Hyperkalaemic quadriparesis secondary to chronic diclofenac treatment

P Patel, B Mandal, M W Greenway

Abstract

A 76 year old woman presented with a quadriparesis associated with hyperkalaemia. She had a 10 month history of treatment with oral diclofenac sodium. On admission she had hyperkalaemic metabolic acidosis with a normal anion gap and mild renal impairment. Her weakness resolved after withdrawal of diclofenac and medical correction of her hyperkalaemia. Non-steroidal anti-inflammatory drugs are known to cause hyperkalaemic acidosis and should be used with caution, especially in the presence of renal impairment.

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Case report

A 76 year old woman with a known history of gouty arthritis had been treated for 10 months with diclofenac sodium, 100 mg/day. She presented with a one day history of acute onset of generalised weakness of all four limbs, being unable to get out of bed. She had a previous history of hypertension with mild renal impairment, hypothyroidism, gout, bilateral hip replacements for osteoarthritis, and carcinoma of the breast with mastectomy four years previously. Her other drugs included allopurinol, omeprazole, nifedipine, tamoxifen, and thyroxine.

On examination at admission, her Glasgow coma scale score was 15/15. Her pulse rate was 70 beats/min, blood pressure 140/65 mm Hg, and respiratory rate 18 breaths/min. She had grade 3/5 power in all four limbs, decreased tone, and depressed deep tendon reflexes. Her plantar responses were equivocal. Examination of the cranial nerves, sensory system, and cerebellar function was normal. There was no evidence of recurrence of breast carcinoma, and the remainder of the examination was within normal limits.

Investigations on admission were as follows: urinalysis, pH 6, otherwise normal; serum potassium 6.9 mmol/l (on duplicate samples); sodium 137 mmol/l; bicarbonate 14 mmol/l; urea 18.9 mmol/l; creatinine 195 µmol/l; anion

gap $[(Na^+ + K^+) - (HCO_3^- + Cl^-)] = 14.3$ (normal 10 to 18); and arterial blood gases in room air: pH 7.42; PCO_2 3.4 kPa; base excess -7 mmol/l; actual bicarbonate 16 mmol/l; PO_2 21.7 kPa. Creatinine clearance was 20 ml/min; 24 hour urinary sodium excretion was 53 mmol (normal 135 to 256) and 24 hour urinary potassium excretion was 26 mmol (normal 35 to 90).

Her corrected serum calcium, magnesium, immunoglobulin electrophoresis, liver function test, thyroid function tests, and glucose levels were all normal.

An ECG and a chest x ray were normal. A plain abdominal x ray revealed a left renal calculus, but an abdominal ultrasound scan showed no evidence of obstructive uropathy and the kidneys were of normal size. Computed tomography of the brain performed on day 3 showed no evidence of parenchymal infarction or haemorrhage.

Diclofenac sodium was discontinued and the hyperkalaemia was urgently treated with dextrose, insulin, and intravenous calcium gluconate. Oral calcium resonium and sodium bicarbonate were started. Her weakness improved as the potassium level decreased with treatment. Table 1 shows her biochemical profile before admission and serial profiles as an inpatient. Calcium resonium was discontinued later and she was discharged on day 8.

Discussion

Our patient had hyperkalaemia, decreased urinary potassium, and a compensated metabolic acidosis. It is difficult to explain the hyperkalaemia on the basis of mild renal impairment, as the creatinine clearance was 20 ml/min, she was not oliguric, and the anion gap was normal.

She had been taking diclofenac sodium for 10 months. Non-steroidal anti-inflammatory drugs can cause hyperkalaemia by producing a syndrome of hyporeninaemic hypoaldosteronism (hyperkalaemia and metabolic acidosis)^{1,2} and inhibiting renin release.³

Neurological features of hyperkalaemia are unusual because cardiotoxicity from hyperkalaemia usually precludes their appearance. In a minority, hyperkalaemia may produce flaccid generalised or focal muscle weakness, rarely

Department of Health
Care of the Elderly,
Glan Clwyd Hospital,
Bodelwyddan, Rhyl,
Denbighshire
LL18 5UJ, UK
P Patel
B Mandal
M W Greenway

Correspondence to:
Dr Patel

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Table 1 Serial biochemical investigations

	10 Months before	3 Months before	Admission	Day 2	Day 2	Day 3	Day 4	Day 6	Day 7	Day 10
K ⁺ (mmol/l)	5.2	4.7	6.9	6.5	5.5	6.4	5.3	5.3	5.3	3.8
Na ⁺ (mmol/l)	138	138	137	133	137	134	130	131	131	128
HCO ₃ ⁻ (mmol/l)	22		14		14			20		19
Cl ⁻ (mmol/l)			102						102	
Urea (mmol/l)	7.4	9.3	18.9	15.6	17.4	13.7	7.8	9.6	11.9	10.3
Creatinine (µmol/l)	133	161	195	176	193	167	142	144	140	147

Abnormal values in bold type.

Learning points

- Secondary hyperkalaemic paralysis is a rare condition of the elderly.
- It can be caused by commonly used drugs.
- Drugs usually involved are β blockers, heparin, ACE inhibitors, potassium sparing diuretics, trimethoprim, pentamidine, cyclosporin A, and non-steroidal anti-inflammatory drugs.
- It may be caused by a partial defect in sodium channels in the cell membranes of muscle cells.
- It usually has a good long term prognosis with treatment.

involving the respiratory muscles, without affecting the cranial nerves. Sensory changes are usually absent.⁴

Patients with hyperkalaemic periodic paralysis have a genetically determined partial or complete defect in the sodium channels of the membranes of muscle fibres. High serum potassium concentrations lead to inexcitability of muscle fibres and paralysis. These episodes are short lasting and rapidly reversible with treatment.² Primary hyperkalaemic periodic paralysis usually presents in the first or second decade of life and is rare in elderly people. However, secondary hyperkalaemic paralysis has been described in the elderly.^{3 4} A search of published reports and inquiries with the Committee for Safety of Medicines (CSM) revealed

no reported cases of hyperkalaemic paralysis associated with diclofenac sodium treatment. The adverse reaction described here has now been reported to the CSM. Drugs known to cause hyperkalaemic acidosis^{5 6} are β blockers, heparin, angiotensin converting enzyme inhibitors, potassium sparing diuretics,¹ pentamidine,⁷ trimethoprim,⁸ and cyclosporin A.

Hyperkalaemic paralysis should be treated as a medical emergency, with the drug responsible withdrawn and the serum potassium reduced by conventional treatment. The paralysis recovers rapidly with treatment.^{2 4}

Hyperkalaemic paralysis secondary to non-steroidal anti-inflammatory drugs is a rare complication in elderly patients. With early recognition and appropriate treatment long term prognosis is good.^{1 3}

- 1 Rado JP. Successful treatment of hyperkalaemic quadriplegia associated with spironolactone. *Int J Clin Pharmacol Ther Toxicol* 1988;267:339–45.
- 2 Goldszer RC, Coodley EL, Rosner MJ, et al. Hyperkalemia associated with indomethacin. *Arch Intern Med* 1981;141:802–4.
- 3 Michelis MF. Hyperkalaemia in the elderly. *Am J Kidney Dis* 1990;16:296–9.
- 4 Gledhill RF. Secondary hyperkalaemic paralysis. *J Neurol Neurosurg Psychiatry* 1998;65:614.
- 5 Perazella MA, Mahnensmith RL. Hyperkalaemia in the elderly: drugs exacerbate impaired potassium homeostasis. *J Gen Intern Med* 1997;12:646–56.
- 6 DuBose TD. Hyperkalaemic metabolic acidosis. *Am J Kidney Dis* 1999;33:XLV–XLVIII.
- 7 Kleiman TR, Roberts C, Ling BN. A mechanism for pentamidine-induced hyperkalemia: inhibition of distal nephron sodium transport. *Ann Intern Med* 1995;122:103–6.
- 8 Perazella MA. Trimethoprim is a potassium-sparing diuretic like amiloride and causes hyperkalemia in high-risk patients. *Am J Ther* 1997;4:343–8.