Hypokalaemic periodic paralysis in a thyrotoxic Polynesian

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Summary: Hypokalaemic periodic paralysis in a thyrotoxic Polynesian is described. The possible pathophysiology is discussed. Though common in Orientals, this condition is uncommon in Caucasians and has not been described before in a Polynesian.

Introduction

A 25 year old man, of half Maori and half English ancestry, presented with hypokalaemia and a hypotonic quadriplegia which responded rapidly to potassium supplements. Hyperthyroid periodic paralysis has not been previously described in a Polynesian to my knowledge.

Case report

A 25 year old man of half Maori and half English extraction developed a sore throat and 2 weeks later was found to have hyperthyroidism. He complained of 21 kg weight loss, increased bowel frequency, tremor, jitteriness, lower limb and back pain with periodic weakness every few days preventing him standing.

On examination he was restless, tremulous, with a pulse of 92, slight proximal weakness of his legs and a small goitre. There was no familial thyroid or muscle disease. His free thyroxine (T₄) was 53 pmol/l (10–26), free tri-iodothyronine 19.3 pmol/l (2.2–6.8), and TSH less than 0.1 mU/l (0.4–4). Plasma potassium was 4.9 mmol/l (3.6–5.2). Anti-thyroglobulin antibody was positive at 1 in 400 and anti-microsomal antibody negative.

A technetium scan showed a diffusely increased thyroid uptake without defect. He was prescribed carbimazole 45 mg/day and metoprolol 100 mg daily but he took only 15 mg of carbimazole. He had some muscle tightness and slight weakness, then after 2 months was admitted with a hypotonic quadriplegia appearing at 4 a.m. on the day of admission when he awoke and was too weak to get out of bed. He had been for a run and fallen from his bicycle the previous day.

Examined on admission he was alert with an

impassive face and marked symmetrical weakness and hypotonia. He was unable to sit up and leg and shoulder power was 1/5 and elbow 2/5, wrist flexion 2/5, extension 4/5 and had grip was 3/5. He had a small goitre, pulse 100/minute, no tremor or lid lag, reflexes depressed but present, normal sensation and a peak expiratory flow rate (PEFR) 280 l/minute (predicted 620 l/min). Guillain–Barré syndrome was suspected but his initial potassium was 2.2 mmol/l and hyperthyroid periodic paralysis was diagnosed. His sodium was 146 mmol/l (136–147), and arterial blood gas analysis showed pH 7.32 (7.35–7.45), PCO₂ 38 mmHg (35–45), PO₂ 100 mmHg (80–100), bicarbonate 20 mmol/l (20–30). His electrocardiogram (ECG) showed hypokalaemic changes with PR interval 0.24 seconds, T-wave flattening and prominent U waves. His free T₄ was 32.4 pmol/l, free T₃ 13.5 pmol/l and TSH 0.05 mU/l. He was given 36 mmol of potassium orally and 40 mmol intravenously in one litre of normal saline over an hour and 20 mmol likewise in the second hour. After 2 hours his potassium was 4.6 mmol/l, PEFR 500 l/minute, ECG improved and strength, facial expressiveness and reflexes had improved considerably. Strength, potassium, PEFR and ECG were normal the following day and remained so.

Two days later he was discharged on carbimazole and potassium supplements. Subsequently he had occasional moderate weakness after large meals but no documented hypokalaemia. He received 20 mCi of radioactive iodine and later became hypothyroid requiring thyroxine replacement. Weakness has not occurred in 2 years of follow-up.

Discussion

Thyrotoxic periodic paralysis with hypokalaemia occurs in 13–24% of Oriental thyrotoxics⁶ but is

uncommon in other races. In a series of 10 cases drawn from 8,972 hyperthyroid patients accumulated over 20 years² (an incidence of 0.1–0.2%), eight were white, one Filipino and one Hispanic. It has not previously been described in a Polynesian. In Orientals it is 70 times commoner in males than females⁶ and usually occurs under 40 years of age. The hyperthyroidism may be mild and is most commonly associated with Grave's disease, but it has also been described in nodular hyperthyroidism.² The syndrome is indistinguishable from idiopathic hypokalaemic periodic paralysis except by the response to low dose intra-arterial adrenaline² which causes no change in the amplitude of compound muscle action potentials in normal or hyperthyroid subjects, but a decrease in these in primary hypokalaemic periodic paralysis.

Our case involved, as is typical, myalgia and weakness in lower more than upper, and central more than peripheral muscles. The muscle weakness may be asymmetrical and usually resolves within 1–36 hours¹ with residual weakness and myalgia sometimes lasting for several days. Mental function and sensation are normal, and ocular and bulbar muscles are rarely involved. Arrhythmias due to hypokalaemia may occur but cardiac arrest is uncommon.⁴ Onset during sleep is common, particularly after exercise or a large carbohydrate intake^{1–3} and exercise may abort an incipient attack.⁵ Glucocorticoid therapy may provoke it, as in the treatment of Grave's ophthalmopathy, connective tissue disease or transplant immunosuppression. Caution in the treatment of Orientals with high-dose steroids is recommended, as potentially fatal hypokalaemia and paralysis may be provoked.^{3,5}

The pathophysiology appears to be a sudden influx of potassium into muscle, caused by increased numbers and activity of sodium–potassium pumps in skeletal muscle,⁶ lymphocytes and platelets,⁶ but not erythrocytes,⁷ in thyrotoxicosis, and

to a greater degree in those with hypokalaemic paralysis. The changes reverse on return to the euthyroid state. Pump-independent potassium influx also seems to be increased.⁶ Rubidium, which is handled like potassium, disappears from plasma more rapidly in thyrotoxicosis, presumably into muscle, and even more rapidly in those with periodic paralysis.⁶ Exercise promotes potassium release from muscle and may thus abort attacks.³ Conversely it also increases insulin and adrenaline plasma levels causing potassium influx, and this may be the mechanism of paralysis during sleep after exercise. Potassium influx may be amplified by the brisk insulin response to a carbohydrate load,² and perhaps other endogenous substances as yet unrecognized, may have a similar action. The mineralocorticoid action of glucocorticoids may accentuate potassium loss,⁵ though it is assumed that total body potassium is not reduced, and there is no increase in urinary or faecal loss during an attack.¹

Treatment requires cardiac, respiratory and electrolyte monitoring, and potassium supplementation with an average dose for treating an attack suggested as 130 mmol, though our patient had largely resolved with 90 mmol over 2 hours. Hyperkalaemia may occur⁴ with large doses of potassium in the absence of net loss, and perhaps aggravated by potassium influx, from muscle. Further attacks of thyrotoxic periodic paralysis can be prevented by beta blockade,^{3,6} anti-thyroid drugs, avoidance of strenuous exercise and carbohydrate loading, and radioactive iodine therapy. Subsequent potassium supplements as given in our case may be unnecessary.

Acknowledgement

I should like to thank Pauline Robertson for secretarial assistance.

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