Medical management of bilateral renal malakoplakia

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Summary

Renal malakoplakia is reported in an 11 year old girl with myelomeningocele and associated neuropathic bladder. She is the first reported child to have survived bilateral renal malakoplakia with full recovery of renal function after medical management.

Malakoplakia is an unusual chronic inflammatory response primarily occurring in debilitated adults, and characterised by aggregates of macrophages containing concentric calciospheres or Michaelis-Gutmann bodies. An immunologic defect of ineffective macrophage phagocytic ability is believed to contribute to its pathogenesis. Although frequently affecting the collecting system of the urinary tract, it only rarely involves renal parenchyma. Earlier published reports 1, 2 state that unilateral renal involvement requires nephrectomy and bilateral involvement is invariably fatal. We report a child with bilateral renal malakoplakia in whom conservative medical management resulted in survival and normal renal function.

Case report

An 11 year old girl was admitted to this hospital with a five day history of fever and abdominal pain. Past medical history included myelomeningocele repair and ventriculocaudal shunt for hydrocephalus at birth with a shunt revision at age 9 years and insertion of a Brantley-Scott prostatic urethral sphincter for urinary incontinence at age 8 years. According to parental reports, the child had not complied in deactivating the sphincter regularly during the previous few months. Two years before hospital admission her intravenous pyelogram had been normal, blood urea nitrogen (BUN) was 3.9 mmol/l (10.9 mg/100 ml) and serum creatinine was 44.2 μmol/l (0.5 mg/100 ml).

Physical examination on admission showed a toxic appearing child with temperature of 38.2°C; heart rate 136/minute; respiratory rate 24/minute; blood pressure 132/80 mm Hg and bilateral flank tenderness with diffuse abdominal pain. Laboratory evaluation on admission included the following values: haemoglobin 10.1 g/dl; haematocrit 28%; white cell count 5.7×109/l with 77% segmented neutrophils; 1% eosinophils; 19% lymphocytes and 3% monocytes; and platelets 98×109/l; erythrocyte sedimentation rate 63 mm in the first hour. Serum sodium was 137 mmol/l; potassium 2.8 mmol/l; chloride 103 mmol/l; bicarbonate 16 mmol/l; BUN 23 mmol/l (61.3 mg/100 ml); and serum creatinine 256 μmol/l (2.9 mg/100 ml). Urine obtained by bladder catheterisation (800 cc) had a specific gravity of 1.010, trace protein, and numerous white blood cells.
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and red blood cells without cellular casts. Urine culture grew *Escherichia coli* (2000 colonies/ml) and several blood cultures were sterile. Initial treatment consisted of intravenous ampicillin for presumed pyelonephritis and bladder drainage with an indwelling Foley catheter.

The urine cultures became sterile during the initial 10 day course of antibiotic treatment; BUN dropped to 5.3 mmol/l (14.8 mg/100 ml) and the creatinine concentration to 88 µmol/l (1 mg/100 ml) within several days of bladder drainage. Despite this, the remainder of her 10 weeks in hospital was marked by persistence of fever (38.5 to 39.0°C). Additional diagnostic studies showed bilateral hydronephrosis on an intravenous pyelogram, bilateral vesicoureteral reflux on a voiding cystourethrogram, and diffusely increased bilateral renal uptake and enlargement on a gallium-67 citrate scan.

An open renal biopsy was performed during the ninth week in hospital, and histology showed malakoplakia (Figs. 1 and 2). She was begun on trimethoprim 160 mg/sulphamethoxazole 800 mg daily, one week after the biopsy, and within several days she became afebrile. Immunologic investiga-

Fig. 1 Light micrograph of renal biopsy showing inflammatory reaction. A few of the numerous Michaelis-Gutmann bodies are indicated by arrows. (Haematoxylin and eosin).

Fig. 2 Electron micrograph of portion of macrophage. Michaelis-Gutmann body, with central nidus of hydroxyapatite and surrounding layers of varying density, is in centre of field. Portion of nucleus is in the top right corner.
tion done six weeks after beginning this treatment including assays for monocyte bactericidal activity and superoxide anion release were normal. During seven months' follow up she has been in good health while maintaining normal renal function with BUN 3·2 mmol/l (8·9 mg/100 ml) and creatinine 61 μmol/l (0·7 mg/100 ml). She has been maintained on trimethoprim/sulfamethoxazole and a regular clean intermittent bladder catheterisation home programme throughout this time.

Discussion

Malakoplakia, first described in 1902 by Michaelis and Gutmann, grossly, consists of variably sized yellow-brown soft plaques. The term malakoplakia is, therefore, derived from the Greek words 'mala-
kos' (soft) and 'plakos' (plaque). Microscopically it is characterised by dense aggregates of large mono-
nuclear phagocytes or histocytes (von Hansemann cells) with an eosinophilic granular cytoplasm that stains positive with periodic acid Schiff reaction. These histocytes also contain the characteristic intracytoplasmic laminated basophilic calciospha-
erules, or Michaelis-Gutmann bodies. (Fig. 1). When fully developed the bodies have a characteristic electron microscopical appearance, with a central core of dense crystals, a light halo, and an outer lamellar crystal formation. (Fig. 2)

The clinical manifestations of renal malakoplakia are often initially indistinguishable from an ordinary urinary tract infection. The fever and flank pain, however, will characteristically persist, as it did in our patient, in the presence of seemingly appropriate intravenous antibiotic treatment and sterile urine cultures. The renal insufficiency of renal malakoplakia may occur in either the presence or absence of urinary tract obstruction. Our patient's initial renal insufficiency was associated with obstruction. This was apparent as her azotaemia resolved when adequate bladder drainage was accomplished through an indwelling Foley catheter. Urinary retention with poor bladder emptying was most probably secondary to the child's non-
compliance at home and at school in deactivating her artificial urethral sphincter regularly.

The pathogenesis of malakoplakia remains unknown, yet it is generally considered that the lesion is associated with a defect in the ability of macro-
phages to digest phagocytosed bacteria, particularly coliform organisms. It is the calcification of these incompletely digested organisms that are thought to produce the Michaelis-Gutmann bodies.

Investigation into the medical management of malakoplakia has recently been directed towards modifying the defective phagocytic ability of the patients macrophages. Urecholine, a cholinergic agonist, has been shown to improve E coli bactericidal activity of monocytes in an adult with rectal malakoplakia, while the intracellularly active antibiotic trimethoprim/sulphamethoxazole improved macrophage bacterial digestion in an adult with ureteral and retroperitoneal malakoplakia. In our patient, monocyte bactericidal activity was normal as determined by an in vitro bactericidal assay and monocyte superoxide production. Since she was already on trimethoprim/sulphamethoxazole treatment when the monocyte studies were performed, and has required continued treatment for urinary prophylaxis, we can only speculate that either defective bactericidal activity may not be a consistent finding in patients with malakoplakia or monocyte dysfunction was improved by the use of the intracellular active antibiotic, or both.

Recognition of renal malakoplakia as both a clinical and pathologic entity is particularly important for those physicians caring for children with neuropathic bladders, in which coliform infection may be quite common. The vast majority of the childhood population with neuropathic bladders is made up of children with myelomingocele. Through recent medical and surgical advances, more and more of these children are surviving through adolescence and into adulthood. As future cases of renal malakoplakia may be identified among these and other children, our patient serves to illustrate that surgical management may not always be necessary. It should only be considered for patients in whom renal damage is progressive in spite of medical management. This medical manage-
ment may require trials of cholinergic agonists or intracellularly active antibiotics, or both.

References

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