Not so acute renal failure with crystals in the urine

Case

A 40-year-old fire fighter presented to an emergency room because of nausea, vomiting and muscle pains in the upper arms and thighs. He had been actively engaged in his profession until the time of admission and denied prior medical illnesses. He denied specific trauma or drug abuse. He was uncertain as to the colour of his urine. Physical examination disclosed a blood pressure of 125/80 mmHg. His muscles were tender to palpation but normal in appearance. The chest was clear, the heart disclosed no murmurs, the abdominal examination was normal and there was no pedal oedema.

The haemoglobin was 13 g/dl, the haematocrit 37 vol%, the white blood cell count was 10 300 and the platelet count 181 000 μl. The serum creatinine was 1010 μmol/l and the urea was 60 mmol/l. A mild metabolic acidosis was present with an anion gap of 15 mmol/l. The serum myoglobin was 38 μmol/l and the creatine kinase (CK) was 261 μmol/l. The CK muscle brain fraction (CKMB) was not elevated. Urinalysis disclosed a positive test for blood and protein ++. Microscopically, few erythrocytes were seen. Instead, numerous hexagonal crystals were observed. A renal ultrasound examination indicated that both kidneys were at the upper limit in size without obstruction or stones. Unfortunately, the urine sediment could not be photographed. However, a low-power electron photomicrograph (×20 000) from the kidney biopsy is depicted in Figure 1, showing hexagonal crystals and needle-like structures that were not observed in the urinary sediment. Crystals were also observed within proximal tubule cells (not shown).

Questions

What is your diagnosis? What therapy would you initiate?
Answers to the quiz on the preceding page

Further questioning disclosed that the patient had felt poorly for \( \sim 1 \) month and had lost 4 kg in weight. A diagnosis of myoglobinuria was favoured by most of the nephrology team, although the CK was not as elevated as is generally observed in that condition and no-one could recall ever having seen hexagonal crystals in myoglobinuria before. Haemodialysis was performed because of the severe renal failure. A serum electrophoresis and urine immune fixation was ordered and a renal biopsy was performed. The serum electrophoresis disclosed a monoclonal gammopathy consisting of IgG immunoglobulins, while the urine immune fixation revealed \( \lambda \) chains (Bence–Jones proteinuria). Figure 2 shows a light photomicrograph (\( \times 50 \)) with Trichrome (Goldner) technique. A tubule is filled with crystalline material. Most tubules were obstructed with proteinaceous casts. Figure 3 shows an immunofluorescent photomicrograph stained with antibody directed against human \( \lambda \) light chains. The patient had multiple myeloma. He felt better with maintenance haemodialysis and was transferred to the haematology service for further care.

Discussion

Acute and chronic renal failures are common in multiple myeloma. Our patient had cast nephropathy (‘myeloma kidney’). The casts typically contain the offending light chain and Tamm–Horsfall protein. Light chains are filtered and resorbed by receptor-mediated endocytosis [1]. The process is saturable, resulting in urinary excretion of Bence–Jones proteins. Haemodynamic studies suggest that elevated intratubular pressures contribute to the decline in glomerular filtration rate. Physico-chemical factors important for light chain precipitation include the light chain concentration, the iso-electric point, acidic intraluminal pH, tubular flow rate and the presence of Tamm–Horsfall protein [2,3]. Colchicine may prevent the

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Fig. 2. Myeloma cast nephropathy with needle-shaped red stained crystals in the tubular lumen (top), and a normal glomerulus (bottom); Trichrome (Goldner) \( \times 50 \).

Fig. 3. Myeloma cast nephropathy with light chains within the tubular casts; immunofluorescence: anti-lambda \( \times 100 \).
formation of casts in this condition by influencing Tamm–Horsfall protein carbohydrate content [4]. The recent localization of a single binding site for immunoglobulin light chains on human Tamm–Horsfall protein may be important to therapeutic interventions because inhibiting the binding of light chains to Tamm–Horsfall protein should preclude development of cast nephropathy. A peptide sequence has been developed that inhibits the binding of these proteins. Interestingly, the sequence requires a cystine residue to block the aggregation of these proteins [5].

We were fascinated by the crystalluria exhibited by our patient that was readily appreciated on urinalysis and in the renal biopsy, especially with electron microscopy. The overall incidence of crystals in kidneys of patients with plasma cell dyscrasia accounts for ~6%. Crystals in large amounts are found in only 1% of cases. In cases of cast nephropathy, crystals in tubular casts and/or tubular epithelium were reported in 18 of 24 patients [6], and in eight of 12 patients with concomitant Fanconi’s syndrome [7]. Our patient presented too far advanced for us to study his acid–base disturbance further. However, renal crystal formation has generally been described in multiple myeloma patients who have the Fanconi syndrome [7]. Our patient presented too far advanced for us to study his acid–base disturbance further. However, renal crystal formation has generally been described in multiple myeloma patients who have the Fanconi syndrome [7]. Our patient presented too far advanced for us to study his acid–base disturbance further. However, renal crystal formation has generally been described in multiple myeloma patients who have the Fanconi syndrome [7]. Our patient presented too far advanced for us to study his acid–base disturbance further. However, renal crystal formation has generally been described in multiple myeloma patients who have the Fanconi syndrome [7]. Our patient presented too far advanced for us to study his acid–base disturbance further. However, renal crystal formation has generally been described in multiple myeloma patients who have the Fanconi syndrome [7]. Our patient presented too far advanced for us to study his acid–base disturbance further. However, renal crystal formation has generally been described in multiple myeloma patients who have the Fanconi syndrome [7]. Our patient presented too far advanced for us to study his acid–base disturbance further. However, renal crystal formation has generally been described in multiple myeloma patients who have the Fanconi syndrome [7]. Our patient presented too far advanced for us to study his acid–base disturbance further. However, renal crystal formation has generally been described in multiple myeloma patients who have the Fanconi syndrome [7].

The messages of our report are that a little CK and myoglobin in serum does not mean myoglobinuric renal failure. Crystals in the urine do not always indicate stone disease. Multiple myeloma with crystal formation is generally indicative of κ light chain acquired Fanconi syndrome, an unusual but important manifestation. Our λ light chain patient represents an exception in that regard.

References

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