The unusual diabetic patient with advanced renal insufficiency on ACE inhibitors
What is the explanation for her persisting hypokalaemia?

Enrique Morales, Juan Carlos Herrero, Beatriz Dominguez-Gil, Agustin Carreño, Gabriel Usera and Manuel Praga

Departments of Nephrology and Pathology1, Hospital 12 de Octubre, Crtra Andalucía, Madrid, Spain

Laboratory data were as follows: Hct 28%, glucose 140 mg/dl, HbA1c 5.3% (normal values 3.8–6.4%), calcium 8.7 mg/dl, phosphorus 10 mg/dl, serum total protein 6.7 g/dl, serum albumin 4.1 g/dl, creatinine 5.3 mg/dl, with a creatinine clearance of 10 ml/min. Serum sodium (S-Na) was 140 mmol/l, and serum potassium (S-K) oscillated between 2.6 and 2.9 mmol/l, with urinary K excretion of 30–40 mmol/l.

24-h protein excretion rate varied between 2.6–4.4 g. Monoclonal gammopathy was excluded by immunoelectrophoresis.

Renal sonography showed normal size kidneys with numerous small cysts. Doppler sonography showed no signs of renal artery stenosis. Percutaneous renal biopsy showed typical nodular glomerulosclerosis (Kimmelstiel–Wilson), with interstitial fibrosis and arteriolar sclerosis.

In view of persistent hypokalaemia with inappropriate urinary K excretion, an effort was made to exclude primary hyperaldosteronism. Potassium supplements were administered until serum potassium had reached normal values; basal serum samples for renin and aldosterone measurements were then obtained with the patient at rest. The dose of captopril remained unchanged. Plasma renin was 39 ng/ml (7–14 normal value) and serum aldosterone 1250 pg/ml (100–150 normal value) under these conditions. A high-resolution CT scan of the adrenal glands showed a nodular mass of 2-cm diameter, suggestive of adenoma.

The patient was discharged with captopril and spironolactone treatment. Blood pressure was 135/85 mmHg during the first visit, with a normal S-K (3.9 mmol/l) and stable S-creatinine (5.5 mg/dl). One month after the discharge, she was admitted to the...
coronary unit because of unstable angina. Given the persistence of ischaemic pain, coronary arteriography was performed; severe stenosis of the right coronary artery was observed. Attempts to perform angioplasty were unsuccessful. The patient died because of myocardial infarction and ventricular arrhythmia.

Necropsic study showed severe atherosclerosis of the aorta but no renal artery stenosis. Both kidneys showed multiple cysts of 1–2 cm diameter. The adrenal glands showed bilateral diffuse hyperplasia; in addition, a well encapsulated tumour with a diameter of 2.2 cm was found in the right adrenal gland. Typical lipid-laden cells were found with vacuolated cytoplasm and nuclear irregularities, which were arranged in small cords.

Discussion

In the face of persisting hypokalaemia in combination with inappropriately high urinary potassium losses in a patient with no diuretic abuse, diarrhea or vomiting, we entertained the diagnostic possibility of primary hyperaldosteronism. We did this although not all features, particularly elevated plasma renin activity, were characteristic for this diagnosis. Primary hyperaldosteronism has been observed repeatedly although rarely in patients with chronic renal failure, [7–9]. It is of note, however, that in these communications, serum potassium concentration was normal or even elevated in a considerable proportion of the cases. Potential compensatory gastro-intestinal loss of potassium is suggested by the observation that hypokalaemia in association with an adrenal adenoma was found in an anuric haemodialysed patient [10]. While a hallmark of primary hyperaldosteronism in patients with normal renal function is suppressed plasma renin activity (PRA), normal or even elevated values were noted in patients with primary hyperaldosteronism and renal failure. This is usually only found in cases of secondary hyperaldosteronism. Elevated PRA was also noted in our case. Elevated PRA should raise the suspicion of renal stenosis. In our case, this diagnostic possibility was excluded, however, by Doppler examination and later on by post-mortem.

In patients with advanced renal failure, normokalaemia is usually maintained by intense kaliuresis of the functioning residual nephrons. It is only in the presence of precipitating factors (such as increased potassium intake, administration of K-sparing diuretics or ACE inhibitors, etc.) that hyperkalaemia ensues. It is remarkable that sustained hypokalaemia with inap-propiate kaliuresis occurred in our patient even in the presence of factors, e.g. diabetes mellitus, administration of ACE inhibitors, that should have favoured development of hyperkalaemia.

We draw attention to the finding of numerous renal cysts in our patient. The association of hyperkalaemia, hyperaldosteronism and renal cysts has been described before [11] and this association appears to be casual, because involution of cysts is noted after removal of adrenal adenoma [12].

Teaching point

In a patient in whom you expect hyperkalaemia (diabetes; renal failure; ACE inhibitors) but who present hypokalaemia, exclude adrenal adenoma (Conn’s disease). The diagnosis should be considered even when (atypically) plasma renin activity is high.

References