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Calcium phosphate stones during long-term acetazolamide treatment for epilepsy

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Summary

We report a case of recurrent renal calculi containing calcium phosphate associated with long-term acetazolamide treatment for epilepsy. Unfortunately, the cause of stone formation was not recognised for many years, by which time irreversible renal damage had occurred.

Keywords: calcium phosphate renal calculi; renal failure; acetazolamide; adverse drug reaction

Patients with recurrent renal calculi may experience serious morbidity. It is important that such patients are adequately assessed in an attempt to identify an underlying cause. This is especially important if preliminary investigations produce unusual results.

Stones composed predominantly of calcium phosphate are uncommon; they accounted for 9.3% of 41 000 stones of renal origin in 11 series from five countries.¹ The majority of patients who form calcium phosphate stones have renal tubular acidosis.²

We report a patient with recurrent calcium-phosphate-containing renal calculi in whom the cause of stone formation was not recognised for a considerable time, despite regular specialist urological review.

Case report

A 32-year-old man was admitted for percutaneous nephrolithotomy (PCNL). He had required four previous PCNLs and numerous extracorporeal shock wave lithotripsy treatments and ureteroscopies since first passing a stone 11 years previously. Stone analysis performed seven years previously had shown calcium phosphate, but this had not been investigated further. The kidneys, initially anatomically normal, were now both scarred, with a small, poorly functioning left kidney (figure 1) and recurrent staghorn on the right (figure 2). Serum creatinine had been abnormal on occasions, probably reflecting episodes of partial obstruction.

Figure 1 DMSA scan showing markedly reduced uptake and scarring on the left

Figure 2 Plain abdominal radiograph showing large staghorn calculus on the right

He had been treated for epilepsy since the age of 11, initially with conventional anticonvulsants and then with the addition of acetazolamide for recurrent seizures. Current medication was acetazolamide 500 mg bid and carbamazepine 600 mg mane, 400 mg nocte.

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Accepted 4 January 1999

Repeat stone analysis on this occasion confirmed pure calcium phosphate. Urine pH was 6.0 with a concurrent venous bicarbonate of 22 mmol/l; serum creatinine and calcium were normal; 24-h urinary calcium excretion was 7.5 mmol and 24-h urinary citrate excretion was low at 72 μ mol/day using an enzymatic assay (hypocitraturia normally being defined as < 1.76 mmol/day).

Discussion

The carbonic anhydrase inhibitor acetazolamide is used in the treatment of glaucoma and, less commonly, in refractory childhood epilepsy.³ It has been known for many years to cause renal calculi,⁴ which are frequently calcium phosphate,⁵ and is used to induce stone formation in experimental animals. The mechanisms include induction of partial renal tubular acidosis with resultant hypercalciuria and hypocitraturia,^{6,7} both recognised risk factors for stone formation.^{8,9} Ordinarily, urinary citrate forms a soluble complex with calcium,

Summary points

- it is important to be aware of and exclude reversible causes of renal calculi
- the presence of calcium phosphate renal calculi should alert the clinician to the possibility of an unusual underlying cause
- acetazolamide causes renal tubular acidosis which can result in calcium phosphate calculi

thereby reducing available ionised calcium, which could otherwise precipitate as an insoluble salt. Hypocitraturia and alkaline urine increase calcium phosphate supersaturation.¹⁰

Calcium phosphate stones are uncommon; renal tubular acidosis is a recognised risk factor for this type of stone.² The occurrence of such stones, therefore, merits early investigation. There is a high probability that this patient's recurrent calcium phosphate nephrolithiasis was caused by acetazolamide. Earlier recognition of this might have enabled irreversible renal damage to be avoided.

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