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Multiple myeloma, severe hypercalcaemia, acute renal failure and multiple organ failure due to calcinosis

Nefrologia 2011;31(2):233-4
doi:10.3265/Nefrologia.pre2010.Nov.10668

To the Editor,

Renal failure in multiple myeloma is frequent; it is found in 20%-40% of cases at diagnosis and is an unfavourable prognostic factor. Myeloma kidney and hypercalcaemia are the most frequent causes. Other contributing factors are dehydration, hyperuricaemia, nephrotoxic drugs and iodine contrasts. Repeated episodes of hypercalcaemia can produce calcium salt deposits in tissues, especially those with an alkaline medium, such as kidneys, lungs or gastric mucosa. We present the case of a 38-year-old man, with multiple myeloma, severe hypercalcaemia, acute renal failure, metastatic calcinosis and multiple organ failure.

The patient had no pathological history, was a smoker of 40 cigarettes/day, and an alcohol consumer. He visited the emergency department with general polymyalgia, nocturia, and oedemas around the ankles for one week. For 48 hours before his visit, he had taken paracetamol every 8 hours.

In the physical examination he had mucocutaneous paleness. Blood pressure: 120/70; temperature: 37.4ºC; auscultation: normal. Abdominal palpation: no findings. Lower limbs had no oedemas.

Laboratory tests showed creatinine: 9.8mg/dl; urea: 198mg/dl; haemoglobin: 9.8g/l; potassium: 4.7mEq/l; sodium: 134mEq/l; haemoglobin: 9.6mg/dl; haematocrit: 27%; leukocytes: 15 900 with 71% neutrophils; platelets: 135 000; creatine phosphokinase (CPK): 4.62IU/l; calcium: 15mg/dl; ionic calcium: 7.71mg/dl. Sediment: proteinuria: 300mg/dl; red blood cells: 5/10/high power field (HPF); leukocytes: 0-5/HPF. The kidney ultrasound showed that the kidneys were of normal size, no hydronephrosis, and increased echogenicity. The chest X-ray was normal. Tests pointed towards acute renal failure with severe hypercalcaemia. Daily haemodialysis was started with low calcium concentrations in the solution and subcutaneous calcitonin. On the third day after admission, the patient developed acute respiratory failure and neurological deterioration. He was therefore transferred to the ICU, with suspected tumoural hypercalcaemia requiring thoracic and cranial CT scans and proteinogram. We observed bilateral alveolar infiltration, right fronto-tempo-parietal subdural haematoma with subfalcine and transtentorial herniation. The haematoma was surgically drained and the patient died 8 hours after the intervention. Monoclonal IgG kappa was detected in the proteinogram. An autopsy was carried out, diagnosing multiple myeloma kappa, affecting the bone marrow; metastatic calcification mainly in the kidneys, stomach, lungs, liver and vessels, and pulmonary haemorrhage with respiratory distress.

Hypercalcaemia is produced in patients with multiple myeloma due to the increased bone resorption caused by osteoclast activation, especially due to the hyperactivity of the RANK/RANK-L receptor. Kidney failure is produced by lesions on the renal tubular epithelium, which alters the ability to concentrate urine and sometimes causes epithelial cell necrosis and obstruction of the tubules. This can then lead to stasis and calcium deposits in the kidney. Treatment should be started quickly, ensuring the patient is hydrated and using anti-myeloma therapy, including steroids. Calcitonin inhibits bone resorption without risk of nephrotoxicity, but its hypocalcaemic effect is modest and transitory. Bisphosphonates, potent osteoclast inhibitors, are very effective for severe hypercalcaemia, but are a risk for kidney toxicity and hypocalcaemia. The most used are pamidronate, and

zoledronic acid, but the latter is not recommended when creatinine levels are above 3mg/dl. Some studies recommend using ibandronate for patients with renal failure, as it is less nephrotoxic, and some authors have even used ibandronate for patients with myeloma and renal failure caused by hypercalcaemia or nephrocalcinosis, recovering renal function and calcium levels. Haemodialysis must be started for oliguric renal failure cases. In our case, we started treatment with calcitonin and daily haemodialysis, but the patient's condition progressed rapidly, with multiple organ failure and respiratory distress due to tumoural calcinosis. In conclusion, we must highlight the need to closely monitor calcium levels in patients with multiple myeloma and start therapeutic measures early. For cases of malignant hypercalcaemia, we recommend bisphosphonates as be the most effective therapy, and for renal failure the least nephrotoxic drugs at an adjusted dosage.

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Rapidly progressive renal failure as the onset of an IgA nephropathy in an elderly patient

Nefrologia 2011;31(2):234-6
doi:10.3265/Nefrologia.pre2010.Nov.10661

To the Editor,

IgA nephropathy is the most frequent primary glomerulopathy in the world.[1,2] It is often presented as macroscopic haematuria (generally preceded by a respiratory infection in the upper airways, especially in children), and persistent microhaematuria with mild proteinuria. Nephrotic syndrome and acute renal failure are the least common manifestations. We describe the case of an elderly patient that was diagnosed with IgA nephropathy, as a result of rapidly progressive renal failure (RPRF).

The patient was a 78-year-old man with a history of prostate carcinoma, treated with brachytherapy and radiotherapy check-ups every 6 months; carpal tunnel syndrome; right hip operation; and no known drug allergies.

His doctor had referred him to the emergency department due to tiredness and pain in his lower limbs. The patient's medical records indicated that he had suffered from nocturia on two occasions. The physical examination performed upon admission indicated that the patient's general condition was fair. He was conscious and aware of his surroundings. He did not have jugular ingurgitation. Blood pressure was 135/85mm Hg, heart rate was 82 beats/min and $SatO_2$: 92%. The heart auscultation was rhythmic and pulmonary auscultation presented hypoventilation with isolated wheezing. The rest of the examination was normal.

The blood analysis (emergency department) was: creatinine: 2.9mg/dl (previous creatinine: 1.2mg/dl); potassium: 5.3mEq/l; haemoglobin: 11.5g/dl; haematocrit: 34.7%; remaining analyses, including venous gasometry and the coagulation test, were normal.

Systematic urine analysis showed: protein +++, blood ++. The sediment test showed haematuria, with isolated hyaline casts.

Chest X-ray and abdominal ultrasound did not show any pathological findings, the kidneys were of normal size, and the excretory tract was not dilated.

The subsequent blood analysis (common) showed: creatinine: 3.9mg/dl; urea: 181mg/dl; albumin: 2.7g/dl; total protein: 5g/dl; calcium: 6.9mg/dl; phosphorus: 8.1mg/dl; uric acid: 8.3mg/dl; sodium: 132mEq/l. 24-hour urine test found microalbuminuria, which was 620μg/min (normal range: 0-15μg/min). Other supplementary tests performed were normal (including viral serology, blood culture, tumour markers and thyroid hormones). The immunological test only showed a decrease in IgG of 574mg/dl (normal value: 751-1560) and an increase in C-reactive protein to 8.7mg/dl. No monoclonal peak was detected on the electropherogram.

The patient had been admitted to the internal medicine department, where progressive deterioration of the renal failure and oligoanuria were confirmed. Renal replacement therapy with haemodialysis was started. Given the rapidly progressive acute renal failure, a kidney biopsy was performed, finding the following: 12 glomeruli per cross-section, none of which was sclerotic.