

## *Please read this bit first*

The HPCSA and the Med Tech Society have confirmed that this clinical case study, plus your routine review of your EQA reports from Thistle QA, should be documented as a "Journal Club" activity. This means that you must record those attending for CEU purposes. Thistle will **not** issue a certificate to cover these activities, nor send out "correct" answers to the CEU questions at the end of this case study.

The Thistle QA CEU No is: **MT00025**.

Each attendee should claim **THREE** CEU points for completing this Quality Control Journal Club exercise, and retain a copy of the relevant Thistle QA Participation Certificate as proof of registration on a Thistle QA EQA.

## CHEMISTRY LEGEND

JULY 2009

### HYPERCORTISOLISM

**Hypercortisolism** is a disease caused by increased production of cortisol, or by excessive use of cortisol, or other steroid hormones.

The most common cause of hypercortisolism is Cushing's disease caused by excessive production of adrenocorticotrophic hormone (ACTH) by the pituitary gland. ACTH stimulates the adrenal glands to produce cortisol.

Hypercortisolism can be caused by a tumour of the pituitary gland, a tumour of the adrenal gland, a tumour somewhere other than the pituitary or adrenal glands (ectopic hypercortisolism), or by long-term use of corticosteroids (drugs commonly used to treat conditions, such as rheumatoid arthritis and asthma).

**Risk factors** are adrenal tumour or pituitary tumour, chronic therapy with corticosteroids, and being female.

The features of hypercortisolism vary from the clinically normal patient, to a patient presenting with an isolated hypokalaemia, to the patient with all the manifestations of Cushing's disease. A high plasma cortisol may be a transient, appropriate response to some disease process, or it may be long-standing as a result of inappropriate secretion by the adrenal cortex. These two types of patients should be identified clinically before embarking on any further investigation. High plasma levels of cortisol (up to 2000nmol/L) can occur in severely stressed patients (physiological, psychological) and moderately increased levels (up to 700nmol/L), which may not suppress in response to Dexamethasone therapy, often occur in patients with severe depressive illnesses. These high plasma cortisol levels are "appropriate" stress reactions and revert to normal when the stress disorder is resolved - these patients do not require further investigation or treatment.

#### Hypercortisolism Symptoms

- moon face (round, red, and full)
- buffalo hump (a collection of fat between the shoulders)
- central obesity with protruding abdomen and thin extremities
- weight gain
- weakness
- backache
- headache
- acne or superficial skin infections

- thin skin with easy bruising
- thirst
- increased urination
- purple striations on the skin of the abdomen, thighs, and breasts
- mental changes
- impotence or cessation of menses
- facial hair growth

**Additional symptoms** of Hypercortisolism that may be associated with this disease:

- weight gain (unintentional)
- skin spots, red
- skin blushing/flushing
- muscle atrophy
- fatigue
- bone pain or tenderness

**Causes of hypercortisolism**

- Physiological - stress, obesity, depression
- Excess ACTH production - Pituitary disease: Cushing's disease
  - Ectopic ACTH: Malignancy - bronchus, thymus, pancreas, ovary
- Excess cortisol (Pituitary independent) - Adrenal tumour: adenoma, carcinoma
  - Alcoholism
  - Iatrogenic: steroid therapy
- Excess cortisol-binding globulin - Oestrogen therapy, oral contraceptives
  - Pregnancy

**Treatment**

The treatment of inappropriate hypercortisolism involves removing the cause of the disorder or if this is not possible, suppression of cortisol production.

**Case Presentation**

A 28 year old woman was referred for investigation of oligomenorrhoea, hirsutism, weigh gain (71kg over 6 months) and easy bruising. She was normotensive, had a "full fattish" face and excessive adipose tissue on the trunk area. Radiology revealed minimal osteoporosis. The pituitary fossa was within normal limits. A urinary free cortisol was 2200nmol/24h (normal 40-250). She was admitted and an overnight 2-mg dexamethasone suppression test was performed. The admission chemistry values were:

Na	142 mmol/L	(132 - 144)
K	3.0 mmol/L	(3.2 - 4.8)
Cl	98 mmol/L	(98 - 108)
HCO <sub>3</sub>	34 mmol/L	(23 -33)
Urea	4.6 mmol/L	(3.0 -80)
Creat	0.08 mmol/L	(0.06 - 0.12)
Cortisol	870 mmol/L	(140 - 690)

The plasma cortisol level at 09h00 after a 2-mg dose of Dexamethasone at midnight was 920 nmol/L

**Differential diagnosis:** Cushing's syndrome - ?pituitary dependent, ?adrenal neoplasm, ?ectopic ACTH syndrome.

A high-dose dexamethasone suppression test and a plasma ACTH estimation was performed with the following results:

Day 1 (8mg Dexamethasone) plasma cortisol (08h00): 1020 nmol/L  
Day 2 (8mg Dexamethasone) plasma cortisol (08h00): 650 nmol/L  
Day 3 (post Dexamethasone) plasma cortisol (08h00): 390 nmol/L  
Plasma ACTH (day 1 08h00): 100 pg/ml (20-40)

This patient's clinical features, plasma electrolyte values (hypokalaemia), high urinary and plasma cortisol concentrations and the results of her overnight Dexamethasone suppression test indicate Cushing's disease. The suppression of her plasma cortisol by the high-dose Dexamethasone suggests that the hypercortisolism is pituitary dependent. The increased plasma ACTH level suggests either Cushing's disease or an ectopic ACTH syndrome. However, the response to high-dose Dexamethasone suggests that the ectopic ACTH syndrome is unlikely.

**Final diagnosis:** The patient was first treated with metyrapone which restored her menstrual cycle and lessened the other clinical features of Cushing's disease. However, when the drug was ceased there was increasing hirsutism and other signs of hypercortisolism. Finally, a pituitary micro adenoma was removed by a trans-sphenoidal resection.

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## References

1. Cases in chemical pathology - A Diagnostic approach 4<sup>th</sup> edition
2. Fundamentals of Clinical Chemistry 3<sup>rd</sup> edition - NW Tietz

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## Questions

1. Discuss the causes and risk factors for hypercortisolism.
  2. Discuss the laboratory findings in a patient diagnosed with Cushing's disease.
  3. What clinical features are associated with hypercortisolism?
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