Nephrology Dialysis Transplantation

Nephroquiz for the Beginner
(Section Editor: M. G. Zeier)

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**Hypercalcaemia and acute renal failure**

A 60-year-old man was admitted to the medical ward with a 1-week history of recurrent falls, increasing confusion, and lower abdominal pain. He was treated with antibiotics for a culture-proven urinary-tract infection. His past medical history was unremarkable apart from episodes of severe dyspepsia for 20 years for which he was taking regular antacids.

On admission the patient was confused and hypertensive, with a blood pressure of 195/107 mmHg; he had no evidence of fluid overload. Systemic examination was unremarkable and there was no neurological deficit. Investigations revealed acute renal failure with a creatinine of 929 μmol/l, urea of 31 mmol/l, and corrected calcium of 3.47 mmol/l. Full blood count revealed a haemoglobin of 11.8 g/dl, white cell count of 14.4 × 10⁹/l, and an erythrocyte sedimentation rate of 107 mm at 1 h. Urinalysis showed microscopic haematuria and proteinuria with the presence of leukocytes and nitrates. Immunological investigations including autoantibodies, immunoglobulins, complement, and serum protein electrophoresis were normal. His creatinine kinase was 419 IU/l and his thyroid function tests were normal. An abdominal ultrasound showed normal sized kidneys. His serum parathyroid hormone levels were 2.9 nmol/l. A skeletal survey did not reveal any lytic lesions.

**Questions**

What additional questions would you ask?
What is your diagnosis?
What further investigations would be helpful?
What treatment would you give?
Answer to the quiz on preceding page

The patient was taking 12–60 tablets of antacids Rennine® (antacid containing calcium and magnesium) a week.

In view of his history of antacid abuse and the unexplained hypercalcaemia, a diagnosis of milk–alkali syndrome was made.

Renal biopsy (Figure 1) showed focal tubular calcification with an attendant epithelial reaction and mild acute tubular necrosis consistent with damage caused by hypercalcaemia.

He was treated with two sessions of haemodialysis. With hydration and withdrawal of the alkali and calcium, his renal function improved dramatically, and his calcium levels normalized. He currently has a creatinine clearance of 62 ml/min and serum creatinine improved from 900 \( \mu \text{mol/l} \) to 164 \( \mu \text{mol/l} \). His blood pressure returned to 125/80 mmHg without any anti-hypertensive treatment.

Discussion

First identified in 1923, the milk–alkali syndrome has become rare since the introduction of \( \beta \)-blockers for the treatment of dyspeptic disease. However, there is a growing popularity of proprietary forms of calcium carbonate, which are being marketed as antacids or as calcium supplements for the prevention of osteoporosis. A resurgence of this syndrome is now being seen. It is therefore crucial to recognize the manifestations of this disorder since the sequelae are potentially reversible in the early stages.

The milk–alkali syndrome is classically characterized by hypercalcaemia, systemic alkalosis, and renal insufficiency. This triad was first described by Cope in 1936 [1]. Three clinical presentations have been recognized [2]. An acute form (toxaemia) described first by Hardt and Rivers [3] develops within 2–30 days after calcium and alkali ingestion, and is characterized by symptoms of hypercalcaemia, alkalosis, and acute renal insufficiency. On withdrawing milk and alkali, there is a rapid relief of symptoms and reversal of biochemical abnormalities. The subacute or intermediate form (also called Cope’s syndrome) is usually seen with therapy with milk and alkali taken intermittently for years [1]. The affected patients have symptoms similar to those in the acute syndrome with additional evidence of soft-tissue calcification. There is gradual improvement on withdrawal of calcium and alkali; however, renal function remains mildly impaired in most patients. Our patient belonged to the subacute group and is making gradual recovery.

In the chronic form (also called Burnett’s syndrome), there is a longer history of calcium and alkali consumption and patients present with signs and symptoms of chronic hypercalcaemia including soft-tissue calcification [4]. The renal failure is more advanced and associated with hyperphosphataemia. Cessation of calcium and alkali ingestion results in gradual recovery from hypercalcaemia. However, renal damage is frequently irreversible. Thus the prognosis is initially favourable but as the chronicity of calcium and alkali ingestion increases, the chances of irreversible renal disease and soft tissue calcification also increase. The pathophysiology of milk alkali syndrome is complex [5–7].

In conclusion, the milk–alkali syndrome is a potentially reversible form of renal failure especially in the early stages and it should be suspected in patients presenting with hypercalcaemia, renal failure, and alkalosis. The diagnosis can be missed if a history of calcium and alkali ingestion is not obtained. When prescribing calcium supplements, physicians should be aware of this syndrome and should educate their patients about the dangerous effects of excessive calcium intake.

References


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Fig. 1. Renal biopsy (H&E × 480). Flattened tubules in keeping with acute tubular necrosis (bottom). Granular calcified material (arrows) in tubules.