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Teaching Point
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The tell-tale urinary chloride

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Introduction

Interpretation of arterial blood gas values is a widely neglected skill. While clinicians routinely order a battery of sophisticated and costly tests to tackle a difficult case, blood gas analysis is rarely utilized. We present a case of profound hypokalaemia in a young woman. Further evaluation initially failed to reveal any of the common causes of hypokalaemia. It was only when arterial blood gas values disclosed severe metabolic alkalosis that an appropriate algorithm revealed a diagnosis.

Case

A 26-year-old female patient presented to her general practitioner with weakness and lassitude of some months duration. Serum potassium was between 2.3 and 2.8 mmol/l on repeated occasions and she was eventually admitted to our department.

The patient reported no further complaints aside from weakness and she had no relevant previous medical history. Moreover, she was on no regular medication. She was employed as a nurse in a tertiary-care hospital. On admission, she did not appear acutely ill. Clinical examination was unremarkable and blood pressure was 90/60 mmHg. Laboratory examinations confirmed hypokalaemia of 2.6 mmol/l and revealed concomitant hypochloraemia of 90 mmol/l. An electrocardiogram showed sinus tachycardia and U waves. Chest X-ray and abdominal ultrasound were normal. A spot urinary potassium was 64 mmol/l (high, particularly in view of the hypokalaemia). At that point, the cause of hypokalaemia remained enigmatic while both renal and non-renal potassium wasting were considered. Arterial blood gas analysis, however, revealed profound metabolic alkalosis (pH 7.56, Pco_2 45.2 mmHg, Po_2 99.3 mmHg, bicarbonate 39.4 mmol/l, base excess 15.5 mmol/l, anion gap 6.8 mmol/l). Urine chloride was very low (5 mmol/l) and urine pH was 8. Another attempt was made to elicit a history of gastrointestinal complaints but the patient reported neither vomiting nor diarrhoea. Repeat clinical examination disclosed fullness of the retromandibular grooves and ultrasound confirmed parotid enlargement; the submandibular glands were also enlarged. A tentative diagnosis of bulimia was made but the patient denied any self-inflicted vomiting, refused counselling and eventually left hospital.

Discussion

They suspected!—they knew! [1]

Acid-base disorders often appear to be very complex and incomprehensible to the medical novice. Our patient presented with weakness that could easily be attributed to hypokalaemia. Among the causative mechanisms of hypokalaemia, increased entry of K^+ into cells, gastrointestinal loss of secretions or renal potassium wasting are most common (Table 1). In our patient, these causes were sought by history taking and clinical examination, all to no avail. Urinary potassium was 65 mmol/l. Before drawing any misleading conclusions from this finding, one must appreciate renal potassium handling and the limitations of urinary potassium assays.

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Table 1. Major causes of hypokalaemia

Increased entry into cells
Insulin
Elevated β-adrenergic activity (stress or beta agonists)
Hypokalaemic periodic paralysis
Increase in blood cell production
Inherited: Autosomal-dominant trait
Acquired: thyrotoxicosis
Alkalosis
Hypothermia
Chloroquine
Increased gastrointestinal potassium losses
Diarrhoea
Vomiting
Tube drainage
Laxative abuse
Increased urinary losses
Diuretics
Mineralocorticoid excess (various causes)
Liquorice intake
Amphotericin B
(increased membrane permeability of the distal tubule)
Salt-wasting nephropathies such as Bartter's or
Gitelman's syndrome
Polyuria
Renal tubular acidosis
Type 1 (some forms)
Type 2, particularly after treatment with bicarbonate
(increased distal sodium and water delivery)
Hypomagnesaemia (mechanism unclear)
In response to loss of gastric secretions
(hyperaldosteronism due to hypotension)
Nonreabsorbable anions (e.g. hippurate in toluene abuse)
Decreased potassium intake
(mostly in combination with another cause of hypokalaemia)
Increased sweat losses

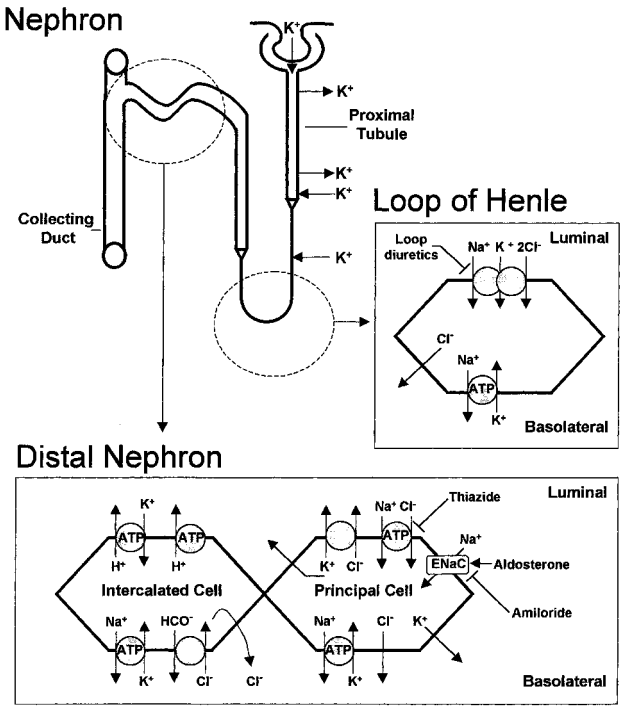

Fig. 1. Renal potassium handling.

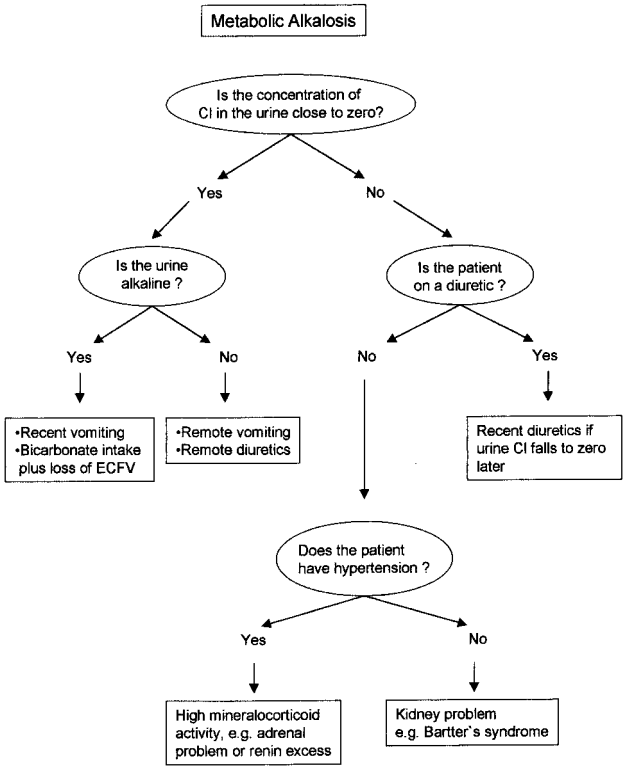

Fig. 2. Algorithm for metabolic alkalosis [3].

Potassium is freely filtered by the glomerulus and reabsorbed along the proximal tubule and the loop of Henle to the effect that urinary potassium excretion is mostly derived from potassium secretion in the distal nephron (Figure 1, lower panel). Potassium movement from the cells is driven by an electrochemical gradient that favours secretion; this gradient is increased by aldosterone-induced sodium reabsorption via the epithelial sodium channel (ENaC). Finally, potassium can also be secreted via an electroneutral K^+Cl^- secretory mechanism. Therefore, with the exception of Bartter's syndrome and intake of loop diuretics, urinary potassium wasting occurs in the distal tubule and involves interaction with the mechanisms described above.

While a spot urinary potassium about 30 mmol/l suggests renal potassium loss, this may not, as exemplified by our case, help with the diagnosis. In particular, it does not exclude gastrointestinal potassium loss due to vomiting. Instead, substantial renal potassium loss may occur, in addition to loss of potassium in gastric secretions, once hypovolaemia and hyperaldosteronism are present [2,3]. In the case reported here, arterial blood gas analysis fortunately revealed severe metabolic alkalosis before any more sophisticated studies were performed. From this point, we proceeded using a simple algorithm (Figure 2) [3]. First, the importance of urinary chloride as a diagnostic tool in metabolic alkalosis must be appreciated [4]. A low urine chloride usually reflects hyperaldosteronism due to volume depletion as it occurs in surreptitious vomiting [4]. In our case, urine chloride was low and from then on we not only suspected but

knew [1] the correct diagnosis. In particular, Bartter's syndrome and abuse of loop diuretics, which might have been another tempting diagnosis in a hypokalaemic health care professional, could be excluded at this point. Likewise, hypokalaemic alkalosis due to liquorice intake [5] could be ruled out. When the urine was found to be alkaline, only gastrointestinal loss of secretions and clandestine ingestion of bicarbonate remained. The latter is rarely encountered in baking soda pica and commonly associated with hypertension [6]. Therefore, we concluded that gastrointestinal chloride loss was present. Gastric fistula could be ruled out on clinical grounds alone. Enlargement of the salivary glands was noted and a diagnosis of bulimia could be made with confidence [7,8]. Hypokalaemia and metabolic alkalosis are not uncommon in patients with bulimia and may account for considerable diagnostic confusion [9,10]. Hypokalaemia can be caused by gastric potassium loss, hyperaldosteronism due to hypovolaemia or metabolic alkalosis due to acid loss. In a particular patient, however, it may be impossible to discern between these mechanisms.

In retrospect, we must be blamed for not making the diagnosis earlier. Blood gas analysis and a spot assay of urinary chloride, had they been performed on the day of admission, could have told the tale early on and at negligible cost.

Teaching points

(i) Surreptitious vomiting is an important cause of hypochloraemic metabolic alkalosis and hypokalaemia due to gastric loss of potassium and protons.

(ii) In this setting, urine chloride is usually low while urinary potassium excretion may even be elevated due to hypovolaemia and hyperaldosteronism.

(iii) Arterial blood gas analysis should be part of the initial evaluation in electrolyte disorders. Disclosing a distinct acid base disorder may occasionally allow for a quick diagnosis using a simple algorithm.

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