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Transient hypercalcaemia following acute renal failure

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Summary

Two patients with transient hypercalcaemia during recovery from acute renal failure are described. The literature is reviewed and possible pathophysiological mechanisms discussed. Patients with renal failure following muscle damage should have regular measurement of plasma calcium.

Introduction

Hypercalcaemia is well recognized in untreated chronic renal failure and following haemodialysis and renal transplantation. The subject has been reviewed by Goldsmith, Johnson and Arnaud (1974) but hypercalcaemia in acute renal failure was not mentioned. Transient hypercalcaemia following acute renal failure was first described by Tavill *et al.* (1964) and since then there have been further reports (Butikofer and Molleyres, 1968; De Morgan and Waterhouse, 1968; Gossman and Lange, 1968; Segal, Miller and Moses, 1968; Turkington *et al.*, 1968; Leonard and Eichner, 1970; Leonard and Nelms, 1970; Grunfeld *et al.*, 1972; Wu *et al.*, 1972; Wilson *et al.*, 1973; Grossman *et al.*, 1974; Lynn, 1975). The highest plasma calcium recorded is 17.2 mg% (4.3 mmol/l) by Gossman and Lange (1968) and the longest period of hypercalcaemia was 25 days (Turkington *et al.*, 1968). There is a striking association with muscle damage, seventeen of the nineteen patients previously described having skeletal muscle damage of some type before renal failure. In the two remaining cases (Turkington, *et al.*, 1968) no cause for renal failure was identified.

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In fourteen cases, hypercalcaemia occurred during the diuretic phase.

Case 1

A 23-year-old male chronic schizophrenic took an overdose of trifluoperazine and had two grand-mal seizures before admission to another hospital. The following day he had apparently recovered and the blood urea was 8.3 mmol/l. Twelve days later he presented with abdominal pain and vomiting, and was found to have generalized oedema. The urine contained a trace of protein and numerous red cells. The haemoglobin was 14.0 g/dl; plasma urea 94.6 mmol/l; creatinine 2334 mmol/l; sodium 121 mmol/l; potassium 7.4 mmol/l; bicarbonate 13 mmol/l; calcium 1.67 mmol/l; phosphate 3.38 mmol/l; alkaline phosphatase 5 KAU; total proteins 66 g/l; albumin 31 g/l. Peritoneal dialysis was undertaken for 3 days. Renal function rapidly improved, the lowest daily urine output being 0.8 l. An intravenous urogram on the fifth day was normal. On the seventh day, the plasma calcium was 2.95 mmol/l and phosphate 1.90 mmol/l. By the ninth day the calcium was 3.85 mmol/l and phosphate 1.92 mmol/l. Sodium cellulose phosphate (20 g daily) was given orally for 3 days to reduce calcium absorption. The plasma calcium fell steadily to 2.62 mmol/l, phosphate 0.68 mmol/l and alkaline phosphatase 11 KAU, on the fifteenth day. On the sixteenth day, plasma parathyroid hormone (PTH) was <0.1 µg/l [normal range, up to 0.73 µg/l. The assay is insensitive for low and normal levels]. He had no corneal calcification. At 6 weeks all biochemistry was normal.

Case 2

A 31-year-old male drug addict developed severe pain in the right leg after injecting a solution of methylphenidate tablets into the right femoral artery. On admission 3 weeks later he complained of painful swelling of the right leg and vomiting. He was dehydrated and had a swollen, hot, tender right thigh, and a right foot drop. Urinalysis was normal and no myoglobin was detected. The haemoglobin was 11.5 g/dl; plasma urea 50.8 mmol/l; creatinine 2.50 mmol/l; sodium 130 mmol/l; potassium 3.9 mmol/l; bicarbonate 19 mmol/l; calcium 2.50 mmol/l; phosphate 2.55 mmol/l; total proteins 75 g/l; albumin 31 g/l; alkaline phosphatase 7 KAu. X-ray of the right thigh showed extensive linear calcification in all muscles. The patient improved rapidly with conservative treatment and was never oliguric. On the twelfth day the plasma calcium was 3.32 mmol/l; phosphate 1.49 mmol/l; alkaline phosphatase 13 KAu. By the nineteenth day the plasma calcium was normal but the alkaline phosphatase had risen to 28 KAu; plasma PTH was $<0.1 \mu\text{g/l}$. Considerable resolution of soft tissue calcification had occurred. At 6 weeks all biochemistry was normal.

Discussion

The cause of renal failure in case 1 is uncertain. The overdose must have played some part, but hypotension was not recorded. The convulsions are of interest as one of the patients with McArdle's syndrome reported by Grunfeld *et al.* (1972) developed myoglobinuria and renal failure following a grand-mal seizure. Renal failure in case 2 probably followed rhabdomyolysis, although myoglobinuria was not detected at presentation.

The cause of hypercalcaemia in these patients is not fully understood but probably results from the fortuitous association of several factors. The association with muscle damage, which is almost absolute, suggests a causal relationship. Grossman *et al.* (1974) postulated that muscle damage results in an endogenous phosphate load predisposing to tissue deposition of calcium phosphate. When the plasma phosphate falls during the diuretic phase this tissue calcium phosphate might be mobilized. In case 1 the plasma phosphate fell from 3.4 mmol/l to 1.92 mmol/l while the plasma calcium was rising. In case 2 and in those reported by Butikofer and Molleyres (1968) and Gossman and Lange (1968), hypercalcaemia coincided with radiological resolution of soft tissue calcification.

There is good evidence for hyperparathyroidism in acute renal failure in humans (Kovithavongs, Becker and Ing, 1972) and in dogs with experimentally induced renal failure (Bergdahl and Boquist, 1973). Plasma PTH levels in the two patients were measured late and were normal, but inappropriate

elevation with respect to plasma calcium was found in the patients described by Leonard and Eichner (1970) and Wu *et al.* (1972).

A further factor might be rapid and inappropriate increase in renal synthesis of 1,25-dihydroxycholecalciferol, the active vitamin D metabolite, as the kidneys recover.

Serial assessment of calcium and phosphate balance, PTH levels, and vitamin D metabolism are required to elucidate the pathogenesis of this condition. It is important to recognize the phenomenon as it may be associated with confusion, lethargy, weakness, vomiting, constipation, conjunctival irritation with calcium deposition, and cardiac dysrhythmias. Patients with renal failure following muscle damage should, therefore, have regular measurement of plasma calcium. Parathyroid surgery is clearly inappropriate as hypercalcaemia is always transient and can be controlled medically.

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Acute renal failure and hypoglycaemia due to sulphadiazine poisoning

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Summary

A 3-year-old girl is described who became oliguric and hypoglycaemic whilst receiving an excessive dose of sulphadiazine. The mechanism of the hypoglycaemia is discussed.

Introduction

Acute renal failure due to sulphonamide administration is now uncommon. This report describes a patient who became oliguric and hypoglycaemic whilst receiving treatment with an excessively high dose of sulphadiazine for meningococcal septicaemia.

Case report

A 3-year-old girl weighing 13 kg was admitted to another hospital, having been generally unwell for 12 hr, and then became comatose and developed a purpuric rash. Meningococcal septicaemia was subsequently proved when the organism was grown from the blood, but not from the cerebrospinal fluid. She was treated with i.v. fluids, hydrocortisone, penicillin and sulphadiazine (450 mg/kg body-weight/24 hr). Her condition improved over the next 48 hr and the dose of sulphadiazine was reduced

to 300 mg/kg/24 hr. Urine output, having been normal, was noted to be much less on days 4 and 5 and because of the appearance of haematuria, the sulphadiazine was stopped. The blood urea was 12 mmol/l but the following day rose to 30 mmol/l and she was transferred to this hospital for further management. On admission she was found to be oedematous and semi-conscious. The blood urea was 30 mmol/l, the sugar less than 1 mmol/l, plasma insulin 22 mu./ml, plasma cortisol 800 nmol/l and the blood sulphonamide 700 mg/l (therapeutic level 120 mg/l). Urine examination showed red cells and typical sulphadiazine crystals. She did not regain consciousness after infusion of 10 g of glucose. Peritoneal dialysis was commenced and her clinical condition slowly improved, the blood urea, glucose and sulphonamide levels reverting to normal as in Fig. 1. However, her urine output did not improve and cystoscopy revealed aggregations of sulphonamide deposits around both ureteric orifices. Bilateral ureteric catheters were inserted and a 2.5% sodium bicarbonate solution was infused at the rate of 2.5 ml/hr in each renal pelvis. Shortly afterwards, she began to pass large volumes of urine, the catheters were removed and she continued with an uneventful convalescence from her illness. At follow-up 2 months later she was physically and mentally normal, a ⁵¹Cr-EDTA clearance was 120 ml/min/1.73 m² and i.v. pyelogram was normal.

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