# Hypokalemia, metabolic alkalosis, and hypertension in a lung cancer patient

Hassane Izzedine[1], Benjamin Besse[2], Anne Lazareth[1], Edward F.G. Bourry[1] and Jean C. Soria[2]

[1]Department of Nephrology, Pitie-Salpetriere Hospital, Paris, France and [2]Medical Oncology, Institut Gustave Roussy, Ville Juif, France

**CASE PRESENTATION**

**A 69-year-old man was admitted to hospital for the evaluation of refractory hypokalemia and metabolic alkalosis. The patient had a 1-year history of a stage pT4N0M1 non-small cell squamous lung carcinoma (NSCLC) that was managed by Pemetrexed (Alimta 500 mg/m$^2$ every 21 days) for the last 6 months. The patient had a 45-pack/y history of smoking without history of alcohol abuse, hypertension, or diabetes mellitus. He was married, had 2 children without health problems and used to work as a truck driver. He had no family history of cancer or metabolic problems. He was in his usual state of health until 1 month before admission. His medication list contained only paracetamol every 6 h.**

Two weeks before admission, he was examined in the emergency department when his family noticed increasing muscle weakness. On admission in nephrology, blood pressure was 170/90 mm Hg, and heart rate was 76 beats per min. There was no peripheral edema, and his mucous membranes were dry. Skin color had recently become generally darker as confirmed by the patient. Cardiovascular and chest examination were unremarkable. Abdominal examination showed no central obesity, nor striae. Neurological examination showed normal reflexes and no localized sensory deficits. Bilateral proximal muscle weakness was noted: 4/5 and 3/5 in upper and lower limbs respectively. Routine peripheral blood and biochemical examination revealed hyperleukocytosis, hypokalemia, metabolic alkalosis, and hyperglycemia. Clinical and laboratory values are listed in Table 1. The patient was managed with oral and intravenous potassium supplementation without improvement. The primary diagnosis was severe dehydration associated with contraction metabolic alkalosis, hypokalemia, hypertension, and type 2 diabetes mellitus (fasting blood sugar 11 mmol/l with glycosuria at 18.6 mmol/l). Supportive treatments included hydration, potassium supplementation, antihypertensive, and oral antidiabetic medications. His alkalosis and hypokalemia partially improved. Endocrine laboratory studies were performed; results are listed in Table 2. Doppler ultrasound study of the renal arteries and adrenal computed tomography (CT) scan were performed.

## CLINICAL DIAGNOSIS

In front of a renal hypokalemia associated with hypertension, excess mineralocorticoids should be evoked including primary and secondary hyperaldosteronism or pseudohyperaldosteronism (algorithm 1). As aldosterone and renin level were normal, primary and secondary hyperaldosteronism could be ruled out. In what concerns the third heterogenous group of pseudohyperaldosteronism, Liddle's syndrome and congenital adrenal hyperplasia can be ruled out because of the late occurrence of signs and absence of suggestive family history. There were no liquorice intake reported by the patient, furthermore these patients usually have markedly lowered renin aldosterone levels. The diagnosis of Cushing syndrome (CS) became then plausible.

Markedly elevated serum cortisol (62.7 μg/100 ml), adrenocorticotropic hormone (ACTH) level (380 pg/ml), and

**Correspondence:** *Hassane Izzedine, Department of Nephrology, La Pitié-Salpêtrière Hospital, 47-80 Boulevard de l'Hôpital, Assistance Publique Hopitaux de Paris, Pierre et Marie Curie University, 75013, Paris, France. E-mail: hassan.izzedine@psl.aphp.fr*

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**Table 1 | Clinical and laboratory values**

| Parameters | Values | | | | |
|---|---|---|---|---|---|
| | Before admission | | | | |
| | Week 8 | Week 4 | Week 2 | Admission | References |
| Blood pressure (mm Hg) | 130/70 | 163/82 | 170/95 | 160/93 | |
| *Serum parameters* | | | | | |
| Sodium | 139 | 141 | 142 | 149 | 132–145 (mmol/l) |
| Potassium | 4.10 | 2.9 | 2.6 | 2.9 | 3.6–5.0 (mmol/l) |
| Chloride | 105 | 100 | 97 | 102 | 95–105 (mmol/l) |
| Bicarbonate | 29 | 35 | 36 | 36 | 22–29 (mmol/l) |
| Glucose | 5 | 9.7 | NA | 10.8 | 3.9–5.8 (mmol/l) |
| Calcium | 2.32 | 2.17 | 2.19 | 2.25 | 2.10–2.65 (mmol/l) |
| Phosphorus | 1.03 | NA | 0.88 | 0.66 | 0.80–1.40 (mmol/l) |
| Uric acid | NA | NA | NA | 136 | 200–420 (μmol/l) |
| Magnesium | 0.82 | NA | 0.85 | 0.80 | 0.74–0.85 (mmol/l) |
| Urea | 4.8 | 3.2 | 3.5 | 4.10 | 2.5–7 (mmol/l) |
| Creatinine | 0.85 | 0.92 | 0.89 | 0.68 | 62–106 (mg/dl) |
| Osmolality | NA | NA | NA | 314 | 280–300 (mOsm/kg) |
| White blood cell count | 6300 | 14,900 | 9900 | 8260 | 4000–7000 per μl |
| Arterial blood pH | NA | NA | 7.52 | 7.50 | 7.38–7.42 |
| Arterial $PCO_2$ | NA | NA | 41.9 | 40.1 | 38–42 (mm Hg) |
| *Urine parameters* | | | | | |
| Sodium | NA | NA | 109 | 82 | 100–200 (mmol/l) |
| Potassium | NA | NA | 40 | 48 | 50–130 (mmol/l) |
| Osmolality | NA | NA | NA | 460 | 100–1400 (mOsm/kg) |

NA, not applicable.

**Table 2 | Endocrine laboratory values**

| Parameters | Values | References |
|---|---|---|
| *Serum* | | |
| Calcitonin | <5 | 0–5 ng/l |
| TSHus | 0.61 | 0.1–4 mU/l |
| Parathormone | 60.2 | 12–65 pg/ml |
| Aldosterone | 19 | 12–125 pg/ml |
| Renin | 2.5 | 3.5–19 pg/ml |
| Cortisol | | |
| Baseline 8 h | 63.7 | 5–25 μg/dl |
| Baseline 16 h | 55.6 | 2.5–12.5 μg/dl |
| After dexamethasone suppression test | 47.8 | |
| ACTH | | |
| Baseline | 380 | 10–45 pg/ml |
| After dexamethasone suppression test | 432 | |
| *Urines* | | |
| Urinary free cortisol by HPLC | 15,576 | 11.1–126.3 (μg/24 h) |

ACTH, adrenocorticotropic hormone; HPLC, high-performance liquid chromatography.

urine-free cortisol excretion rates (15,576 μg/24 h) were found. An overnight dexamethasone suppression test (8 mg) reduced plasma cortisol levels to 61.2% of baseline values. CS was made. The generation and maintenance of hypokalemia, metabolic alkalosis, and hypertension in this patient were likely the result of sustained activation of circulating cortisol. Abdominal and pelvic CT scans showed normal adrenal glands and confirm previously known hepatic metastases. Brain magnetic resonance imaging (MRI) showed normal pituitary gland and no cerebral metastases. These results supported the diagnosis of ectopic ACTH secretion.

## CLINICAL FOLLOW-UP

The patient was first managed with spironolactone and potassium supplementation reaching subnormal serum potassium (3.2 mmol/l) and bicarbonates (31 mmol/l) values, but he had no remission. He was then treated with metyrapone to counteract ectopic ACTH production. At 1 week after switching spironolactone for amiloride 10 mg and metyrapone 1000 mg/d in accordance to endocrine tests, he made a dramatic recovery: serum potassium levels increased to 4.1 mmol/l with serum carbon dioxide levels decreasing to 27 mmol/l. Hypertension control (average 120–130 mm Hg systolic blood pressure) was obtained by amlodipine 10 mg/d in addition to amiloride. Glycemic control was partial (treated fasting blood sugar 7.2 mmol/l) using repaglinide 1 mg TID (Novonorm).

## DISCUSSION

We described a case of CS. Because he had no pituitary adenoma and primary adrenal disorders, non-small-cell lung cancer (NSCLC) was suspected as the source of the excess ACTH.

### Clinical aspects of CS

The name of Harvey Cushing (1869–1939) was immortalized in the history of medicine, by his discovery, in 1912, of Cushing's disease, an endocrine syndrome caused by a malfunction of the pituitary gland.[1] CS is characterized by truncal obesity with 'moon face', facial plethora, 'buffalo hump' but loss of subcutaneous fat, purplish abdominal striae, ecchymoses and proximal myopathy, accompanied by nonspecific symptoms like edema, hypertension, fatigability