Nephroquiz
(Section Editor: M. G. Zeier)

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Electrolyte abnormalities with a fatal implication

Case

A 72-year-old caucasian male presented with a 1-month history of decreased appetite, 6 kg weight loss with alteration in pattern of micturition; namely a tendency to pass most of his urine overnight, estimated at 2 to 2.5 l. He also gave a 1-week history of progressive ankle swelling. Over this period of time he felt increasingly clumsy on his feet especially on turning abruptly. He denied fever, sweats, myalgia, arthralgia, prostatic and gastrointestinal symptoms. He was a non-smoker, infrequently drank alcohol and was a retired businessman. His past medical history included a diagnosis of prostatic carcinoma made 18 months prior to his current presentation. He had been treated with hormonal medication and subsequently TURP 4 months after diagnosis. He was under urological follow-up with a recent PSA value of 0.1 μg/l.

On clinical examination he was a thin gentleman with a single non-tender lymph node in the left supraclavicular space. Urinalysis revealed 3+ glucose only. Skin turgor was reduced, extremities were cold and he had a sinus tachycardia with an occasional ectopic beat. Heart sounds were normal, blood pressure 140/80 mmHg with no postural drop; he had 1+ ankle oedema only. Auscultation of his chest was normal, abdominal examination unremarkable. Neurological examination revealed gait ataxia on heel-toe testing only. Current medication prescribed by his general practitioner included Sando-K 2 tabs qds, Slow sodium 2 tabs qds.

Initial investigations were as follows: sodium 135 mmol/l, potassium 2.9 mmol/l, urea 7.2 mmol/l, creatinine 115 μmol/l, bicarbonate 35 mmol/l, corrected calcium 2.34 mmol/l, phosphate 0.86 mmol/l, albumin 29 g/l, magnesium 0.78 mmol/l, random glucose 8.5 mmol/l, creatinine clearance 38 ml/min, proteinuria 0.36 g/d, PSA 1.1 μg/l, CRP 1.7 mg/l, Hb 13.6 g/dl, WCC 7.9×10⁹/l, platelets 210.10⁹/l. Twenty-four hour urinary electrolyte values were sodium 112 mmol/day (50–200), potassium 121 mmol/day (30–100), calcium 8.9 mmol/day (2.5–7.5) and magnesium 2.7 mmol/day (3.0–5.0) with a total volume of 2.7 l.

Questions

1. What is the biochemical abnormality?
2. What additional investigations would you undertake and why?
3. What is your diagnosis and differential diagnosis?
**Answers to the quiz on the previous page**

1. The biochemical abnormality is that of a hypokalaemic metabolic alkalosis with urinary electrolytes in keeping with a Bartter’s-like syndrome.

2. Additional investigations should be directed towards assessing the underlying aetiology. The history is all-important. This was suggestive of an underlying malignancy whilst the alteration in micturition pattern was suggestive of partial urinary tract obstruction. Further investigations would include: chest X-ray, renal ultrasound scan, DTPA scan with frusemide, CT scan of head (gait ataxia), chest abdomen and pelvis, and lymph node biopsy.

3. Initial diagnostic possibilities considered included malignancy of the prostate, lung or lymphoid system with retroperitoneal involvement causing partial urinary tract obstruction. A less likely possibility was occult loop diuretic abuse with or without underlying malignancy.

Abdominal ultrasound revealed two normal sized kidneys. A large post micturition residual bladder volume (500 ml) was found, the bladder wall appeared trabeculated and thickened posteriorly. Aortic lymphadenopathy was noted. DTPA scan with frusemide demonstrated minor hold-up of tracer in the pelvicalyceal systems bilaterally. Differential function was 33% left and 67% right. CT scan demonstrated normal liver and gallbladder; kidneys, adrenal glands, spleen and pancreas also appeared normal. A large volume of lymph nodes in the para-aortic region surrounding the aorta and inferior vena cava from the level of the superior mesenteric artery to the aortic bifurcation with extension to the proximal iliac chain was found. Supraclavicular lymph node biopsy demonstrated metastatic carcinoma consistent with an undifferentiated prostatic carcinoma.

The diagnosis was therefore one of the malignant retroperitoneal adenopathy with bladder outlet obstruction most likely related to a de-differentiated prostatic carcinoma.

**Discussion**

This gentleman’s biochemical profile reflected renal electrolyte losses, which occurred in the setting of partial obstruction secondary to malignant retroperitoneal lymphadenopathy and bladder outlet obstruction. Serum and urinary biochemical profiles were similar to that of Bartter’s syndrome with hypokalaemic metabolic alkalosis, hypercalciuria and hypomagnesuria [1,2]. One could therefore regard this as a pseudo-Bartter’s or Bartter’s-like syndrome. The molecular basis of Bartter’s syndrome has been demonstrated to be due to ion channel abnormalities in the medullary thick ascending limb of the Loop of Henle (mTAL). Mutations resulting in loss of function of the sodium-potassium-chloride cotransporter (NKCC2) or the ROMK1 channel, an apical ATP-regulated potassium channel, are the major abnormalities. The mechanism of the acquired defect in the patient presented here is unknown.

In the obstructed urinary tract and post-obstructed state a range of neurohormonal and endocrine factors are operative such as the renin-angiotensin-aldosterone system (RAAS), prostanoids, atrial natriuretic peptides (ANP) and anti-diuretic factors (ADH) [3,4]. Most of the experimental work concerning the changes observed during ureteric obstruction has been undertaken in animal models. Information available about the effects of urinary tract obstruction on human GFR are sparse, though a marked reduction in GFR occurs and in the setting of bilateral incomplete obstruction progressive renal impairment can develop. Chronic partial ureteric obstruction has been associated with a number of abnormalities such as impaired concentrating ability, a salt-losing state and an acidification defect. Experimental work has been undertaken to assess changes that occur in the post-obstructed state, which may also be relevant to partial obstruction. Release from bilateral ureteric obstruction often results in a profound diuresis and natriuresis, provided the patient is not dehydrated. Contributory factors to this state include an osmotic effect secondary to retained poorly reabsorbable solutes, intrinsic tubular damage resulting in loss of medullary concentration gradients, increased circulating levels and local levels of ANP and an acquired nephrogenic diabetes insipidus due to down regulation of aquaporin-2 expression during the period of obstruction [5].

A factor more pertinent to the patient discussed here is the possible role of prostaglandin E(2), a major renal cyclooxygenase metabolite of arachidonate. PGE(2) is induced in obstructed and more especially in post-obstructed kidneys; one would assume that this also applies to the partially obstructed state, although this has not been assessed [6]. PGE(2) mediates different effects on different renal structures due to differential receptor expression [7]. Thus, PGE(2) attenuates vasoconstrictive factors operative on the glomerular afferent arteriole whereas at the level of the mTAL, PGE(2) inhibits sodium reabsorption. In children with Bartter-like syndromes, increased urinary excretion of PGE(2) has been demonstrated. Therefore, a possible mechanism to account for the biochemical abnormality observed in the patient presented here, might be that of excessive PGE(2) production in the mTAL consequent to partial obstruction resulting in reduced sodium reabsorption with consequent activation of the RAAS resulting in the observed biochemical profile.

For our patient, the apparent excellent response of the tumour to hormonal therapy, as defined by normalization of PSA value (600 µg/l to 0.1 µg/l), was misleading. In this case the development of PSA-negativity reflected progressive de-differentiation of the tumour resulting in hormonal escape with ultimately fatal consequences.
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References


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