Introduction

- Metabolic alkalosis is characterized by elevated serum bicarbonate levels and pH.
- Requires both accumulation of excess bicarbonate and the inability to excrete this.
- When severe, it can have many adverse effects including altered mental status, reduced seizure threshold, cardiac arrhythmias and hypotension.
- The mortality of alkalosis with pH > 7.55 is ~ 45% and 80% at pH > 7.65.1
- We present an unusual case of severe, life-threatening metabolic alkalosis with prescribed fludrocortisone being the main inciting factor.

Case

- An 89 year old presented confused with reduced mobility and oral intake over the preceding week. She had a background of orthostatic hypotension with recurrent falls and fludrocortisone 0.2mcg was commenced 9 months previously. 2 weeks prior to admission hydrochlorothiazide was commenced for hypertension and codeine for headaches.
- On presentation GCS was 14, blood pressure 130/63, HR 59bpm, examination was remarkable only for volume depletion and upper limb dyskinetic movements.
- Initial bloods (Table 1) revealed AKI with hypokalaemic, hypochlorinaemic metabolic alkalosis, spot urinary chloride was 61mmol/L and spot urinary K 34mmol/L, suggesting renal losses.
- Of note, serum creatinine kinase was markedly elevated at 13,649U/L. ECG was consistent with hypokalaemia (T wave flattening with prominent U waves).
- Initial management included holding hydrochlorothiazide and fludrocortisone and fluid resuscitation with normal saline and KCl.
- Mrs. X continued to decline with worsening renal failure and GCS.

Table 1

<table>
<thead>
<tr>
<th>Creat</th>
<th>Urea</th>
<th>Na</th>
<th>K</th>
<th>Cl</th>
<th>HCO3</th>
<th>Urine</th>
<th>Plasma</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.8</td>
<td>21.0</td>
<td>148</td>
<td>2.4</td>
<td>77</td>
<td>49</td>
<td>7.45</td>
<td>91</td>
</tr>
</tbody>
</table>

Discussion

This case eloquently demonstrates the complexities underlying renal acid-base homeostatic mechanisms. The metabolic alkalosis was multifactorial:

(1) Fludrocortisone

- A state of mineralocorticoid excess:
- Stimulation of luminal H+ ATPase in distal tubule secretion of H+ & Na+ reabsorption to maintain electroneutrality.
- Stimulation of ENa channel of distal tubule Na+ reabsorption with H+ and K+ secretion to maintain electroneutrality.

(2) Hydrochlorothiazide

- Inhibits Na-Cl co-transporter in the distal convoluted tubule, increasing distal Na+ delivery allowing for further Na+ reabsorption in exchange for H+ and K+ secretion.

(3) Hypokalaemia

- Developed by the above mechanisms causes transcellular shift and IC acidosis of proximal convoluted tubule cells2 causing:
- Ammoniogenesis from glutamine is stimulated, with formation of bicarbonate – this is absorbed
- Inhibits excretion of organic ions (such as citrate) – compromising removal of dietary alkali
- Stimulation of distal H+K+ATPase transporters encourages K+ reabsorption and H+ secretion.

(4) Renal failure

- Reduces renal capacity to excrete excess bicarbonate.
- It is hypothesized renal failure occurred in the setting of volume depletion and rhabdomyolysis. The latter is suggested by the significantly elevated creatinine kinase on admission, and felt to be spontaneous in the context of prolonged immobility.
- The primary cause of alkalosis was 2o to mineralocorticoid excess, this was later confirmed when admission renin and aldosterone levels returned suppressed (2.9pg.ml and 11pg/ml, respectively).
- The development of this had been manifested earlier with hypertension and the addition of a thiazide to manage this inadvertently worsened the metabolic scenario.
- The respiratory acidosis was greater than expected for this degree of alkalæmia and this was likely secondary to reduced GCS as a consequence of codeine accumulation in renal impairment, in combination with neurological effects of severe alkalosis.

Learning points

- High urinary chloride levels in metabolic alkalosis:
- Suggest ‘chloride-resistant alkalosis’ and predict failure of NaCl treatment.
- In combination with hypokalaemia should lead to suspicion of mineralocorticoid excess.
- Hypokalaemia potentiates metabolic alkalosis and without its resolution alkalosis will persist.
- In refractory metabolic alkalosis with AKI, renal replacement therapy is an effective intervention.
- In this case the combination of 3 commonly used medications resulted in a cascade of events precipitating a life-threatening metabolic state. This illustrates the importance of awareness of medication interactions and vigilance when prescribing, especially in the frail, elderly population.

References