Reminder of important clinical lesson

Hypokalaemia: common but not always benign. Severe, persistent hypokalaemia secondary to ectopic ACTH from a carcinoid tumour

Muhammad Muzaffar Mahmood,¹ Kurien John²¹Department of Cardiology, Sunderland Royal Hospital, Sunderland, UK²Department of Endocrinology and Diabetes, Weston General Hospital, Weston-Super-Mare, UK

Correspondence to Dr Muhammad Muzaffar Mahmood, muzafar.mahmood@gmail.com

Summary

Hypokalaemia is a common and often benign observation. There is usually an obvious underlying cause for the anomaly. However, hypokalaemia can very rarely be the sole presentation of a more sinister disease. A high index of suspicion and a systematic approach are therefore required to avoid delays in the management, especially in the context of presentation to a medical team. We present a case of a patient with severe and persistent hypokalaemia due to ectopic adrenocorticotrophic hormone (ACTH) secretion secondary to a carcinoid tumour. The case report is followed by a brief discussion on the approach to the management of hypokalaemia and additional tests to confirm ectopic ACTH.

CASE PRESENTATION

A 60-year-old woman presented to her general practitioner with a 4-week history of tiredness. Examination at the surgery was unremarkable but routine blood tests revealed severe hypokalaemia (2.0 mmol/l). She was referred to the local hospital a couple of weeks later for the management of persistent hypokalaemia despite adequate oral replacement. She had also noticed easy bruisability of both upper limbs. Her medical history was unremarkable and she was not on any regular medications. She had a 20 pack-year history of smoking but was a teetotaler.

Initial evaluation revealed hypertension (BP 180/96 mm Hg) with facial plethora and extensive pink abdominal striae.

INVESTIGATIONS

Initial laboratory investigations are outlined in table 1.

Twenty-four-hour urinary cortisol output was >2444 nmol/24 hour (N <120 nmol/24 hour). Morning serum cortisol was >1650 nmol/l (N <50 nmol/l) following an overnight dexamethasone suppression test (1 mg administered orally the night before the blood test). Baseline serum adrenocorticotrophic hormone (ACTH) was 175 ng/l. A 48-hour high-dose (8 mg/day) dexamethasone suppression test failed to suppress the cortisol,

>2081 nmol/l (N <50 nmol/l). A corticotropin-releasing hormone stimulation revealed a raised morning baseline ACTH level of 237 ng/l with a peak level of 256 ng/l at 90 min. The chest x-ray was normal. A CT scan of the chest, abdomen and pelvis revealed extensive liver metastasis and two peripheral lung nodules (4 mm each) in both lower lobes. The adrenal glands appeared normal. Further laboratory investigations (table 2) including pituitary hormone profile were suggestive of hypopituitarism.

The MRI scan of the brain and pituitary revealed a normal pituitary gland with a possible metastasis adjacent to the right sylvian fissure. Tumour markers (CA 125, CA 19-9, CA 15-3, CEA) were not significantly elevated. A biopsy of the metastatic liver lesion was consistent with chromogranin-positive neuroendocrine carcinoma.

DIFFERENTIAL DIAGNOSIS

At presentation in view of the short history, clinical findings, severe hypokalaemia and metabolic alkalosis, a diagnosis of Cushing's syndrome secondary to ectopic ACTH secretion was suspected.

The final diagnosis after biochemical, radiological and histological reports was metastatic carcinoid tumour

Table 1 Initial laboratory investigations

	Patient result	Normal values
Serum sodium	142 mmol/L	136–143 mmol/L
Serum potassium	2.2 mmol/L	3.7–5.1 mmol/L
Serum bicarbonate	37.2 mmol/l	24.0–32.0 mmol/l
Serum calcium	2.47 mmol/l	2.25–2.63 mmol/l
Random glucose	5.5 mmol/l	<7.7 mmol/l
Serum creatinine	59 µmol/l	59–96 µmol/l

Table 2 Endocrine profile

Test	Patient result	Normal laboratory values
TSH	0.5 mIU/l	0.3–6.0 mIU/l
Free T3	3.0 pmol/l	3.8–6.0 pmol/l
Free T4	6.1 pmol/l	7.5–21.0 pmol/l
Oestradiol	<100 pmol/l	
FSH	2.0 IU/l	
LH	<0.5 IU/l	
Prolactin	321 mIU/l	<700 mIU/l
24-hour Ur. 5-HIAA	9.30 mmol/mol	0.00–4.00 mmol/mol

secreting ectopic ACTH. Although not confirmed by histology, in view of the CT chest finding of lung nodules, it was felt a bronchial carcinoid was the culprit.

TREATMENT

She soon developed diabetes and proximal myopathy. Palliative chemotherapy with carboplatin and etoposide was started. She received metyrapone to control and manage hypercortisolemia. An ACE inhibitor was initiated to improve blood pressure. A small daily dose of thyroxine 25 µg was added as well.

OUTCOME AND FOLLOW-UP

Owing to severe proximal myopathy she was in a wheelchair when she returned to oncology 3 weeks later. At that time she needed insulin to control her deteriorating glycaemic state. It is very likely that the metastatic lesions in the liver secreted the ectopic hormone as well. Two weeks later she was admitted with bilateral severe bronchopneumonia from which she did not recover.

The cause of the patient's deranged pituitary profile remained unexplained.

Her hypokalaemia was recurrent despite oral and intravenous replacement. It improved to 3.5 mmol/l during the initial admission. When she was admitted with bronchopneumonia it was once again low at 2.9 mmol/l.

DISCUSSION

Cushing's syndrome and hypokalaemia

Hypokalaemia is much more prevalent (57% patients in one review¹) in Cushing's syndrome caused by ectopic ACTH secretion than in patients with other causes of Cushing's syndrome.¹

Incidence of hypertension is however similar between the two subgroups.

1. In a patient suspected of Cushing's syndrome, presence of severe hypokalaemia would be a useful clue towards the possibility of an ectopic ACTH source, especially if associated with rapid onset of aggressive symptoms. Cushingoid features are often minimal in patients with malignancies and in some a paraneoplastic wasting syndrome can mask features of hypercortisolaemia.²
2. A high index of suspicion is therefore required. Small-cell lung carcinoma is the commonest cause of

ectopic ACTH secretion. Bronchial carcinoid as well as many other endocrine tumours (phaeochromocytoma, pancreatic neuroendocrine tumours, gut carcinoids) are other causes, although up to a third of the cases may remain unidentified.

3. In patients suspected of Cushing's syndrome, hypercortisolaemia can be confirmed from screening tests, such as an overnight dexamethasone suppression test or by estimation of 24-hour urinary cortisol secretion.² This can be initiated in an acute or general medical ward pending an expert endocrinal review. However, once hypercortisolaemia has been confirmed, further diagnostic evaluation of the source of cortisol secretion would be best undertaken by an endocrinologist.

Learning points

- Rapid onset of severe hypokalaemia warrants urgent investigations. Serum potassium concentration <2.5 mmol/l with severe muscle weakness and/or ECG changes requires immediate treatment.
- Hypokalaemia associated with hypertension may suggest salt-losing nephropathy, Conns syndrome or renal artery stenosis. Severe persistent hypokalaemia may be a presentation of ectopic adrenocorticotrophic hormone (ACTH) syndrome.
- Small-cell lung carcinoma, carcinoid (commonly bronchial) and other endocrine tumours are known causes of ectopic ACTH secretion, although up to a third of the cases remain unidentified.

Competing interests None.

Patient consent Obtained.

REFERENCES

1. **Torpy DJ**, Mullen N, Ilias I, *et al*. Association of hypertension and hypokalaemia with Cushing's syndrome caused by ectopic ACTH secretion: a series of 58 cases. *Ann N Y Acad Sci* 2002;**970**:134–44.
2. **Newell-Price J**, Bertagna X, Grossman AB, *et al*. Cushing's syndrome. *Lancet* 2006;**367**:1605–17.

Copyright 2012 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.

BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Please cite this article as follows (you will need to access the article online to obtain the date of publication).

Mahmood MM, John K. Hypokalaemia: common but not always benign. Severe, persistent hypokalaemia secondary to ectopic ACTH from a carcinoid tumour. *BMJ Case Reports* 2012;10.1136/bcr-2012-007193, Published XXX

Become a Fellow of BMJ Case Reports today and you can:

- Submit as many cases as you like
- Enjoy fast sympathetic peer review and rapid publication of accepted articles
- Access all the published articles
- Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow