GFR impaired			
			Blood	Urine				
Ravel ²	3	F	-	+	+	2		Dead
Trillo and Lorentz ³	9.5	F	-	+	+	1	Nephrectomy	Full recovery
Deridder <i>et al</i> ⁴	3	F	-	+	-	1	Nephrectomy	Full recovery
Charney <i>et al</i> ⁵	11	F	-	+	+	2		Full recovery
Wigginkhuizen <i>et al</i> ⁶	0.5	M	+	+	+	2		Dead
	0.5	M	+	+	+	2		Full recovery
Saleem <i>et al</i> ⁷	0.15	F	+	+	+	2	Prednisolone and azathioprine	Full recovery
							Methylprednisolone	Full recovery
Honjo <i>et al</i> ⁸	0.09	M	+	+	+	2		Full recovery
Present study	3.5	F	+	-	+	2		End stage renal failure

*Medical therapy excludes antibiotic treatment, which they all received.

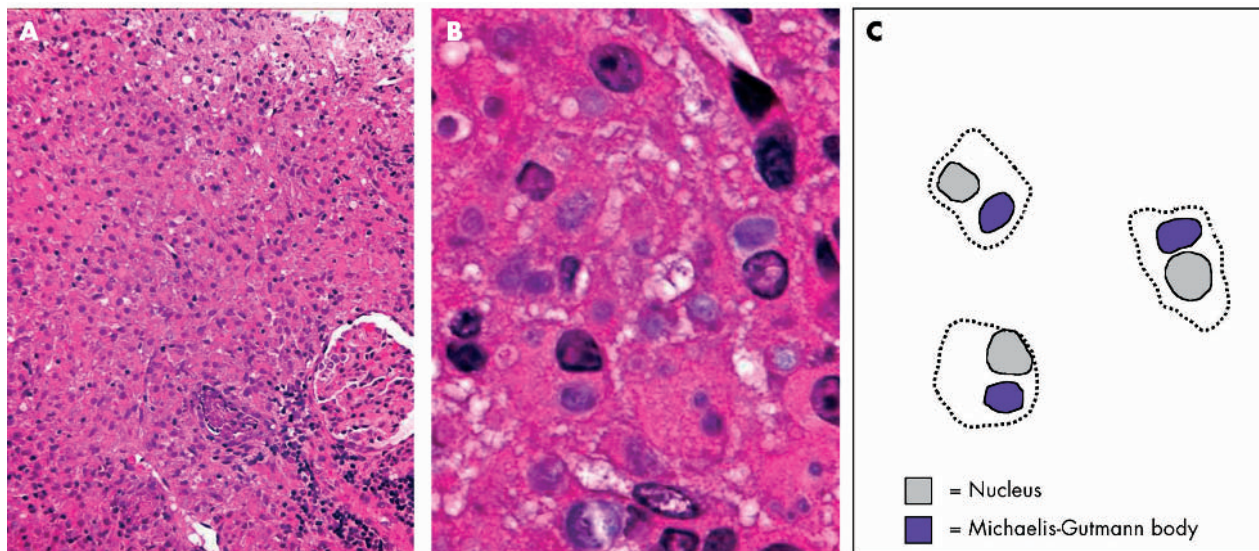


Figure 1 Renal biopsy. (A) Low power shows massive expansion of the interstitium by a cellular infiltrate. (B) High power shows abundant large histiocytes with eosinophilic cytoplasm that contain Michaelis-Gutmann bodies, diagnostic of malakoplakia. (C) This cartoon shows three examples of the large histiocytes shown in figure B, with the nuclei in grey and the Michaelis-Gutmann bodies in purple.

DISCUSSION

Childhood renal parenchymal malakoplakia is rare; our case is only the ninth in the English literature, and the first ever to develop end stage renal failure. Unlike the majority of adult cases,¹ she had no malignancy, immunodeficiency syndrome, or autoimmune disease, and had not been receiving steroids or immunosuppressant drugs. Indeed, analysis of her leucocyte function showed no abnormalities of bacterial killing. Despite that, we felt it appropriate to give prophylactic cotrimoxazole to augment the intracellular bacterial killing.⁹

However, we did not immunosuppress her with steroids or azathioprine as others have reported,^{7,8} because this has been implicated in the genesis of malakoplakia.¹ Indeed, patients who developed malakoplakia while on immunosuppressive therapy for other reasons have been shown to have reversal of their clinical and leucocyte abnormalities after withdrawal of these agents.¹⁰ This poses a difficult management dilemma in our patient; renal transplantation is universally recognised to be the long term treatment of choice in children, but inevitably requires lifelong immunosuppression. If this can induce rare cases of de novo malakoplakia in the transplanted kidney¹¹ and other organs¹⁰ of patients with no previous history of this condition, we fear that our child may be at particularly high risk of a recurrence of malakoplakia in the graft. Nonetheless, because of the much better quality of life that paediatric renal transplantation provides we plan to undertake this, using minimal immunosuppression, and long term cotrimoxazole.

Authors' affiliations

S Hegde, M G Coulthard, Department of Paediatric Nephrology, Royal Victoria Infirmary, Newcastle, UK

Correspondence to: Dr M G Coulthard, Department of Paediatric Nephrology, Royal Victoria Infirmary, Newcastle NE1 4LP, UK; malcolm.coulthard@nuth.northy.nhs.uk

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REFERENCES

- 1 Dobyas DC, Truong LD, Eknoyan MD. Renal malakoplakia reappraised. *Am J Kidney Dis* 1993;**22**:243–52.
- 2 Ravel R. Megalocystic interstitial nephritis: an entity probably related to malakoplakia. *Am J Clin Pathol* 1967;**47**:781–9.
- 3 Trillo A, Lorentz WB, Whitley NO. Malakoplakia of kidney simulating renal neoplasm. *Urology* 1977;**10**:472–7.
- 4 Deridder PA, Koff SA, Gikas PW, et al. Renal malakoplakia. *J Urol* 1877;**117**:428–32.
- 5 Charney EB, Witzleben C, Douglas SD, et al. Medical management of bilateral renal malakoplakia. *Arch Dis Child* 1985;**60**:254–6.
- 6 Wiggelinkhuizen J, Mills A, Emms M. Bilateral renal malakoplakia in infancy. *Child Nephrol Urol* 1988;**9**:101–5.
- 7 Saleem M, Milford DV, Raafat F, et al. Renal parenchymal malakoplakia—a case report and review of the literature. *Pediatr Nephrol* 1993;**7**:256–8.
- 8 Honjo K, Sato T, Matsuo M, et al. Renal parenchymal malakoplakia in a four-week-old infant. *Clin Nephrol* 1997;**47**:341–4.
- 9 Mederazo EG, Berlin BB, Morhardt C. Treatment of malakoplakia with trimethoprim-methoxazole. *Urology* 1979;**13**:70–3.
- 10 Biggar WD, Crawford L, Cardella C, et al. Malakoplakia and immunosuppressive therapy. Reversal of clinical and leukocyte abnormalities after withdrawal of prednisolone and azathioprine. *Am J Pathol* 1985;**119**:5–11.
- 11 Arnesen E, Halvorsen S, Skjorten F. Malakoplakia in a renal transplant. Report of a case studied by light and electron microscopy. *Scand J Urol Nephrol* 1977;**11**:93–6.