Nephrology
Dialysis
Transplantation

Nephroquiz for the Beginner
(Section Editor: T. J. Rabelink)

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Metabolic acidosis, hypokalaemia and acute renal failure with a normal urine output

Case

A 72-year-old man was admitted with a 3-week history of general debility and diarrhoea, passing copious amounts of watery, brown stool through the day and night. He had had no abdominal pain and had started to vomit the day before presentation. On examination he was dehydrated and mildly disorientated. He had a tachycardia of 110/min, and a blood pressure of 90/70 mmHg, with a postural drop to 60/30 mmHg. His abdomen was soft and non-tender, with tinkling bowel sounds. No masses were felt on palpation or rectal examination. His biochemistry on presentation is shown on Table 1.

His stool volume was recorded in excess of 3 l per day, and with a urine output of 50 to 100 ml/h. Dipstix testing showed a trace of haematuria and proteinuria with the presence of ketones. A chest X-ray was normal, and a plain film of the abdomen showed occasional loops of non-dilated bowel. He had normal sized, unobstructed kidneys with normal cortical thickness on ultrasound. Cultures of blood, urine and stool were all negative for bacteria and parasites. Haemoglobin, magnesium, amylase and carcinoembryonic antigen were normal. He was rehydrated with potassium-containing crystalloid to euvolaemia. His electrolytes normalized over 5 days, and his creatinine fell to 105 µmol/l.

Question

What is the most likely diagnosis? Why is the patient polyuric in the face of profound dehydration?

Table 1. Initial results

<table>
<thead>
<tr>
<th>Biochemistry on presentation</th>
<th>Normal range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium</td>
<td>121 mmol/l</td>
</tr>
<tr>
<td>(135–145 mmol/l)</td>
<td></td>
</tr>
<tr>
<td>Potassium</td>
<td>2.9 mmol/l</td>
</tr>
<tr>
<td>(3.5–5.0 mmol/l)</td>
<td></td>
</tr>
<tr>
<td>Chloride</td>
<td>83 mmol/l</td>
</tr>
<tr>
<td>(95–110 mmol/l)</td>
<td></td>
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<tr>
<td>Bicarbonate</td>
<td>6 mmol/l</td>
</tr>
<tr>
<td>(22–26 mmol/l)</td>
<td></td>
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<tr>
<td>Urea</td>
<td>90 mmol/l</td>
</tr>
<tr>
<td>(2.8–8.9 mmol/l)</td>
<td></td>
</tr>
<tr>
<td>Creatinine</td>
<td>960 µmol/l</td>
</tr>
<tr>
<td>(75–115 mmol/l)</td>
<td></td>
</tr>
<tr>
<td>Glucose</td>
<td>4.9 mmol/l</td>
</tr>
<tr>
<td>(3.9–6.1 mmol/l)</td>
<td></td>
</tr>
<tr>
<td>pH</td>
<td>7.261</td>
</tr>
<tr>
<td>(7.35–7.45 pH units)</td>
<td></td>
</tr>
<tr>
<td>pCO₂</td>
<td>2.28 kPa</td>
</tr>
<tr>
<td>(4.7–6.0 kPa)</td>
<td></td>
</tr>
<tr>
<td>Serum osmolality</td>
<td>334 mosm/kg</td>
</tr>
<tr>
<td>(280–296 mosm/kg)</td>
<td></td>
</tr>
<tr>
<td>Urine osmolality</td>
<td>404 mosm/kg</td>
</tr>
<tr>
<td>Urinary sodium</td>
<td>2 mmol/l</td>
</tr>
<tr>
<td>Urinary potassium</td>
<td>28 mmol/l</td>
</tr>
</tbody>
</table>
Answer to quiz on preceding page

This patient presented with a life threatening volume depletion syndrome with hyponatraemia, hypokalaemia, and hypochloraemic metabolic acidosis with acute pre-renal failure. On admission he was in a state of cardiovascular collapse, but unusually for his degree of hypovolaemia, had a well-maintained urine output. Given his fluid deficit, his urine was inappropriately dilute. Simple dehydration may account for the hypovolaemia and acute renal failure but would usually be associated with oliguria and highly concentrated urine. The electrolyte abnormalities may also be found in chronic renal failure, with a good output of dilute urine: normalization of plasma biochemistry by rehydration ruled this out.

The metabolic acidosis on admission was associated with hypochloraemia, and a raised anion gap (35, normal range 6–12). Diabetic ketacidosis may present with similar chemistry, but a normal blood sugar would be atypical. Lactic acidosis accompanying tissue hypoperfusion and subsequent anaerobic glycolysis will show a raised anion gap as well, but would be marked by hypokalaemia—in this case lactic acid may have played a part in the abnormalities, but would not account for them all. The history of our patient’s complaint seems to be against salicylate poisoning, or methanol or ethylene glycol ingestion, both of which lead to raised anion gap acidoses caused by lactate and formate respectively. The retention of protons and organic acids in acute renal failure played a major role in this case, but hypokalaemia is not typical, and suggests an alternative diagnosis. Hypokalaemia with metabolic acidosis can be caused by renal tubular acidosis or ureterosigmoidostomy. However, the anion gap is usually normal, and these conditions are rarely associated with renal dysfunction [1].

The depletion syndrome characterized by cardiovascular collapse, acute renal failure, hyponatraemia and a hypokalaemic, hypochloraemic metabolic acidosis is a rare complication of a rectal villous adenoma [2] (Fig. 1). Characteristically there is watery, mucinous diarrhoea with bowel actions as frequent as 20 times a day, not uncommonly for up to 15 years prior to recognition of the cause. At the outset, the fluid and electrolyte losses are easily compensated for by increased oral intake and renal regulation. As the tumour size increases these losses overwhelm compensatory mechanisms and the patient may seek medical attention. The profound metabolic disturbance, associated with vague symptoms and few signs, frequently leads to initially inaccurate diagnosis. In particular, digital examination of the rectum will miss even large tumours in many cases due to their soft, mucin-covered surface, often described as velvet-like.

The mechanism of fluid and electrolyte loss is unclear. Locally released prostaglandin E₂ has been suggested as the secretagogue responsible for salt wasting [3], as has cyclic adenosine monophosphate [4]. Resultant losses can amount to 1.5–3.5 l of fluid containing 40–160 mmol/l sodium, 15–105 mmol/l potassium and 80–165 mmol/l chloride [5]. Rectal losses of sodium chloride are isotonic whereas potassium losses are well in excess of plasma concentrations, with active secretion in the stool accounting for up to 150 mmol/day [6]. This is crucial to the clinical syndrome as chronic hypokalaemia inhibits the normal compensatory mechanisms in electrolyte and water deprivation. A state of nephrogenic diabetes insipidus develops due to reduction in collecting duct responsiveness to vasopressin, mediated via decreased expression of aquaporin-2 [7]. This response is restored within weeks of correcting hypokalaemia. In addition to rectal loss of potassium, urinary losses (84 mmol/day in our patient) further exacerbate the metabolic upset. This urinary loss occurs due to secondary hyperaldosteronism in the face of volume contraction, leading to salt conservation at the expense of potassium.

Pointers to the diagnosis in our patient were hypokalaemia, the magnitude of fluid replacement required to maintain euvolaemia and an inappropriately good urine output with low osmolality. With prompt recognition of the diagnosis, recourse to haemodialysis is rarely necessary. Established acute tubular necrosis is a surprisingly rare complication considering the severity of the circulatory collapse developing in patients characteristically into their seventh or eighth decade. There is experimental evidence to suggest that hypokalaemia provides cytoprotection against hypoxic proximal tubular injury by inactivating potassium channels [8]. Similarly, profound acidosis provides protection against proximal tubular injury by inhibition of the mediators of cell damage [9].

Fig. 1. An extensive papilliferous, circumferential tumour extending from the anal verge (but sparing the sphincter) to 15 cm into the rectum, characteristic of this lesion.
Reversal of the biochemical derangement is the cornerstone of successful management. The magnitude of the fluid and electrolyte deficit cannot be over emphasized. An accurate daily record of urinary and colonic losses is essential to ensure adequate replacement. Once resuscitated, immediate surgical resection of the tumour is the treatment of choice.

References


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