Malakoplakia

A case report and review of the renal manifestations and immunopathology

G. M. CARNEY, J. J. FAURE, S. K. PRICE

Summary

A case of renal malakoplakia associated with prednisone therapy is reported; clinical recovery had taken place 6 months later, after nephrectomy and cessation of corticosteroid administration.

Case report

A 25-year-old Coloured woman presented for the first time in 1968, complaining of dysphagia. Physical examination revealed a multinodular goitre and anaemia. She was normotensive and urinalysis was negative. A subtotal thyroidectomy was performed, and a histological diagnosis of Hashimoto's thyroiditis was made. The patient was given thyroxine supplements and because she had iron deficiency anaemia, attributed to 5 previous uneventful pregnancies, she was also treated with iron supplements.

She was seen again in 1978, complaining of palpitations, ankle oedema, dyspnoea on exertion, and poor appetite. She had failed to take her thyroxine supplements for 10 months. Physical examination revealed a blood pressure of 160/100 mmHg, grade II retinopathy, and an auscultatory sound thought to be a pericardial friction rub. Chest radiography revealed cardiomegaly and an echocardiogram a pericardial effusion. Urinalysis showed haematuria 3+ and proteinuria 2+. An intravenous pyelogram was normal. Urine culture produced a pure growth of Escherichia coli.

She was anaemic with a haemoglobin concentration of 7.9 g/dl and hypothyroid. The serum creatinine level was 85 µmol/l and the serum urea level 3.5 mmol/l. The serumanalysis showed haematuria 3+ and proteinuria 2+, and on microscopic examination the urine was found to contain red cells and numerous pus cells. Urine culture produced a pure growth of Escherichia coli. An intravenous pyelogram showed the right kidney to be normal; however, the left kidney was grossly enlarged, with poor definition of the collecting system. A cystogram showed gross lesions of the bladder with prominent thumbprint impressions of the urothelial lining (Fig. 1). Ultrasound examination of the left kidney demonstrated gross enlargement with cystic areas suggestive of hydronephrosis or multiple abscess formation. A left renal angiogram revealed an

haematuria. She had been taking her medications, consisting of thyroxine 0.1 mg twice a day, prednisone 60 mg/d and 2 amiloride-hydrochlorothiazide tablets twice a day.

On physical examination she was distressed, her temperature was 38°C, and she had a marked cushingoid appearance. She was clinically anaemic. Her blood pressure was 110/70 mmHg and her pulse rate 104/min; there was no evidence of cardiac failure. There was a large, tender, palpable mass in the left abdomen extending into the flank. Her haemoglobin concentration was 9.5 g/dl and her white cell count was 15 500/µl, with a neutrophilia. The serum creatinine level was 181 µmol/l and the serum urea level 13.5 mmol/l. Urinalysis showed haematuria 3+ and proteinuria 2+, and on microscopic examination the urine was found to contain red cells and numerous pus cells. Urine culture produced a pure growth of E. coli. An intravenous pyelogram showed the right kidney to be normal; however, the left kidney was grossly enlarged, with poor definition of the collecting system. A cystogram showed gross lesions of the bladder with prominent thumbprint impressions of the urothelial lining (Fig. 1). Ultrasound examination of the left kidney demonstrated gross enlargement with cystic areas suggestive of hydronephrosis or multiple abscess formation. A left renal angiogram revealed an

Departments of Nephrology and Pathology, Groote Schuur Hospital, Cape Town

G. M. CARNEY, M.B. B.S.

S. K. PRICE, M.B. CH.B., M.MED. PATH.(ANAT.), F.F. PATH. (SA.)

Department of Urology, Conradie Hospital, Cape Town

J. J. FAURE, M.B. CH.B., F.R.C.S.

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Reprint requests to: Dr S. K. Price, Dept of Pathology, UCT Medical School, Observatory, 7925 RSA.
enlarged kidney, and in the nephrogram phase there was irregularity of the kidney contour and stretching of the intrarenal arteries. There was no neovascularity, and it was concluded that the left angiogram was consistent with a hydronephrotic kidney (Fig. 2). Cystoscopy revealed a chronically inflamed bladder with a cobblestone appearance. The left ureteric orifice could not be identified. A bladder biopsy subsequently showed malakoplakia of the bladder. The patient began a course of co-trimoxazole and was transfused. The prednisone dose was decreased by 5 mg every second day to 10 mg/d, and then slowly reduced and stopped after another 2 weeks. At operation the left kidney was found to be grossly enlarged with multiple adhesions and perinephric abscess formation. It was removed and histological examination confirmed malakoplakia of the kidney. The patient had a stormy postoperative course, requiring several courses of parenteral antibiotics. A gallium scan was performed during the postoperative phase, and this showed positive areas in the left renal bed and also in the right kidney. A second exploratory and drainage procedure was performed in the left renal bed area. No active intervention was contemplated for the right kidney. Eventually the patient's pyrexia settled and she recovered.

The patient was seen again 7 months later. She had no urinary symptoms, and was well, but complained of ankle swelling. Her blood pressure was 190/105 mmHg. She had proteinuria 1+ on Dipstix urinalysis. Her serum urea level had fallen to within the normal range and her haemoglobin concentration was 13.6 g/dl. A rheumatoid factor test was positive (latex 1/320), but the antinuclear factor test was negative.

**Pathological examination**

The kidney was pale yellow in colour, weighing 1093 g and measuring 18.5 x 10 x 8 cm (Fig. 3). There were adhesions to surrounding tissue and the capsule could not be stripped. The cut surface revealed bulging confluent masses of soft pale yellow tissue, with necrotic centres resembling caseation. These masses had replaced most of the renal parenchyma. Smaller yellow plaques were present throughout a dilated caliceal system.

Light microscopy revealed a renal parenchyma largely replaced by aggregates of macrophages with eosinophilic granular cytoplasm (von Hansemann's cells) (Fig. 4). The granules varied in size and were periodic acid-Schiff (PAS)-positive and diastase-resistant. Numerous intracytoplasmic calciospherules in various stages of formation (Michaelis-Gutmann bodies) were present. The largest of these were concentrically laminated structures, which stained positively for calcium (von Kossa stain) (Fig. 5). The remaining parenchyma showed changes of chronic pyelonephritis. Many glomeruli were intact and showed no features of underlying glomerulonephritis. Electron microscopy confirmed the presence of Michaelis-Gutmann bodies (Fig. 6).

No intact bacteria were demonstrated.
Fig. 4. Renal glomerulus surrounded by granular macrophages with tubular obliteration (PAS x 100).

Fig. 5. Michaelis-Gutmann bodies (von Kossa x 400).

Fig. 6. Electron micrograph of Michaelis-Gutmann body (x 15 000).

**Discussion**

Malakoplakia was first reported in 1902 by Michaelis and Gutmann, and in 1903 by von Hansemann. It has been described in the gastro-intestinal tract, mesenteric lymph nodes and retroperitoneum, bone, lung, skin and brain; the commonest site is the bladder and lower urinary tract. E. coli is the pathogen most frequently associated with malakoplakia; however, other Gram-negative, Gram-positive and atypical mycobacteria and viral pathogens have been reported. Malakoplakia has been found at the site of benign and malignant tumours.

The patient with localized disease in the bladder usually presents with dysuria and E. coli urinary tract infection. Renal parenchymal malakoplakia is commonly associated with flank pain, fever, anaemia and a palpable renal mass. There are no characteristic radiographic findings. The intravenous pyelogram may vary from normal to complete non-visualization of the kidney, depending on the degree of obstruction or intrinsic involvement of the kidney and ureter. The renal arteriographic features are also nonspecific. Usually arteriography shows a grossly enlarged kidney with diminished renal blood flow and stretching of the renal arteries. The differential diagnosis includes pyohydronephrosis, cyst, xanthogranuloma and perinephric abscess. Two case reports described renal malakoplakia in which the arteriogram showed an avascular lesion, with neovascularity in the periphery of the lesion suggesting renal tumour. The cystoscopic findings are multiple raised yellow to brown soft plaques, giving the bladder a cobbledstone appearance with occasional ulceration. As with renal parenchymal malakoplakia, the diagnosis is made on histological examination.

The immunopathogenesis of malakoplakia has been clarified by recent studies. Terner and Lepin demonstrated that the Michaelis-Gutmann inclusion body contained glycolipid dissimilar to human polysaccharide lipid and also calcium, phosphate and iron. Electron microscopy has identified inclusion bodies in macrophages involved in malakoplakia. These have been shown to be of bacteria in various stages of degeneration in cases associated with bacterial infection. The inclusion bodies could be viral particles or cell debris in cases associated with viral infection. Lov and Teplitz suggested that the Michaelis-Gutmann body was the result of coalescent enlarged phagolysosomes around bacterial inclusions in varying stages of degeneration within the macrophage. Subsequent deposition of calcium, phosphate and iron within this structure results in the formation of the concentric lamination (calciosphere) characteristic of the lesion. The structure of the lesion suggests an impaired macrophage response to an invading organism. Many cases described in the literature have been in the clinical setting of impaired immunity, such as hypogammaglobulinaemia, cellular immunodeficiency or administration of steroids or immunosuppressives, or associated with alcoholic liver disease. Studies of cellular immunity in malakoplakia by several workers have shown some conflicting results when measuring circulating T-cell numbers and responses to mitogens, as well as chemotactic ability of monocytes. A consistent finding, however, is decreased bactericidal function of monocytes. Abdou et al. have associated this finding with decreased monocyte cyclic guanine monophosphate, resulting in impaired lysosome function and enzyme release. Administration of cholinergic agonists in vivo and in vitro corrects monocyte chemistry and function.

Prognosis in malakoplakia depends on the site of involvement. Localized disease in the bladder is recurrent but benign. Renal parenchymal disease is cured only by nephrectomy if unilateral and is fatal if bilateral. A major therapeutic problem is persistent disease and sepsis at the site of surgery in spite of seemingly appropriate antibiotic therapy. Trimethoprim-sulphamethoxazole (co-trimoxazole), which is thought to enhance intracellular killing of bacteria, has been reported successful in 1 case. In 4 cases of malakoplakia resistant to conventional antimicrobial therapy, a cure or marked improvement resulted from treatment with the cholinergic agonist, bethanechol chloride.

Our patient had a history of auto-immune thyroiditis, with positive tests for antinuclear factor and rheumatoid factor. The onset of renal parenchymal malakoplakia corresponded to the
administration of a large dose of steroid. Following nephrectomy and cessation of steroids she made a good clinical and biochemical recovery.

REFERENCES


Acute massive hydrothorax — a rare complication of peritoneal dialysis

A case report

A. R. SEEBARAN, P. L. PATEL

Summary

Acute massive hydrothorax, a rare complication of peritoneal dialysis, in a 45-year-old woman is described. It occurs at about the 24th hour of dialysis and is right-sided; the glucose content of the pleural fluid is high. There were similarities in chemical composition of the pleural and ascitic fluids. The danger of misdiagnosing this condition as a worsening of cardiac failure is pointed out and its management and pathogenesis are discussed.

During peritoneal dialysis (PD) the patient may become dyspnoeic because of exacerbation of congestive cardiac failure, pneumonia, atelectasis or purulent bronchitis. A more recently discovered and rare cause of dyspnoea is development of massive acute hydrothorax, the first case having been described in 1967. Subsequently 13 case reports have appeared in the literature. In 8 cases PD was being performed for chronic renal disease and in 5 for drug intoxication. Two cases have occurred in children. We describe a further patient who developed this complication while undergoing PD for chronic renal disease.

Case report

The patient was a 45-year-old Indian woman attending the R.K. Khan Hospital, Durban. She had been treated as an outpatient from 1971 for hypertension and recurrent urinary tract infection. Her first admission to hospital had been on 6 October 1979, at which time her blood pressure was 210/120 mmHg. Serum biochemical values at that time included: sodium 139 mm01/l, potassium 4,8 mmol/l, chloride 107 mmol/l, urea 10 mmol/l and creatinine 365 mm01/l. The creatinine clearance rate was 22 ml/min. An intravenous pyelogram showed bilateral shrunken kidneys, probably due to chronic pyelonephritis. A chest radiograph showed no pleural effusion (PE) and was normal.

The patient was readmitted to hospital on 6 February 1980 with hypertensive heart failure and uraemia. The serum biochemical values were now: sodium 134 mmol/l, potassium 6,2 mmol/l, chlorides 100 mmol/l, urea 37 mmol/l and creatinine 1 340 μmol/l. A chest radiograph showed cardiomegaly and congestion but no PE. Hypotensive drugs, a...