CLINICAL REPORTS

Extreme metabolic alkalosis with fludrocortisone therapy

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Summary

We present an unusual case of extreme metabolic alkalosis resulting from severe hypokalaemia caused by unmonitored fludrocortisone therapy. Biochemical aspects of the disorder are discussed, as is the successful treatment with diuretics and potassium replacement. Some dangers of this therapy and necessary precautions are emphasized.

KEY WORDS: metabolic alkalosis, hypokalaemia, hypercapnia, fludrocortisone, postural hypotension.

Introduction

Severe metabolic alkalosis is encountered in clinical practice usually as a result of loss of hydrogen ions as in prolonged vomiting and less often secondary to hypokalaemia. The former, where symptoms precede the metabolic upset, is usually recognized early and is rarely life-threatening. The case here reported is an example of the latter where insidious onset of hypokalaemia resulted in a near fatal degree of metabolic upset.

Case report

A woman, aged 71 years, was admitted with a 7-day history of increasing peripheral oedema. Anuria had been present for 36 hr. History revealed that postural hypotension had been treated with fludrocortisone, 0.2 mg daily, for 1 year.

Clinically, she was semi-conscious with a pulse rate of 64 per min, respiratory rate of only 10 per min and blood pressure of 110/80 mmHg. Jugular venous pulse was markedly elevated and there was gross

peripheral and sacral oedema. Fine inspiratory basal crackles were heard. Otherwise, examination was unremarkable.

Blood biochemistry gave the following results: sodium 145 mmol/litre, bicarbonate 39 mmol/litre, chloride 88 mmol/litre, potassium 1.9 mmol/litre, urea 7.4 mmol/litre, glucose 6.6 mmol/litre, P_{aO_2} 7.4 kPa (56 mmHg), P_{aCO_2} 8.9 kPa (67 mmHg), pH 7.46, standard bicarbonate 40.1 mmol/litre and base excess 16.5 mmol/litre (note the picture of hypokalaemia, metabolic alkalosis, hypoxia and hypercapnia). Chest X-ray was normal.

Treatment was commenced with 24% oxygen, intravenous diuretic (frusemide 160 mg) and potassium chloride (40 mmol, 4 hourly) along with 500 ml of 1.9% sodium chloride solution, 6 hourly. Four hours after initiation of therapy the patient's condition deteriorated, P_{aCO_2} rising to 11.7 kPa (88 mmHg), P_{aO_2} 9.2 kPa (70 mmHg), pH 7.54 and bicarbonate 54 mmol/litre. In view of the increasing hypercapnia, oxygen therapy was discontinued. After 24 hr and a good diuresis, her clinical condition improved with clearing of pulmonary crackles and spironolactone, 100 mg twice daily was commenced. Repeat biochemistry including arterial blood gases showed a return to normal over the following 48 hours.

In view of hypercapnia, the patient completed the MRC Questionnaire on Respiratory Symptoms (MRC, 1966) and there were no features of chronic bronchitis. Moreover, respiratory function as measured by spirometry (Vitalograph), performed after recovery, revealed a normal forced expiratory volume/forced vital capacity (FEV_1/FVC) ratio and values of FEV_1 and FVC were near those predicted normal. The patient was discharged home after several weeks when her postural hypotension

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was well-controlled by a pair of support stockings and ephedrine, 30 mg thrice daily.

Discussion

We believe that hypokalaemia and metabolic alkalosis of such a degree have not been reported previously as a complication of fludrocortisone therapy. Presumably in this patient, fludrocortisone, predominantly a mineralocorticoid, had caused sodium and water retention as evidenced by peripheral and pulmonary oedema along with intracellular potassium depletion.

The combination of fludrocortisone therapy (effectively an iatrogenic Conn's syndrome) and hypokalaemia would increase the rate of ammonium synthesis in the kidney thus leading to hydrogen ion excretion exceeding that of endogenous hydrogen ion production and causing a renal metabolic alkalosis.

The entity of hypercapnia as a result of compensatory respiratory suppression in metabolic alkalosis has been debated. Some disclaimed its existence arguing that hypoxia limits the degree of hypoventilation (Goldring *et al.*, 1968) though more recent workers have shown that it does indeed occur (Fulop, 1976). Our patient's P_{aCO_2} of 8.9 kPa (67 mmHg) lies outside the 95% confidence limits for metabolic alkalosis described by Shear and Brandman (1973) and Bia and Thier (1981), and suggests an independent respiratory suppression. This apparently was transient and not due to chronic obstructive airways disease as later pulmonary function tests showed and could be explained in terms of a hypokalaemic myopathy causing respiratory muscle weakness. This mechanism could explain the discrepancy in our figures with those of Bone *et al.*, (1974) who were describing pure metabolic alkalosis with their curvilinear relationship between hydrogen ion concentration and bicarbonate. The potassium and bicarbonate concentrations correlate well with those of Kassirer *et al.* (1970) which is to be expected as they studied hyperaldosteronism which was mimicked in our patient by the exogenous administration of fludrocortisone.

Postural hypotension is a common clinical problem particularly in the elderly. Treatment of the condition is difficult and many therapeutic tools of marginal benefit are available to the clinician. Increasing the extracellular fluid volume compartment by way of sodium retention is the rationale behind using a potent mineralocorticoid such as fludrocortisone. Potassium depletion is a recognized but rarely mentioned side effect even of prolonged fludrocortisone therapy (Campbell, Ewing and Clarke, 1976; Chobanian *et al.*, 1979; Watt, Tooke and Perkins, 1981). Nicholls and colleagues (1979) who studied 6 healthy men, given 1 mg of fludrocortisone per day experimentally, observed significant

reductions in serum and whole body potassium which were reversed by the mineralocorticoid antagonist spironolactone in doses of between 50 and 200 mg per day. Spironolactone was used in our patient to promote the necessary diuresis, but also because of its specific antimineralocorticoid action. Presumably, the resultant potassium retention reversed the entire metabolic abnormality.

This case is reported because the metabolic upset was of a severity never previously described with fludrocortisone therapy. It illustrates well the biochemical abnormalities of metabolic alkalosis in its extreme form and serves to warn clinicians of the real hazards of fludrocortisone therapy not least of which is the temptation to ventilate subjects with profound hypercapnia. Though fludrocortisone therapy is of real benefit in some patients incapacitated by postural hypotension, we believe it can only be safely prescribed if used sparingly with regular biochemical checks and in most cases with the additional use of potassium supplements.

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