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CASE REPORT

When hidden steroids cause harm: Secondary adrenal insufficiency from unrecognised exposure

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Abstract

Introduction: Adrenal insufficiency is a life-threatening condition that often presents with non-specific symptoms, complicating diagnosis in elderly patients. *Case report:* We report a case of a 77-year-old man with diabetes mellitus, hypertension and a history of cerebrovascular accident who presented with nausea, vomiting, weight loss and persistent giddiness. Laboratory tests revealed hyponatraemia and low serum osmolality. Further endocrine evaluation showed low morning cortisol, a suboptimal response to the short Synacthen test and suppressed adrenocorticotropic hormone levels confirming secondary adrenal insufficiency. The patient later disclosed recent use of a traditional Chinese medicine suggesting possible hidden glucocorticoid exposure and suppression of the hypothalamic-pituitary-adrenal axis. He improved after initiation of hydrocortisone replacement and discontinuation of the suspected products. *Discussion:* This case emphasises the need for greater awareness of the potential adulteration of traditional Chinese medicines with glucocorticoids. It also highlights the critical role of laboratory testing in diagnosing adrenal insufficiency, detecting hidden adulterants and recognising the limitations of immunoassays in interpreting adrenal function tests.

Keywords: adrenal insufficiency, adulterant, glucocorticoid, hyponatraemia, traditional Chinese medicine

INTRODUCTION

Adrenal insufficiency is caused by failure of the adrenal cortex to produce cortisol. It is categorised into primary and secondary forms based on the level of dysfunction within the hypothalamic–pituitary–adrenal (HPA) axis.[1] Exogenous glucocorticoids have been identified as adulterants in traditional medicine and their prolonged use can suppress the HPA axis, leading to adrenal insufficiency.[2] We report a case of secondary adrenal insufficiency in a patient who had consumed traditional Chinese medicine suspected to be adulterated with exogenous glucocorticoids.

CASE REPORT

A 77-year-old Chinese man with diabetes mellitus, hypertension and a history of cerebrovascular accident presented with one week of nausea, vomiting and anorexia preceded by two weeks of generalised weakness and epigastric discomfort. His medications included aspirin, metformin, perindopril, amlodipine and simvastatin. Additionally, he reported three months of unintentional 3 kg weight loss, chronic constipation and one year of persistent giddiness despite multiple clinic visits. A colonoscopy one month earlier was unremarkable. He denied fever, headache, seizures or the use of corticosteroids or traditional medicines. On examination, he was non-obese and appeared lethargic. Vital signs were stable with no postural hypotension and capillary glucose was 5.8 mmol/L. Given his giddiness and unsteady gait, a posterior circulation infarct was suspected in the emergency department (ED) but computed tomography brain imaging revealed only multifocal old infarcts, cerebral atrophy and microvascular changes. He was admitted for further evaluation.

Laboratory investigations (Table 1) revealed moderate hyponatraemia with normal potassium,

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suggesting preserved mineralocorticoid function. Other electrolytes, renal profile, liver function, total protein and glucose were normal, excluding renal impairment, hepatic cirrhosis, hyperproteinaemia and hyperglycaemia as causes of hyponatraemia. High-sensitivity troponin T (hs-Trop T) was performed in the ED despite no chest pain. The electrocardiogram was unremarkable and hs-Trop T was below the cut-off. Full blood count showed no evidence of anaemia or infection while normal tumour markers and a negative immunochemical faecal occult blood test further reduced the likelihood of colorectal malignancy. Low serum osmolality (262 mmol/kg) confirmed hypo-osmolar hyponatraemia with inappropriately normal urine osmolality and elevated urine sodium (92 mmol/L) suggesting renal sodium loss. Urine pH and venous blood gas were normal excluding renal tubular acidosis and metabolic acidosis. Normal thyroid function test excluded hypothyroidism. Morning cortisol was low at 67.2 nmol/L and the short Synacthen test (SST) demonstrated a suboptimal peak cortisol response of 292 nmol/L, confirming adrenal insufficiency. Plasma adrenocorticotropic hormone (ACTH) was suppressed at 0.59 pmol/L, consistent with secondary adrenal insufficiency.

On further questioning, the patient disclosed consuming a traditional Chinese medicine for bowel regulation over the preceding three months, which was discontinued one week before symptom onset. This raised strong suspicion of hidden steroid content causing HPA axis suppression. He was started on oral hydrocortisone with symptomatic improvement and remained well on follow-up with ongoing therapy to maintain adrenal function.

DISCUSSION

Traditional and complementary medicine (TCM) is widely used in Malaysia. Although the Ministry of Health (MOH) regulates TCM practitioners and products, public awareness regarding their safety and content remains limited.[3] Under the Sale of Drugs Act 1952, adulteration is defined as mixing or diluting a drug with substances that reduce its efficacy, lower its commercial value, cause harm or fail to meet prescribed standards.[4] A major concern is adulteration with undeclared pharmaceuticals, particularly glucocorticoids which can cause Cushing syndrome or adrenal suppression.

Secondary adrenal insufficiency is most often caused by prolonged glucocorticoid exposure through prescribed therapy but ingestion of adulterated products can also be a contributing factor. Symptoms are frequently non-specific, leading to delayed diagnosis.[5] In this case, the patient presented with constitutional and gastrointestinal symptoms, hyponatraemia and no hyperpigmentation, features consistent with secondary adrenal insufficiency. However, documentation regarding Cushingoid features prior to presentation was lacking.

Glucocorticoid-adulterated products suppress the HPA axis via negative feedback on corticotropin-releasing hormone (CRH) and ACTH secretion. Prolonged suppression leads to adrenal cortex atrophy with recovery varying by dose, potency, duration and individual susceptibility.[6] In this case, no other causes of secondary adrenal insufficiency were found aside from a three-month history of unregulated TCM use. Although the product was not analysed, a previous study has documented undeclared corticosteroids in traditional medicine.[7]

According to the Endocrine Society Clinical Practice Guideline, a morning cortisol level below 140 nmol/L is strongly suggestive of adrenal insufficiency.[1] In this patient, the diagnosis was supported by a low morning cortisol and confirmed by a suboptimal SST peak (Table 1). Interpretation should be cautious as the Roche Elecsys Cortisol II assay can cross-react with exogenous corticosteroids (e.g., prednisolone, 6-α-methylprednisolone, prednisone, 21-deoxycortisol). Given the patient's use of unregulated traditional medicine possibly containing glucocorticoids, cortisol levels may be falsely elevated and true endogenous levels lower. Low plasma ACTH indicates secondary adrenal insufficiency and preanalytical handling protocols were strictly followed to avoid false suppression.[9]

Proper preparation before the SST is crucial for reliable results. Hydrocortisone was withheld for 24 hours and the SST was performed according to the standard protocol with a cut-off of 500 nmol/L in our laboratory. This value is assay-specific and each laboratory should establish its own cut-off to avoid false-positive results.[9] As the SST utilises the same immunoassay as baseline cortisol, it remains susceptible to assay interference.

Adrenal insufficiency significantly increases the risk of a life-threatening adrenal crisis during periods of stress due to an impaired cortisol response. Although incomplete suppression

Table 1: Biochemical laboratory investigation results obtained during the patient's inpatient admission

Serum/Plasma	**Result**	**Reference interval**
Urea, mmol/L	1.6	2.8-8.1
Sodium, mmol/L	126	136-145
Potassium, mmol/L	3.6	3.5-5.1
Chloride, mmol/L	87	98-107
Creatinine, µmol/L	69	62-106
Calcium, mmol/L	2.27	2.20-2.55
Phosphate, mmol/L	1.30	0.81-1.45
Magnesium, mmol/L	0.69	0.66-0.99
Total protein, g/L	61	64-83
Total bilirubin, µmol/L	10	<24
Albumin, g/L	39	35-52
Globulin, g/L	22	25-39
Alanine transaminase, IU/L	17	10-50
Aspartate transaminase, IU/L	23	10-50
Alkaline phosphatase, IU/L	104	40-129
High sensitivity troponin T, ng/L	7	<14
Free thyroxine, pmol/L	20.1	11.9-21.6
Thyroid stimulating hormone, mIU/L	1.58	0.27-4.20
Cortisol (am), nmol/L	67	133-537
Adrenocorticotropic hormone, pmol/L	0.59	1.60-13.90
Prostate specific antigen, µg/L	2.8	<4.4
Carcinoembryonic antigen, µg/L	2.3	<5.0
Alpha-fetoprotein, IU/ml	3.1	<5.8
Carbohydrate antigen 19-9, IU/ml	26.9	<27.0
Serum osmolality, mmol/kg	262	275-300
Venous blood gas		
pH	7.41	7.35-7.45
PCO_2, mmHg	41	35-48
HCO_3, mmol/L	26	18-23
Short Synacthen test	**Result**	**Reference interval**
Cortisol 0 min, nmol/L	193	
Cortisol 30 min, nmol/L	266	133-537
Cortisol 60 min nmol/L	292	
Comment: Peak serum cortisol did not reach 500 nmol/L, indicating a poor adrenal response to the Synacthen stimulation test. Please correlate clinically.		
Urine	**Result**	**Reference interval**
Urine osmolality, mmol/kg	237	50-1400
Urine sodium, mmol/L	92	-
Urine biochemistry	urine pH: 6.5, no other abnormality detected.	
Faeces	**Result**	
Immunochemical faecal occult blood test	negative	

from adulterated products may reduce this risk, elderly patients with comorbidities remain highly vulnerable.[10] This patient improved with oral hydrocortisone replacement and ongoing periodic HPA axis assessment is crucial to ensure adrenal recovery.

In this case, no specific details on traditional medicine were documented. Future cases should include thorough TCM documentation and where possible, obtain and submit product samples to the National Pharmaceutical Regulatory Agency (NPRA), MOH for adulterant testing.

CONCLUSION

Unrecognised glucocorticoid exposure from unregulated traditional medicines is a common but often overlooked cause of HPA axis suppression. Collaboration among clinicians, laboratorians, pharmacists and regulatory agencies is crucial to confirm adulteration, detect hidden glucocorticoids in traditional medicines, guide management, prevent adrenal crisis and control unsafe products.

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