PHOTO QUIZ

Failing hormones

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CASE REPORT

A 70-year-old female patient presented to the outpatient clinic with general malaise, salt craving, and hypotension. She had been treated for severe asthma with 15 mg prednisone daily without interruptions for at least ten years. This treatment was complicated by the development of diabetes mellitus and severe osteoporosis. In addition, she suffered from generalised myopathy and skeletal pain, for which she took naproxen 500 mg three times a day.

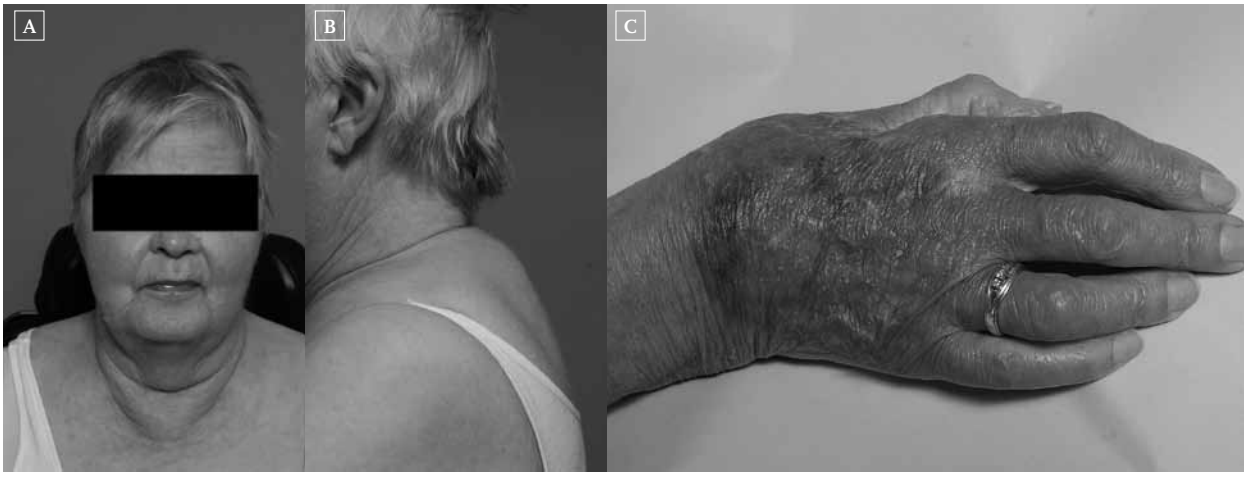
On clinical examination, a wheel-chair dependent, 71-year-old woman was seen with a moon face, buffalo hump, abdominal fat accumulation, and severe muscle atrophy (*figure 1*). Her blood pressure, however, was low (110/60), both in supine and in upright position.

Sodium concentration was 126 mmol/l, potassium 4.9 mmol/l, creatinine 59 umol/l and plasma osmolality 244 mOsm/kg. Urinary sodium concentration was 43 mmol/l. ACTH was suppressed (<5 ng/l), with a normal afternoon cortisol level (0.293 µg/l). Plasma renin activity was undetectable (<0.10 µg/l/hour), and aldosterone concentration was low (0.13 nmol/l, reference range 0.0 to 0.35 nmol/l). The transtubular potassium gradient (TTPG = (Urine potassium/ (urine osmol/serum osmol))/ serum potassium)) was 3.7 (reference >7)

WHAT IS YOUR DIAGNOSIS?

See page 532 for the answer to this photo quiz.

Figure 1.



A. Moon face
B. Buffalo hump
C. Muscle atrophy of the right hand

ANSWER TO PHOTO QUIZ (PAGE 528)

FAILING HORMONES

DIAGNOSIS

The clinical signs, symptoms and laboratory investigations point towards symptomatic hyporeninaemic hypoaldosteronism in the presence of exogenous Cushing's syndrome.

The syndrome of hyporeninaemic hypoaldosteronism is characterised by decreased angiotensin II production secondary to diminished renin release and an intra-adrenal defect of a local renin-angiotensin system, both of which suppress aldosterone secretion.[1]

Hyporeninaemic hypoaldosteronism is a relatively common disorder in patients with mild diabetic and other forms of nephropathy, in particular those associated with non-steroidal anti-inflammatory drugs (NSAIDs).[2] Patients are often asymptomatic and present with hypertension despite diminished aldosterone levels, because of volume expansion in the presence of chronic kidney disease and normal levels of cortisol, which exhibits mineralocorticoid activity (MA). In our patient, chronic treatment with supraphysiological doses of prednisone caused Cushing's syndrome but also symptomatic tertiary adrenal insufficiency. In agreement, ACTH levels were suppressed but cortisol levels were within the normal range, which is most likely due to the interference of prednisolone (171% cross-reactivity) in the cortisol assay (Modular E170 immunoanalyser Roche Diagnostics, Germany). With the additional presence of hypoaldosteronism, MA is primarily dependent on the active prednisolone, which is converted out of prednisone by 11β-hydroxysteroid dehydrogenase type 1 (11β-HSD1). In contrast, 11β-HSD2 inactivates glucocorticoids,[3] which is more effective for prednisolone than for cortisol, explaining the reduced MA of prednisolone.[4]

Treatment with fludrocortisone, which is 125 times more potent than cortisol, rapidly improved the patient's well being, normalised blood pressure, and restored electrolyte concentrations and TTPG, which confirmed the diagnosis of adrenal insufficiency.

The combination of hyporeninaemic hypoaldosteronism due to diabetic nephropathy and chronic use of NSAIDs, suppression of endogenous cortisol secretion, and the negligible MA of prednisolone, resulted in symptomatic adrenal insufficiency.

Glucocorticoids given in supraphysiological dosages do not always display effective mineralocorticoid activity when symptomatic hypoaldosteronism is present. Therefore, when hyponatraemia and hyperkalaemia are not fully understood in a symptomatic patient, physicians should consider adrenal insufficiency, even in the presence of synthetic glucocorticoids.

REFERENCES

1. Schambelan M, Sebastian A, Biglieri EG. Prevalence, pathogenesis, and functional significance of aldosterone deficiency in hyperkalemic patients with chronic renal insufficiency. Kidney Int. 1980;17:89-101.
2. Karet FE. Mechanisms in hyperkalemic renal tubular acidosis. J Am Soc Nephrol. 2009;20:251-4.
3. Edwards CR, Stewart PM, Burt D, et al. Localisation of 11 beta-hydroxysteroid dehydrogenase--tissue specific protector of the mineralocorticoid receptor. Lancet. 1988;2:986-9.
4. Diederich S, Eigendorff E, Burkhardt P, et al. 11 beta-hydroxysteroid dehydrogenase types 1 and 2: an important pharmacokinetic determinant for the activity of synthetic mineralo- and glucocorticoids. J Clin Endocrinol Metab. 2002;87:5695-701.