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*Nephroquiz*
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# Hypokalaemia and hypertension early after kidney transplantation

## Case

A 48-year-old Caucasian male underwent a cadaveric renal transplantation in November 2000 after 15 months of haemodialysis. He was treated by nifedipine (30 mg o.d.) and nisoldipine (20 mg o.d.) for arterial hypertension evidenced more than 20 years before. No laboratory investigation was performed until May 1999, when he was admitted for chest pain. Blood pressure was 185/95 mmHg and serum creatinine was 6.0 mg/dl. Urinary microscopy was unremarkable. Proteinuria was 570 mg/24 h. Renal ultrasonography showed normal-sized kidneys with a lack of corticomedullary distinction. Renal biopsy showed aspecific interstitial fibrosis and tubular atrophy. A diagnosis of nephroangiosclerosis complicating long-lasting primary arterial hypertension was considered. Coronarography showed a 75% stenosis on a diagonal artery, not requiring revascularization. The treatment was changed to atenolol (50 mg o.d.) and furosemide (160 mg o.d.). Renal function progressively deteriorated, and haemodialysis was started in August 1999. At the time of transplantation, the homolateral native kidney was removed (a routine procedure in our centre) and histological examination showed end-stage kidney disease. Delayed graft function required four haemodialysis sessions. The results of a laboratory examination obtained 4 days after the last haemodialysis session (day 12) are provided in Table 1. The patient was discharged on day 17 (Table 1). Serum creatinine and potassium were 2.1 mg/dl and 3.05 mEq/l, respectively. The patient had no diarrhoea. He was not taking diuretics. Blood pressure at home and at the outpatient clinic averaged 150/90 mmHg. Maintenance therapy included tacrolimus 5 mg b.i.d., mycophenolate mofetil 500 mg b.i.d., prednisolone 10 mg o.d., dipyridamole 200 mg b.i.d., valaciclovir 1 g t.i.d. and citalopram 20 mg o.d. Urinary sodium, potassium and chloride excretion were 77, 27 and 86 mEq/l, respectively. Hypokalaemia persisted despite oral supplementation with potassium (40 mEq o.d.) and magnesium (1.5 g o.d.) (Table 1). Metabolic alkalosis appeared progressively. Blood and urinary cortisol were 487 nM (Nl 260–540) and 144 μg/24 h (Nl $<90$), respectively.

## Questions

How do you explain hypokalaemia?
What kind of complementary tests would you recommend to confirm your diagnosis?

**Table 1.** Evolution of biochemical parameters after renal transplantation in November 2000

| | Normal values | Day −10 | Day 12 | Day 17 | Day 22 | Day 40 | Day 71 | Day 175 |
|---|---|---|---|---|---|---|---|---|
| Plasma | | | | | | | | |
| Creatinine (mg/dl) | 0.8–1.3 | 13.2 | 3.9 | 2.1 | 1.85 | 2.2 | 2.5 | 2.5 |
| K (mEq/l) | 3.5–5.0 | 6.65 | 3.3 | 3.05 | 2.7 | 2.7 | 3.4 | 4.4 |
| Na (mEq/l) | 135–145 | 134 | 133 | 142 | 145 | 142 | 140 | 137 |
| Cl (mEq/l) | 97–107 | 97 | 100 | – | 105 | 102 | 100 | 113 |
| Total $CO_2$ (mEq/l) | 24–28 | 15.5 | 25.5 | – | 29.5 | 31 | 28 | 20 |
| Mg (mEq/l) | 1.45–1.9 | – | 2.2 | – | 1.5 | 1.1 | 1.3 | 1.5 |
| Urine | | | | | | | | |
| Na (mEq/l) | | – | – | – | 77 | – | – | – |
| K (mEq/l) | | – | – | – | 27 | – | – | – |
| Cl (mEq/l) | | – | – | – | 78 | – | – | – |
| Ca (mg/24 h) | 50−300 | – | – | – | 113 | – | – | – |

## Answer to the quiz on preceding page

A stepwise diagnostic approach of hypokalaemia is summarized in Figure 1 [1]. In this patient, an extra-renal $K^+$ loss was easily ruled out by the absence of diarrhoea and the elevated amount of urinary $K^+$ excretion. At that point, the level of blood pressure would be the next diagnostic clue in most patients. However, this step is less discriminating in renal transplant recipients, given the high prevalence of systemic hypertension in such patients [2].

Could tacrolimus intake have played a role in this renal transplanted patient? Anticalcineurins have been shown to increase urinary magnesium excretion leading to hypomagnesaemia [3]. Pure magnesium depletion in humans can induce hypokalaemia and increased renal $K^+$ losses [4]. However, both tacrolimus and cyclosporin are known to inhibit aldosterone secretion, thereby causing hyperkalaemia, together with metabolic acidosis [5,6]. Similarly, the causes of normotensive hypokalaemia with metabolic alkalosis and a high urinary $Cl^-$ excretion may be considered (Figure 1). However, none of these possibilities were

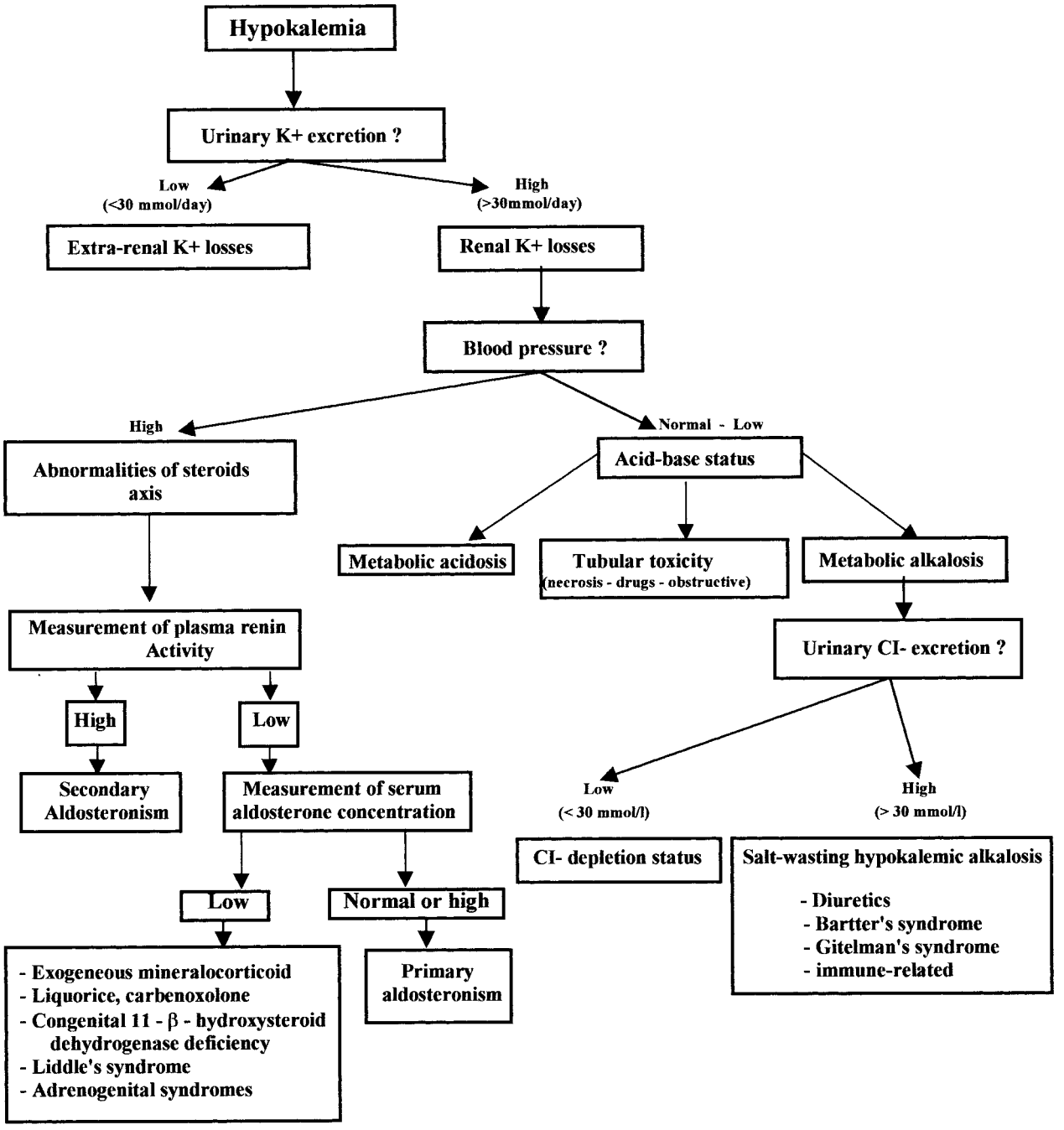



**Fig. 1.** A stepwise diagnosis of chronic hypokalaemia.

plausible; the patient was not given diuretics, and he had no signs or symptoms of Bartter's or Gitelman's syndromes.

We have thus to consider the causes of hypokalaemia associated with hypertension (Figure 1). As indicated above, blood and urine cortisol were normal, which excluded hypercorticism. Rather, the association of hypokalaemia, inappropriate kaliuresis, and a long-lasting history of mild hypertension evokes a diagnosis of hyperaldosteronism. Complementary laboratory investigations included serum aldosterone level and plasma renin activity (PRA). PRA was very low (<0.2 ng/ml/h (Nl <5)), while serum aldosterone concentration (PAC) was high (2.3 nM (Nl <0.4)). These results are highly suggestive of primary hyperaldosteronism. The various causes of pseudohyperaldosteronism (Liddle's syndrome, abuse of liquorice, apparent mineralocorticoid excess, deoxycorticosterone excess) can be excluded by the high aldosterone level. The next step is thus to perform MRI or CT scans of the adrenals. Abdominal MRI showed a left adrenal mass of $4.5 \times 3 \times 1.5$ cm (Figure 2a). Adrenal vein catheterism confirmed excessive aldosterone production by the left adrenal gland (Figure 2b). Spironolactone treatment (100 mg o.d.) readily corrected electrolytic disorders (Table 1). Left adrenalectomy showed an adrenal adenoma with two areas of hyperplasia. Spironolactone treatment was withdrawn with a persistently normal ionogram at day 175 (Table 1).

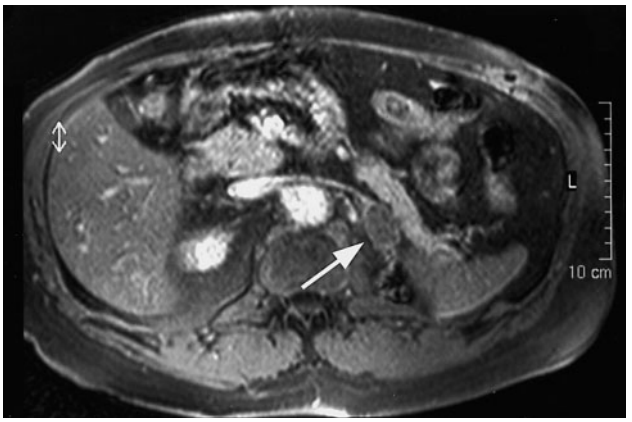
*A posteriori*, the May 1999 laboratory findings before the initiation of haemodialysis were already suggestive (Table 2). At that time, mild hypokalaemia (probably attenuated by the metabolic acidosis secondary to renal failure), together with a high $K^+/Na^+$ ratio in the urine, pointed to hyperaldosteronism. During haemodialysis, hypokalaemia was masked by both anuria and metabolic acidosis (Table 1, day −10). After the onset of diuresis secondary to renal transplantation, hypokalaemia reappeared within 4 days because of excessive urine $K^+$ losses together with the correction of acidosis.

Thus, in this renal transplanted patient it was the association of ion abnormalities with mild hypertension that led to the diagnosis of hyperaldosteronism. The low PRA in the face of elevated serum aldosterone values, associated with adrenal tumor detection by MRI, homolateral excessive aldosterone production evidenced by selective catheterism, and pathological examination following surgery, confirmed the

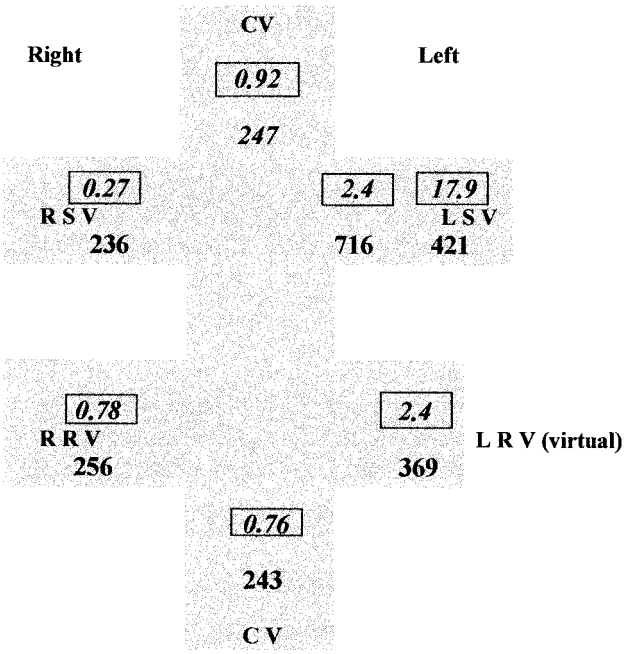
**Table 2.** Biochemical parameters in May 1999

| | Values on 25 May 1999 |
|---|---|
| Plasma | |
| Creatinine (mg/dl) | 6.0 |
| Urea (mg/dl) | 154 |
| Na (mEq/l) | 141 |
| K (mEq/l) | 3.35 |
| Cl (mEq/l) | 103 |
| $CO_2$ (mEq/l) | 21 |
| Urine | |
| Na (mEq/l) | 6 |
| K (mEq/l) | 23 |

Normal values are identical to those in Table 1.




(a)




(b)

**Fig. 2.** (**a**) T1-wrighted MRI of the left adrenal gland showing $4.5 \times 3.0 \times 1.5$ cm adenoma (white arrow). (**b**) Adrenal catheterism measures confirming excessive aldosterone production by the left adrenal gland. Aldosterone (nM); cortisol (nM); CV, cava vein; RSV, right surrenal vein; LSV, left surrenal vein; RRV, right renal vein; LRV, left renal vein (amputated during nephrectomy).

diagnosis of primary hyperaldosteronism (Conn's syndrome).

Finally, the nephroangiosclerosis diagnosed in this patient may have been related to long-lasting primary hyperaldosteronism.

## References

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